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Cross allergic reactions in infants and toddlers with atopic dermatitis

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ABSTRACT

Purpose: Prevalence and clinical significance of cross sensitization in children up to 3 years old, diagnosed with atopic dermatitis.
Material and Method: The retrospective study included 69 children up to 3 years old with atopic dermatitis. Allergological diagnostics was performed based on skin tests, determination of total IgE concentration and allergen-specific IgE.
Results: Cross sensitization was found in 26% of children. Other patients were qualified to the control group. The sensitization to trees pollen and fruits as well as grass pollen and vegetables were the most frequent types of cross allergy. The patient's family history was positive with regard to atopy in 72% of children from the study group vs. 31% of children from the control group. The statistically higher prevalence of allergic rhinitis and bronchial asthma as well as co-existence of sensitization to house dust mite and animal dander were revealed in the study group. The total concentration of IgE, eosinophilia and SCORAD values were statistically higher in the study group. Children with cross sensitization required systemic steroid therapy more frequently.
Conclusion: In children up to 3 years with atopic dermatitis and sensitization to plant pollen, the role of a pollen-food allergy syndrome must be taken into account in the pathogenesis of the disease. In children with cross sensitization, the course of atopic dermatitis is more severe; the symptoms from the respiratory and digestive system co-exist. The positive family history is a factor, predisposing to the development of cross sensitization in infants and toddlers.

Key words: Atopic dermatitis, Cross sensitization, Infants

INTRODUCTION

Atopic dermatitis is a disorder conditioned by numerous factors, allergic, environmental and genetic, among others. Food sensitization is regarded as the most important and pathogenic cause of skin lesions in infants and toddlers. Clinical observations indicate that proteins of cow's milk and hen's egg are the first allergens responsible for development of skin lesions in infants. On one hand, the spectrum of allergizing foods widens with time, on the other, a child acquires the immunological tolerance [1, 2]. Studies also show that some of the children manifest simultaneously sensitization to one allergen (monoallergy), other to several different allergens (polyallergy). Observations of children with atopy show that sensitization to numerous, usually, food allergens is frequently reported in the youngest patients. The phenomenon of polyallergy is a natural course of an allergic process and most frequently affects older children, especially, with a positive family history of atopy. They usually demonstrate the symptoms from the respiratory system. Therefore, to date examinations have referred to the influence of polyvalent sensitization on the frequency of

wheezing incidents in children [3, 4]. Cross allergy, a special type of sensitization to food and inhalant allergens, resulting from homology of the amino acids sequence, among others, is an object of research and observation in older children and adults. So far, this ailment has been regarded to affect mainly children above 3 years old and all studies concentrate on this age group [5, 6]. In the literature, the attention is paid to the role of food and inhalant allergens in the pathogenesis of atopic dermatitis, taking into consideration only the influence of polyvalent sensitization on the course of the disease [2, 7, 8]. In many cases, the role of an allergic factor in the pathogenesis of this disease is unquestionable and the clinical significance of cross allergy is the most frequently considered in regard to the syndrome of oral cavity allergy and pollinosis [5, 9]. However, the observations carried out in our clinical center indicate that cross allergy is more and more frequently reported in younger children, demonstrating multi-organic clinical symptoms. Therefore, the attempt has been made to analyze that problem in infants and toddlers with the most frequent manifestation of allergy at this age, which is atopic dermatitis.

The aim of the study was to assess the prevalence of cross sensitization in children up to 3 years old with atopic dermatitis, the influence of the character of sensitization on the course of the disease and its treatment and the presence of other diseases of the allergic background.

MATERIAL AND MEHODS

The retrospective study included 69 children (26 girls, 43 boys) aged from 1 year old to 36 months old, hospitalized in the Department in the years 2009-2011 due to atopic dermatitis. The diagnosis of atopic dermatitis according to the criteria of Sampson [10] for children up to 1 year old and Hanifin and Rajka [11] for children above 1 year old, as well as, the patient's history, indicating the time relation between skin lesions and the activity of food and/or inhalant allergens was a criterion qualifying children for the clinical analysis.

The following diagnostic examinations (skin tests, determination of serum total IgE concentration, allergen-specific IgE antibodies) were performed to define the background of allergic skin lesions and the spectrum of sensitizing allergens. Food skin tests were done by the „prick by prick" method with native allergens (a standard kit, containing basic allergens: milk, egg white and yolk, fish, wheat) and plant-derived allergens, taking part in cross reactions: apple, nut, peach, tomato, celery, sesame, carrot, soy. Skin tests with inhalant allergens were performed with standardized allergens of Allergopharma firm (a basic kit + birch). The result was read out after 15 min., regarding a wheal with a diameter of more than 3 mm as a positive reaction. The serum total IgE concentration and allergen-specific IgE antibodies were determined [12].

The serum total IgE concentration and allergen-specific IgE antibodies were measured, collecting on a one – off basis about 2 ml of serum. The examination was carried out with allergens of Pharmacia Upjohn firm by the fluoroimmunoenzymatic method (UniCAP) according to the rules, worked out by the manufacturer. The value > 0.7 kU/l was considered as a positive result.

Smear culture of the skin lesions to inoculation was collected to a standard test tube at the child's admission to hospital; before instituting the local and systemic treatment, on the first day of hospitalization.

Based on the results of examinations, 18 children with atopic dermatitis and sensitization to food and inhalant allergens, were qualified to the study group (children with cross allergy). Other 51 patients with atopic dermatitis were qualified to the control group.

The total concentration of IgE, peripheral blood eosinophilia, the skin superinfection with Staphylococcus aureus, incidence of other diseases than atopic dermatitis, ailments of the allergic background (symptoms from the respiratory system and gastric and intestinal), frequency of systemic corticotherapy were compared to evaluate the severity of the disease. The clinical intensity of skin lesions was assessed based on the scale of SCORAD, taking into consideration extensity, topography of skin lesions and subjective symptoms: itch, sleep disorders [13]. The information above, as well as the results of accessory examinations were obtained, based on to date documentation of children hospitalized in the Department. The results were analyzed statistically.

Statistical analysis

The distribution of values for each parameter in the study patients and in each group was reported using the mean (x), standard deviation (SD), minimum (min) and maximum (max) value and median (Me). Due to the lack of normal distribution of the parameters in statistical interference, we used nonparametric methods. The differences in the distribution of quantitative variables between the two groups of patients were assessed using the Mann-Whitney test. All the hypotheses were verified at the level of statistical significance p=0.05. Most of the calculations were carried out based on the statistical package Statistica 9.0, StatSoft.

RESULTS

The study included 69 children with atopic dermatitis. In 18 (26%) of them, sensitization to food and inhalant allergens, characteristic of cross sensitization, was proved based on accessory tests (the study group). Fifty one other (74%) patients were qualified to the control group. Both groups were comparable with regard to the age (24.00±8.38 months vs. 15.37±10.73 months; p=0.003). Cross sensitization was

reported more frequently in boys with atopic dermatitis than in girls, but the difference was statistically insignificant (p=0.236).

Analysis of prevalence of allergic diseases (food allergy, bronchial asthma, allergic rhinitis) among first and second degree relatives of the study children indicated the statistically higher incidence of a positive family history in the families of children with cross allergy (72% in the study group vs. 31% in the control group; p=0.003). No statistically significant differences were determined with regard to the prevalence of atopic dermatitis in the families of both groups (*Tab. 1*).

Multi-organic allergy manifestation (2 or more organs) was observed in 50% of the study children and in 39% of the controls. The signs from the respiratory system (bronchial asthma in early childhood – 33%, allergic rhinitis – 22%) and from the digestive system (gastroeosophageal reflux – 22% and reduced body weight) were the most frequent. The syndrome of the oral cavity allergy affected 11% of the examined; these were children above 2 years old (*Tab. 1*). Except of atopic dermatitis, 50% of children were asymptomatic.

The analysis of atopic dermatitis severity, measured with the scale of SCORAD, proved statistically higher values in the children with cross sensitization compared to the control group (p=0.015) (*Fig. 1*).

The statistically higher values of both total IgE concentration and peripheral blood eosinophilia were determined in the study group (p=0.0001) (*Fig. 2* and *Fig. 3*). Similarly, superinfection with Staphylococcus aureus more frequently affected patients with cross sensitization (67% vs. 39%; p= 0.045).

Specific IgE antibodies to inhalant and food allergens were stated in all children form the study group, but 49% of children with atopic dermatitis from the control group were negative for IgE antibodies to both groups of allergens. Based on allergen-specific IgE, the birch –apple and grass pollen–vegetables syndromes were the most frequent types of the cross reaction sensitization that affected 39% and 83% of the study children, respectively. Other types of cross allergy were observed in 6% of patients. The prevalence of sensitization to main food and inhalant allergens varied between groups. Sensitization to house dust mite was reported in 61% of the study group and in 8% of the control group. Coexisting sensitization to animals' fur affected more frequently children with cross allergy (22% vs. 2%). There was statistically significant difference of sensitization to grass and trees pollen between study and control group (*Tab. 2*).

Sensitization to milk proteins concerned 72% of the study children and 31% of the control one (*Fig. 4*). In the study group, in most of cases the sensitization to food vegetal allergens was related to sensitization to pollen allergens; generally homologous allergens.

Table 1. **Characteristics of the study and control group.**

Examined parameter	Study group (n=18)	Control group (n=51)	Value of p
Gender (boys)	72%	59%	0.236
Age (months)	24.00±8.38	15.37±10.73	0.003
Family history	72%	31%	0.003
Other allergic diseases : a/ bronchial asthma b/ allergic rhinitis c/ gastrointestinal symptoms d/oral allergy syndrome	50% 33% 22% 22% 11%	39% 8% 4% 35% 0%	0.427 0.024 0.060 0.466 0.109

Figure 1. **Comparison of the severity of skin lesions according to the SCORAD scale in the study and control group.**

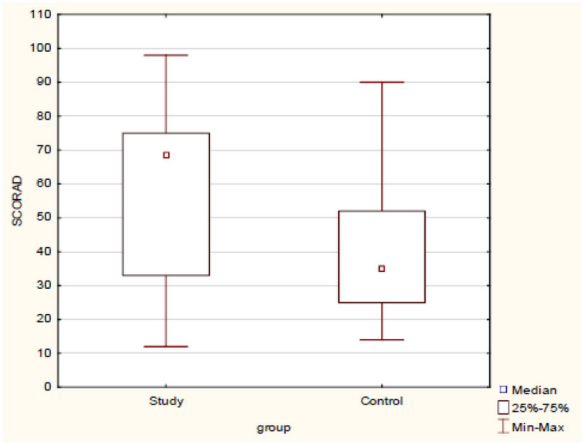


Figure 2. **Comparison of total IgE level in the study and control group.**

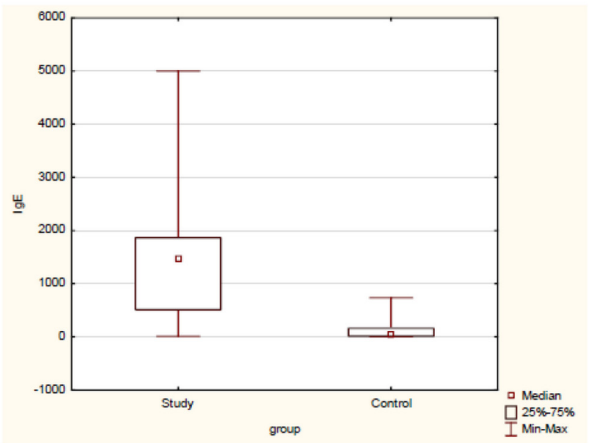


Figure 3. **Comparison of peripheral blood eosinophilia in the study and control group.**

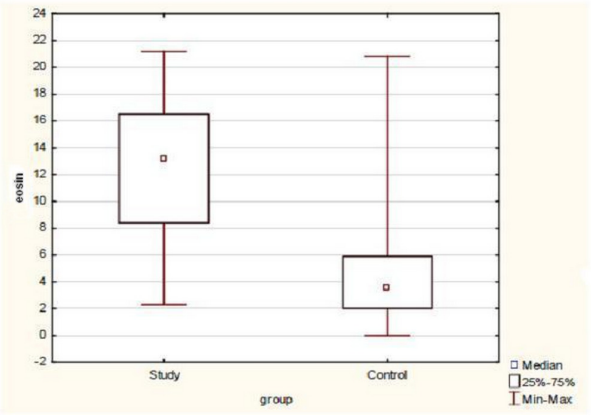


Table 2. **The prevalence of sensitization to main food and inhalant allergens in the study and control group.**

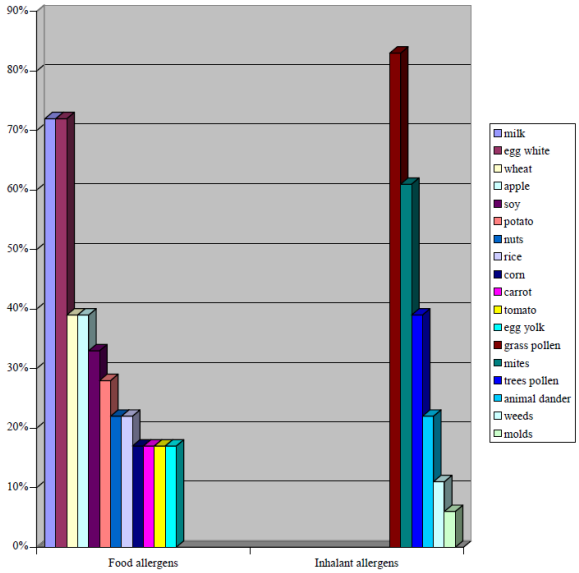
Allergens	Study group (n=18)	Control group (n=51)	Value of p
milk	72%	31%	0.003
egg white	72%	25%	0.003
mites	61%	8%	0.007
animal dander	22%	2%	0.005
grass pollen	83%	15%	0.0001
trees pollen	39%	7%	0.023
weeds pollen	11%	0%	0.109

When taking into consideration pharmacotherapy (local steroid therapy, systemic therapy and antihistamine therapy), systemic steroids were statistically more frequently administered in children with cross sensitization (61% vs. 12%; p=0.0001).

DISCUSSION

Cross allergy is a clinical problem taken the most frequently into consideration in adults allergic to plant pollen and demonstrating symptoms from the respiratory system or the oral cavity mucosa (oral allergy syndrome), present after consumption of some the most frequently fresh raw vegetables and fruit. At present, this dependence is defined as the pollen-food allergy syndrome [9]. Milk, hen's egg white and soy played a pathogenic role in children with atopic dermatitis. However, the recent studies indicate that pollen-food allergy syndrome is more and more frequently reported in children above 3 years old [14]. Our clinical observations have suggested that this problem could also affect the youngest patients up to 3 years old. This has become a reason for conducting examinations among the youngest age group, in which sensitization of the cross allergy type was reported in more than ¼ of the children with atopic dermatitis. This relatively high prevalence of this

Figure 4. **Sensitization to food and inhalant allergens in the examined group of children (n=18).**



phenomenon could be explained by the fact that children most frequently hospitalized due to severe exacerbations of the disease were analyzed in our study. It seems that in regard to the population of the children with an allergy, this percentage would be lower, however, such research has not been carried out so far.

To date studies referred to mono- and polyvalent sensitization in children, according to the data published by de Jong et al. [6] after the retrospective population studies carried out in children up to 18 years old, sensitization to one or more allergens was determined in about 40% of them. More than 80% of children sensitized to soy had positive sIgE against inhalant allergens. However, the authors regard this as manifestation of a severe type of the atopic phenotype, not cross allergy to allergens, showing homology of the amino acids sequence [6]. Similar observations refer to the course of sensitization in children with atopic dermatitis. Positive skin tests to inhalant allergens were reported in about 80% of children that had the increased total IgE, after the age of 7 [5]. The age of 3 to 4 is given as a border age, above which the sensitization to inhalant allergens develops. The earlier presence of inhalant allergy in our infants and toddlers may result from the fact that a sensitizing agent was searched for even in the youngest children. However, sensitization in these patients does not always correlate with clinical symptoms of the disease, because no symptoms of bronchial asthma or allergic rhinitis were found in 56% of these patients. This correlation is more frequent in older age groups [15]. From the other hand, there are also papers indicated that children suffering from atopic dermatitis are more predisposed to pneumonia and bronchitis, that may be an important risk factor for asthma [16]. The frequency of asthma in the study

group is probably related to high frequency of sensitization to perennial allergens, but not to cross sensitization.

In the literature, the expression of pollen-food allergy syndrome has been adapted in regard to patients, sensitized to allergens of plant pollen and food allergens homologous to them. In case of finding such sensitization in children, the expression mentioned above seems not to be appropriate, because asymptomatic manifestation of hypersensitization can be observed at this age. About half of our investigated children were asymptomatic and didn't demonstrate, except of atopic dermatitis, typical for cross allergy symptoms as allergic rhinitis or bronchial asthma. The studies carried out only indicate the fact that cross sensitization is observed in the youngest children, not as it has been suspected before, in the teenagers and adults. As our earlier studies confirm, sensitization to plant-derived food allergens is often reported in young children without sensitization to plant pollen or in patients, not showing clinical symptoms of pollinosis [9, 17].

Pollen-food allergy syndrome in children is a subject of few findings in the literature. In the study publication, devoted to the role of food allergy in atopic dermatitis, Werfel et al. [14] turns attention to the presence of sensitization to inhalant allergens in children above 3 – 4 years old with the possibility of sensitization to pollens as early as in the first months of life. The symptoms from the respiratory system are the most frequent clinical manifestations of such sensitization. However, according to the authors, its relation with atopic dermatitis is still unclear [14]. There is a relation between the exacerbation of skin lesions and food consumption in patients with birch-apple allergy syndrome [18], which is the most common form of cross allergy and its model example. In the study group of children, this type of sensitization affected about 40% of the examined. In the rest of patients, we observed sensitization of the cross allergy type to allergens of grass pollen and vegetables.

In studies performed by Werfel et al. [19] and Reekers et al. [18], exacerbation of skin lesions after food consumption is observed in more than 50% patients with sensitization to birch pollens and the pollen-food allergy syndrome. In the study group, statistically significant differences were revealed between the SCORAD value in the study and control groups as well as the more frequent incidence of symptoms of early childhood bronchial asthma and allergic rhinitis in children with cross allergy. However, the assumption that cross allergy in correlation with atopic dermatitis predisposes to the prevalence of the diseases mentioned above requires further investigations in the more numerous group of patients. It is worth mentioning that the development of bronchial asthma and allergic rhinitis in children with atopic dermatitis is a consequence of an allergic march. Moreover, cross allergy more frequently occurs in patients with asthma and allergic rhinitis, which results from sensitization to plant pollen [20]. In other studies performed in children aged from 3-9 years old, with a pollen-food allergy syndrome and atopic dermatitis, a delayed skin reaction to foods consumed was reported in more than 30% of them and three children had an immediate reaction, requiring the systemic steroid therapy [15]. In our study group, 61% of children required the systemic corticotherapy. The co-existence of sensitization to house dust mite and animals' fur seems to have a significant influence on the severity of atopic dermatitis, which was reported in 61% and 22% of the examined, respectively.

In light of the considerations presented above, the examinations carried in our study have confirmed only the sensitization of the cross type, but have not proved its role in the development and exacerbation of skin lesions. In case of sensitization to plant-derived food allergens, a food provocation test may be the proof of their harmful effect; in case of inhalant allergens, there is no a gold standard of provocation and the relation between sensitization to them and absence of skin lesions can be established, based only on the results of the tests [8].

The first multi-centered clinical studies, confirming the harmful effect of food and inhalant allergens after the contact with the skin of patients with atopic dermatitis, were published in 2004 year. Interestingly, sensitization to allergens of celery, the known cross-reacting allergen, and more frequent positive results of sIgE and patch tests were observed in comparison with data from the patient's history, confirming its influence on skin lesions [8]. Similarly, in our study group, positive results of the examinations do not always correlate with their clinical significance. Based on the data from the patient's history, exacerbation of skin lesions after consumption of cross reacting allergens was reported in 22% of children sensitized to fruit and in 33% of children sensitized to vegetables. It should be emphasized that data from the patient's history may not be reliable in such cases. In the study by Breuer et al. [15], based on food provocation, carried out in children with sensitization to birch allergens and birch homologous food allergens, the authors proved that of all children with a positive result of the food provocation test, only one child reported the exacerbation of skin lesions after consuming sensitizing foods. The special attention should be paid to the possibility of immediate reactions from the respiratory system or even anaphylactic reactions after e.g., nuts, which can occur during such tests.

A clinical problem is to find out whether skin lesions are really induced by food consumption [14, 21]. Thus, in some studies, birch pollen-homologous foods were given on consecutive days, after which the skin condition was assessed according to the scale of SCORAD to distinguish after-food skin lesions from early skin lesion [15, 19, 22].

It was proved that patients with the pollen-food allergy syndrome that presented exacerbation of skin lesions after food provocation showed no significant statistical differences with regard to the total IgE concentration, the history of inhalant allergy symptoms, age or severity of atopic dermatitis [22, 23]. Similarly, determination of specific IgE did not permit

to differentiate patients, with a positive or a negative result of the food provocation test [15, 19]. The positive results of patch tests might suggest the role of delayed delayed food reactions in the induction of skin lesions. However, their diagnostic significance in allergy to plant-derived foods is questioned in children up to 3 years old [24]. The studies mentioned above involved adults; so far such studies have not been performed in the pediatric population. Our study is an initial stage of further research and was focused on establishing the presence of sensitization of the cross allergy type, not finding the cause and effect relation with clinical symptoms.

The conclusion that the problem of cross allergy affects also the youngest children with atopic dermatitis may suggest the change in the therapeutic attitude in the management of this disease, taking into consideration an appropriate elimination diet and a specific immunotherapy in the future [25].

CONSLUSIONS

In children up to 3 years with atopic dermatitis and sensitization to plant pollen, the role of a pollen-food allergy syndrome must be taken into account in the pathogenesis of the disease. In children with cross sensitization, the course of atopic dermatitis is more severe; the symptoms from the respiratory and digestive system co-exist. The positive family history is a factor, predisposing to the development of cross sensitization in infants and toddlers.

REFERENCES

1. Heratizadeh A, Wichmann K, Werfel T. Food allergy and atopic dermatitis: how are they connected? Curr Allergy Asthma Rep. 2011 Aug;11(4):284-91.

2. Dynowska D, Kolarzyk E, Schlegel-Zawadzka M, Dynowski W. Udział alergenów pokarmowych i powietrznopochodnych w patogenezie atopowego zapalenia skóry [The contribution of food and airborne allergens in the pathogenesis of atopic dermatitis]. Przegl Lek. 2002 Jun;59(6):453-6. Polish.

3. Park JH, Ahn SS, Sicherer SH. Prevalence of allergy to multiple versus single foods in a pediatric food allergy referral practice [abstract]. J Allergy Clin Immunol. 2010 Feb;125(2) Suppl 1:AB216.

4. Kaczmarski M, Żur E, Cudowska B, Wasilewska J, Matuszewska E, Chrzanowska K. Alergia wielopokarmowa w wieku dziecięcym – aktualny problem kliniczny diagnostyczny i leczniczy [Multiple food allergy in childhood – current clinical, diagnostics, and therapeutic problem]. Gastroenterol Prakt. 2012 Mar;4:23-30. Polish.

5. Gustafsson D, Sjöberg O, Foucard T. Sensitization to food and airborne allergens in children with atopic dermatitis followed up to 7 years of age. Pediatr Allergy Immunol. 2003 Dec;14(6):448-52.

6. de Jong AB, Dikkeschei LD, Brand PL. Sensitization patterns to food and inhalant allergens in childhood: a comparison of non-sensitized, monosensitized, and polysensitized children. Pediatr Allergy Immunol. 2011 Mar;22(2):166-71.

7. Wanat-Krzak M, Kurzawa R. Diagnostyka i leczenie wyprysku atopowego [Diagnosis and treatment of atopic dermatitis]. Alerg Astma Immunol. 2006 Mar;11(1):11-21. Polish.

8. Darsow U, Laifaoui J, Kerschenlohr K, Wollenberg A, Przybilla B, Wüthrich B, Borelli S Jr, Giusti F, Seidenari S, Drzimalla K, Simon D, Disch R, Borelli S, Devillers AC, Oranje AP, De Raeve L, Hachem JP, Dangoisse C, Blondeel A, Song M, Breuer K, Wulf A, Werfel T, Roul S, Taieb A, Bolhaar S, Bruijnzeel-Koomen C, Brönnimann M, Braathen LR, Didierlaurent A, André C, Ring J. The prevalence of positive reactions in the atopy patch test with aeroallergens and food allergens in subjects with atopic eczema: a European multicenter study. Allergy. 2004 Dec;59(12):1318-25.

9. Katelaris CH. Food allergy and oral allergy or pollen-food syndrome. Curr Opin Allergy Clin Immunol. 2010 Jun;10(3):246-51.

10. Sampson HA. Pathogenesis of eczema. Clin Exp Allergy, 1990 Sep;20(5):459-67.

11. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Dermatovener. 1980 June;59 Suppl 92:44-7.

12. Dreborg S, Frew A. Position paper: Allergen standardization and skin tests. Allergy. 1993 Feb; 48 Suppl s14:49-54.

13. Kunz B, Oranje AP, Labrèze L, Stalder JF, Ring J, Taïeb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. Dermatology. 1997;195(1):10-9.

14. Werfel T, Breuer K. Role of food allergy in atopic dermatitis. Curr Opin Allergy Clin Immunol. 2004 Oct;4(5):379-85.

15. Breuer K, Wulf A, Constien A, Tetau D, Kapp A, Werfel T. Birch pollen-related food as a provocation factor of allergic symptoms in children with atopic eczema/dermatitis syndrome. Allergy. 2004 Sep;59(9):988-94.

16. Frankowska J, Kamer B, Trznadel-Budźko E, Rotsztejn H. The retrospective evaluation of pneumonia and bronchitis cases in infants and small children with atopic dermatitis in the practice of a family doctor - personal observations. Adv Med Sci. 2010;55(2):250-3.

17. Cudowska B, Kaczmarski M, Restani P. Lipid transfer protein in diagnosis of birch-apple syndrome in children. Immunobiology. 2008;213(2):89-96.

18. Reekers R, Busche M, Wittmann M, Kapp A, Werfel T. Birch pollen-related foods trigger atopic dermatitis in patients with specific cutaneous T-cell responses to birch pollen antigens. J Allergy Clin Immunol. 1999 Aug;104(2 Pt 1):466-72.

19. Werfel T, Reekers R, Busche M, Schmidt P,

Constien A, Wittmann M, Kapp A. Evidence for a birch pollen-specific cutaneous T-cell response in food-responsive atopic dermatitis. Int Arch Allergy Immunol. 1999 Feb-Apr;118(2-4):230-1.

20. Stajminger G, Marinović-Kulisić S, Lipozencić J, Pastar Z. Most common inhalant allergens in atopic dermatitis, atopic dermatitis/allergic rhinitis, and atopic dermatitis/bronchial asthma patients: a five-year retrospective study. Acta Dermatovenerol Croat. 2007;15(3):130-4.

21. Dai VS. Allergens in atopic dermatitis. Clin Rev Allerg Immunol. 2007 Dec;33(3):157-66.

22. Werfel T, Reekers R, Busche M, Schmidt P, Constien A, Wittmann M, Kapp A. Association of birch pollen-related food-responsive atopic dermatitis with birch pollen allergen-specific T-cell reactions. Curr Probl Dermatol. 1999;28:18-28.

23. Amon U, Koch M, Zehnder S, Porsch S, Cavcic A. Incidence of pollen-associated food allergies in patients with atopic dermatitis [abstract]. J Allergy Clin Immunol. 2009 Feb; 123(2) Suppl 1;S38.

24. Devillers ACA, De Waard-van der Spek FB, Mulder PGH, Oranje AP. Delayed- and immediate-type reactions in the atopy patch test with food allergens in young children with atopic dermatitis. Pediatr Allergy Immunol. 2009 Feb;20(1):53-8.

25. Wang J. Management of the Patient with Multiple Food Allergies. Curr Allergy Asthma Rep. 2010 July; 10(4): 271–7.