

## Role of the skin patch test in diagnosing food allergy in children with atopic dermatitis

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**Key words:** atopic dermatitis, children, skin patch test.

**Summary.** The aim of the study was to determine peculiarities of food allergy in children with atopic dermatitis and to evaluate the significance of skin patch test in determining the main food allergens.

**Methods.** One hundred and eight children (57 boys and 51 girls) with atopic dermatitis were examined. Atopic dermatitis was diagnosed by standard diagnostic criteria, severity of the progress of the disease was determined using SCORAD index and the amount of total IgE in blood, skin prick and patch tests with the main food allergens were performed.

**Results.** The age of the patients varied from 6 months to 16 years, however, almost half (41%) of them were toddlers (1–3 years old). Mild form of atopic dermatitis was dominating (52%). Analysis of the total IgE amount in blood showed different degree of sensitivity of the children tested. Normal amount of the total IgE in blood was found in 73.1% of children with atopic dermatitis, and the increased total IgE amount was found only in 26.9% of children. Positive skin prick test with the standard and the most common food allergens was found only in 4.63% of children with atopic dermatitis, while the positive skin patch test with 25 food allergens was found in 68.5% of children. Depending on the type of the allergic reaction, immediate type reaction dominated only in 10.3% of children with atopic dermatitis, while the delayed type allergic reactions were characteristic to food allergies in 48.3% of children with atopic dermatitis. Food allergy was not found in one fifth of children with atopic dermatitis.

**Conclusions.** Skin patch test is an informative and reliable diagnostic test in evaluating the delayed type allergic reactions. In about half of the tested persons with atopic dermatitis, food allergy appeared in delayed type allergic reactions. Therefore it is very important to do the skin patch test for toddlers and pre-school age children. The most common allergens found with the help of skin patch test are soy, milk, peanuts, carrot, egg whites, wheat, and corn.

### Introduction

Atopic dermatitis (AD) is the most common skin disease especially in children (1). The number of children with this disease is increasing. The number of adults with this disease did not change during the last five years, however, the number of children with this disease has increased twice (2). Epidemiological data showed that AD was diagnosed in 4% of children in Lithuania, although twice as many children have the signs of this disease, and AD symptoms were found in 17% of children (3). The interaction of genetic, immunity and surrounding factors has influence on the appearance of AD. Children with AD often are sensitive to food allergens. Many researchers indicate that 80% of children with AD are allergic to food (4).

Food allergy may be mediated by IgE (immediate type, type I) and also by other than IgE factors, e.g. type IV, delayed type reactions mediated by T cells (5, 6). Type I and IV allergic reactions are dominant in the pathogenesis of AD. Usually studies were done with the immediate type immunity reactions (mediated by IgE), the beginning of which is from several minutes up to 1–2 hours after the contact with the food allergen. When child eats one product and symptoms of allergy appear within several minutes, then the product that caused the allergic reaction may be easily suspected. However, the food product that mediated food allergy is very hard to identify when the delayed type reactions are dominating. Then the allergy symptoms may appear even in a few days (7). Therefore,

delayed type immunity reactions and their new diagnostic method *in vivo* - skin patch test - are more and more recognized in AD pathogenesis in the last decade. In 1996, E. Isolauri and K. Turjanmaa were the first to declare the data about the significance of the skin patch test in diagnosing the food allergy in small children with AD (8). It is not difficult to diagnose AD and to determine its causes in children who have increased total IgE amount in blood according to the age, their skin prick test for the main food and inhalation allergens are positive, and when there are specific IgE for individual food products. Difficulties arise when the increased total IgE in blood of a child with AD is not found and the skin prick test is negative. Then the cause of the food allergy may be determined by making a skin patch test.

The list of allergic products, which more often cause allergies in different countries of the world, is different. Allergy to food depends on the age of the child, eating traditions of the family and the country. However, such food allergens as milk, soy, eggs, wheat, nuts and fish are usually listed among the main reasons for the development of AD. Theoretically allergic reactions may be caused by all food products that contain protein. In the first years of life allergic reactions are usually caused by the protein in cow milk, eggs, wheat, soy, and in older children allergic reactions are caused by nuts (peanuts, hazelnuts) and fish (9, 10). It is not easy to diagnose food allergy since more than one food allergen may be responsible for the flare-up of the skin symptoms.

The aim of our study was to determine the peculiarities of the food allergy in children with AD and the significance of the skin patch test by determining the main food allergens.

### Material and methods

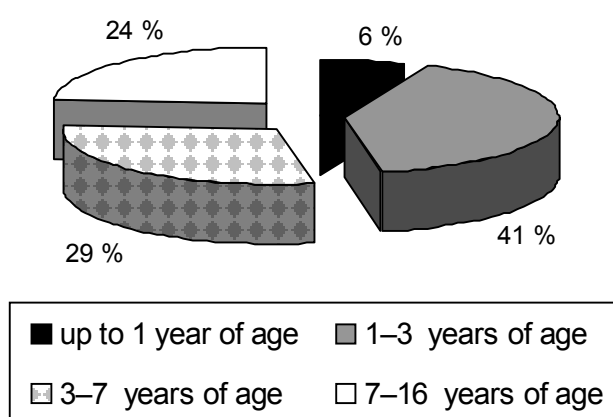
One hundred and eight children from 6 months to 16 years of age, who had only AD, were examined. The disease was diagnosed by standardized diagnostic criteria (according to J. M. Hanifin and G. Rajka (11)); the severity of the disease was evaluated according to SCORAD index (2). All children were tested by determining the total IgE amount in blood by enzyme-immune method, skin prick tests were performed with the standard food allergens (milk, eggs, wheat, rice, cod, pork, chicken, carrot), which helped to determine the immediate type (type I) sensitivity to food mediated by IgE. Moreover, based on the recommendations of Finnish scientists (8), the skin patch test was carried out with 25 food allergens, which helped to evaluate the delayed type (type IV) reaction, which occurs without the participation of IgE. All patients were tested at the remission of the disease in outpatient department.

### Results

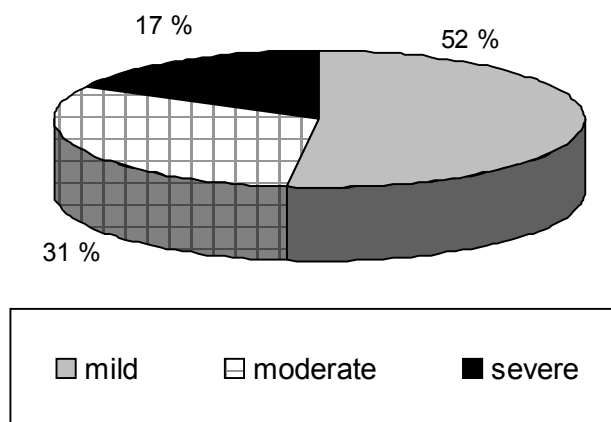
The age of the patients with AD was from 6 months to 16 years of age, although the majority were toddlers (1-3 years of age) (Fig. 1).

Distribution according to the gender of tested patients was almost equal - there were 57 boys (52.8%) and 51 girls (47.2%). Children were grouped into three groups according to the severity of AD. The first group - (SCORAD index 1-24 points) children, who were diagnosed mild AD, the second group - (SCORAD index 25-50 points) children, who were diagnosed moderate AD, and the third group - (SCORAD index >50 points) children, who were diagnosed severe AD. Mild form of AD was dominating (Fig. 2).

Analysis of the total IgE amount in blood showed



**Fig. 1.** Distribution of children with AD according to the age groups



**Fig. 2.** Distribution of patients according to the severity of AD

different degree of sensitivity of the tested children. The increased amount of the total IgE, which shows immediate type allergic reactions, was found only in 29 (26.9%) children with AD. The normal amount of the total IgE was found in 79 (73.1%) children with AD. The increase of the total IgE amount, as well as the positive skin prick tests with food allergens helped to determine immediate type food allergy in children with AD. Positive skin prick tests with the standard and most common food allergens were found in 5 (4.63%) children with AD. One child had very severe reaction to egg.

Skin patch tests with 25 food allergens were performed for all children. Delayed type allergic reactions were evaluated according to the characteristic skin changes found on the spots where the allergens were placed. Skin patch test is considered to be slightly positive if there is erythema or edema, strongly positive - if there is pronounced erythema, edema, vesicles, and very strongly positive - if there is erythema, edema, merging vesicles, and cysts. Seventy four (68.5%) children had positive skin patch test and 34 (31.5%) - negative. The most common delayed type allergic reactions are showed in Fig. 3.

There were less common allergic reactions to cod, chicken, oranges, cacao, barley, beef, buckwheat, egg yolk, potato, banana, honey, whey, rice, pork, cabbage, and oat (Fig. 4, 5). There were no cases of the de-

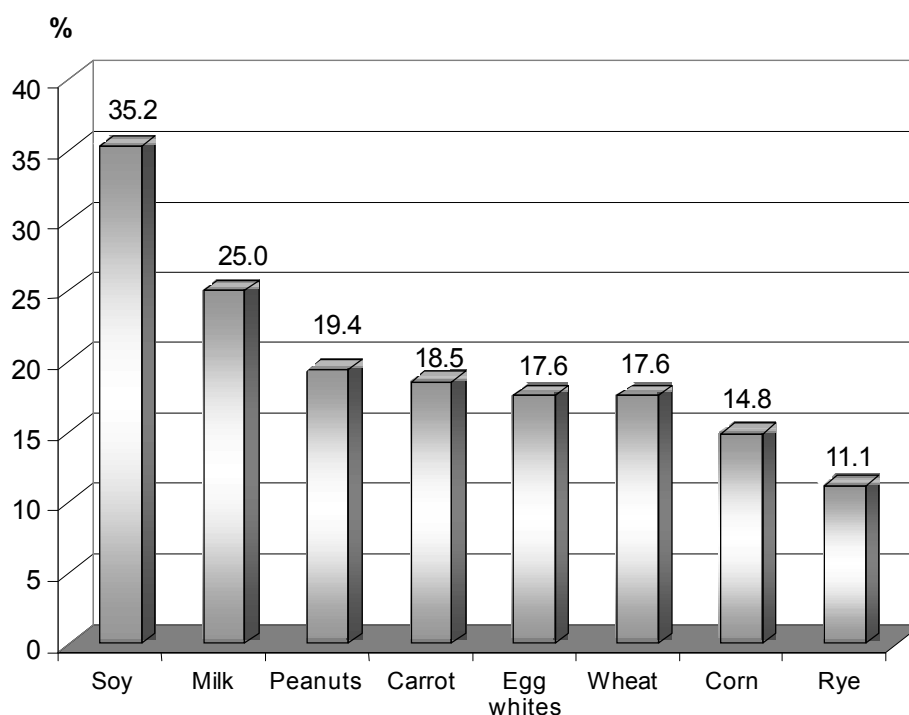
layed type allergic reaction to apple.

Delayed type severe reactions to corn were noticed in 6 (37.5%) cases, peanuts - 5 (23.8%), banana - 4 (66.7 %), soy - 4 (10.5%), cod - 3 (33.3%), whey and honey - 2 (33.3%), chicken and orange - 2 (25%), egg whites - 2 (18.2%), rye - 2 (14.3 %), carrot - 2 (10%), cacao and potato - 1 (16.7%). A very severe reaction to banana was noticed in a 6-year-old girl.

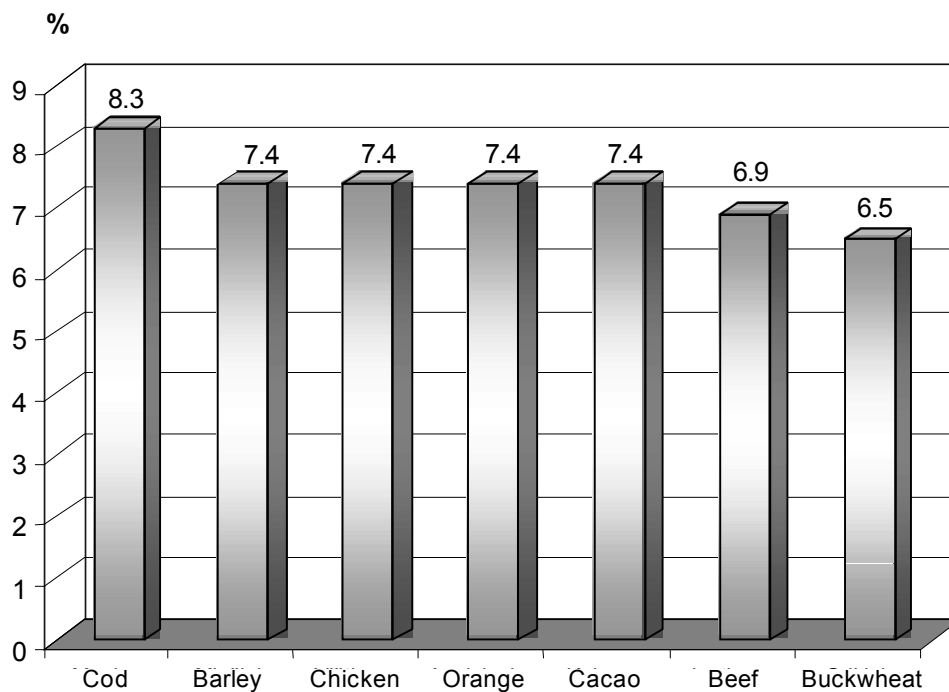
Distribution of the results of skin patch test and total IgE amount in blood among children with AD depending on the age of the child are presented in Table 1.

All children with AD were grouped into 6 groups according to the type of allergic reaction (Table 2).

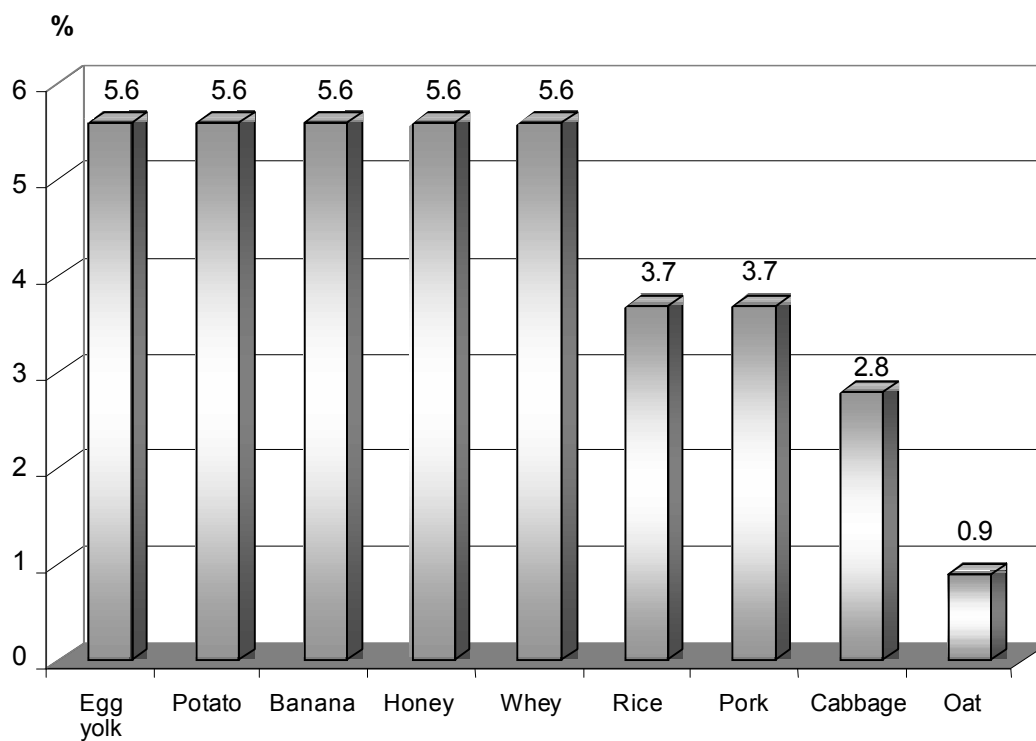
Patients in groups I and VI as a result of the performed tests were diagnosed the immediate (type I) allergic reactions, patients in group IV - delayed type (type IV) allergic reactions, patients in groups II and III had both types allergic reactions (immediate and delayed). Children from group V were not diagnosed any type of allergic reactions; AD symptoms in them were likely to be caused by non-immunological reactions. According to our study data, immediate type reactions were dominant only in 11.1% of children with AD, while more often the food allergy appears in delayed type allergic reactions in of children with AD (49.07%). Food allergy was not diagnosed in one fifth of children with AD.



**Fig. 3. Food products that most often cause slow type allergic reactions in children with AD**



**Fig. 4.** Food products that rarely cause slow type allergic reactions in children with AD



**Fig. 5.** Food products that rarely cause slow type allergic reactions in children with AD

**Table 1. Distribution of skin patch test results and total IgE amount in blood among children with AD according to the age of the child**

Age of child (years)	Number of children with AD	Positive skin patch test	Negative skin patch test	Increased total IgE	Normal total IgE
		number ( % )	number ( % )	number ( % )	number ( % )
Up to 1	7	7 (100)	0	1 (14.3)	6 (85.7)
1–3	44	37 (84.1)	7 (15.9)	9 (20.5)	35 (79.5)
3–7	31	19 (61.3)	12 (38.7)	6 (19.4)	25 (80.6)
7–10	13	8 (61.5)	5 (38.5)	6 (46.2)	7 (53.8)
10–14	7	3 (42.9)	4 (57.1)	3 (42.9)	4 (57.1)
14–16	6	0	6 (100)	4 (66.7)	2 (33.3)

**Table 2. Groups of children with AD based on the results of performed tests**

Group	Skin prick test	Total IgE amount in blood	Skin patch test	Number of children with AD	
				number	%
I	+	↑	–	1	0.93
II	+	↑	+	10	9.23
III	–	↑	+	11	10.19
IV	–	n	+	53	49.07
V	–	n	–	22	20.37
VI	–	↑	–	11	10.19

↑ – increased total IgE in blood; n – normal total IgE in blood for that age;

+ – positive skin prick and patch tests; – – positive skin prick and patch tests.

## Discussion

Food allergy plays an important role in the pathogenesis of AD (12). However, increased amounts of total and specific IgE in blood and sensitivity to food and environment allergens are not found in about 20% of patients with AD to whom classic AD clinic is characteristic (1). It may be concluded that non-immunological reactions (pharmacological and of undetermined etiology) are dominating in the pathogenesis of atopic dermatitis in one fifth of children with AD. This was confirmed by the data of our study.

According to the data of various scientific studies, skin patch test is positive in 33-86% of cases. According to the doctoral thesis of O. Rudzevičienė, positive skin patch test to milk was in 33.3% of children with AD up to 2 years of age. Statistically significant positive skin patch test (33.3%) was determined more often than positive skin prick test (6.1%) (13). Other

researchers presented similar data as well. H. Majamaa et al (14), having tested 143 children with AD up to 2 years of age, determined that skin prick test was positive in 14% cases and skin patch test - in 43% cases in children, whose allergy to milk was confirmed by double blind, placebo controlled test. According to the data of E. Isolauri et al (8), positive skin patch test to milk was determined in 52.5% cases and positive skin patch test - in 68% cases. According to the data of other researchers, positive skin patch test to cow's milk in children up to 2 years of age was found in 44% (4), and to grain in 86% (15). According to our data, skin prick test was positive in 4.63%, while skin patch test was positive in 68% cases. According to the literature, skin patch test is positive in 89% of children, whose skin prick test is negative (8).

Although the list of the most allergic products differs by countries, milk, soy, egg, wheat, nuts and fish

are considered to be the most common food allergens that cause AD. This is reflected in our tests as well. Every third child was diagnosed delayed reactions to soy, every fourth - to milk, every fifth - to peanuts, carrot, egg whites and wheat. Neither delayed nor immediate type reactions to apple were found in any of the children. According to our data, positive skin patch test is most often found in children from 6 months to 7 years of age (100% and 61%, respectively). This is confirmed by the data of various authors as well (16). In infancy skin patch tests are positive disregarding the amount of IgE in blood. The younger the child is, the greater the possibility that the skin patch test is positive. We think that the physiological characteristics of the skin (permeability of the skin, sweating, response to irritants, and sensitivity to light) of an infant or a small child have influence on that. It is not expedient to perform skin patch test in children with AD in adolescence. It is very important to diagnose the food allergy as soon as possible. Early determination of food allergens protects infants and small children from unnecessary empirical strict diets that may cause impaired development, decreased resistance of the organism to infections and the imbalance of the immune system, it may improve child's health and performs the role of secondary prevention, protecting from further food allergy development. Many children grow

out of the food allergy, especially to milk and eggs; however, they often remain allergic to nuts and fish all their lives. The literature indicates that among children allergic to food (mediated by IgE), 26% become tolerant to the specific food product within the first year of diet, and 11% - within the second year (4). Symptoms of the food allergy may remain in the older age as well; only they demonstrate themselves with different symptoms, e.g. slow down of growth, and functional diseases of digestive tract (17). Although the AD frequency decreases as the child grows, a great risk remains for the development of bronchial asthma (4).

### Conclusions

Skin patch test is informative and reliable diagnostics method, when determining delayed type allergic reactions in children with AD. It is necessary to perform skin patch test for infants and pre-school children, when total IgE amount in blood is normal and skin prick test are negative. The most common food allergens, determined by skin patch tests were soy, milk, peanuts, carrot, egg whites, wheat and corn. Delayed type food allergic reactions were found in one half of the tested children with AD. One fifth of tested children were diagnosed non-allergic AD type.

## Odos lopo mėginio reikšmė diagnozuojant alergiją maistui atopiniu dermatitu sergantiems vaikams

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**Raktažodžiai:** atopinis dermatitas, vaikai, odos lopo mėginys.

**Santrauka.** Tyrimo tikslas. Išanalizuoti atopiniu dermatitu sergančių vaikų alergijos maistui ypatybes bei įvertinti odos lopo mėginio reikšmę nustatant pagrindinius maisto alergenų.

**Metodika.** Kompleksiškai ištirti 108 vaikai (57 berniukai ir 51 mergaitė), sergantys tik atopiniu dermatitu. Liga diagnozuota remiantis standartizuotais diagnostikos kriterijais, nustatytas ligos eigos sunkumo laipsnis (SCORAD indeksas), bendras IgE kiekis kraujyje, atlikti odos dūrio ir lopo mėginiai su pagrindiniais maisto alergenais.

**Rezultatai.** Tirtų ligonių amžius svyravo nuo 6 mėn. iki 16 metų, tačiau maži vaikai (1–3 metų) sudarė 41 proc. Pagal atopinio dermatito eigos sunkumo laipsnį (SCORAD indeksą), vyravo nežymus atopinis dermatitas (52 proc.). Bendrojo IgE kiekio kraujyje pokyčių analizė parodė skirtingą tirtų vaikų įsijautrinimo laipsnį. Normalus bendrojo IgE kiekis kraujyje rastas 73,1 proc. atopiniu dermatitu sergančių vaikų, o padidėjęs bendras IgE kiekis rastas tik 26,9 proc. Teigiamas odos dūrio mėginys su standartiniais didžiausiais maisto alergenais nustatytas tik 4,63 proc. atopiniu dermatitu sergančių vaikų, o teigiamas odos lopo mėginys su 25 maisto alergenais rastas 68,5 proc. Atsižvelgiant į alerginės reakcijos tipą, greitojo tipo reakcijos vyravo tik 10,3 proc. atopiniu dermatitu sergančių vaikų, o lėtojo tipo alerginėmis reakcijomis alergija maistui pasireiškė 48,3 proc. atopiniu dermatitu sergančių vaikų. Penktadaliui atopiniu dermatitu sergančių vaikų alergijos maistui nenustatyta.



Išvados. Odos lopo mėginys – informatyvi ir perspektyvi diagnostikos priemonė vertinant lėtojo tipo alergines reakcijas. Apie pusę tirtųjų, sergančių atopiniu dermatitu, alergija maistui pasireiškia lėtojo tipo alergenėmis reakcijomis. Odos lopo mėginį tikslinga atlikti kūdikiams ir ikimokyklinio amžiaus vaikams. Dažniausi maisto alergenai, nustatyti atlikus odos lopo mėginį, yra šie: soja, pienas, žemės riešutai, morkos, kiaušinio baltymas, kviečiai, kukurūzai.

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