

Food Allergy in Adults with Atopic Dermatitis

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Atopic dermatitis is a disease with a multifactorial etiology. Atopy may be defined as the genetic predisposition of the immune system to react inappropriately, with a marked IgE production to otherwise harmless environmental antigens (inhalants, foods). Atopy is probably the main causative factor in atopic dermatitis, but other nonallergenic environmental factors may influence pathogenesis [1]. The sensitivity of the skin for these non-allergenic factors is called *hyperreactivity*. Factors that may aggravate the disease and play a role in its maintenance are numerous: cutaneous infections and irritants, climatological circumstances, emotional and physical stress.

The complex pathogenesis makes it difficult to judge the relative importance of inhalant and food allergens in modulating the expression of the disease, both in terms of their capacity to act as triggers and in terms of the benefit that interventions, such as housedust mite avoidance or elimination diets, may have. Patients with atopic dermatitis differ from those with asthma and hay fever in having higher total IgE levels that tend to parallel the extent and severity of the disease. They have a higher frequency of positive immediate skin tests to food and higher levels of food-specific IgE [2]. A fairly significant number of patients experience food-induced hypersensitivity reactions of immediate onset, both localized and generalized [1]. However, the results of diets are disappointing with regard to the course of the chronic skin lesions in atopic dermatitis, especially in case of adults. Nevertheless, the question whether food allergens do play a role in the pathogenesis of the skin lesions remains intriguing.

The role of food allergy has best been studied in infancy; the most important food allergens in childhood being egg, cow's milk, peanut, fish, wheat and soybean. According to Sampson [3], almost 60% of children with severe atopic dermatitis have positive food challenges to one or two of these foods. Sensitization to these potent allergens occurs mainly in the vulnerable period of the first year of life, when the mucosa of the gut is still easily permeable, and devoid of defense mechanisms like endogenous IgA production. With increased maturity of the gut barrier, egg and cow's milk allergy tend, though not always, to disappear [4–6]. Fish and especially peanut allergy often remain a life-long problem [5–7].

When the atopic subject gets older and sensitization to common inhalants, especially birch and mugwort pollen, comes into effect, there is an ever increasing possibility of simultaneous sensitization to food allergens of vegetable origin that share epitopes with the formerly mentioned allergens. This cross-sensitivity is often widespread and may account for a multitude of positive skin tests to vegetable food with only a few being of clinical relevance. In explaining the acute, often generalized food-allergic reactions (urticaria, anaphylaxis) that may occur in patients sensitized to birch and mugwort pollen, but without atopic dermatitis, a careful clinical history, knowledge of the characteristic sensitization patterns, insight in food preparation habits and the components of prepacked food, is usually sufficient to pinpoint the relevant positive skin test. However, patients with atopic dermatitis clearly find it very difficult to judge which food allergens and to which extent, influence the severity of their disease, thus creating a greater need for challenge tests. Apart from being time-consuming these challenge tests have other flaws. Food allergy has a variable expression and symptomatology depends on the amount of food eaten, the way it was prepared, presence or absence of a combination with alcohol and physical exercise. So the causative food may not induce a reaction if it is not eaten under exactly the right circumstances [1]. Furthermore, it is not clear if only one or repeated challenges are necessary to provoke this chronic allergic disease.

Considering the drawbacks of challenge tests, a careful selection of food items that are most likely to be of influence is an absolute prerequisite to obtain a positive challenge test, if ever. In our opinion this selection has to be done according to certain basic principles: taking a detailed clinical food history, doing skin tests with and specific IgE measurements for a careful chosen panel of food allergens, and making a neatly arranged – preferably one page – overview of these data. These points are discussed in detail below.

The Clinical Food History

This includes more than the question if the patient noticed 'ill effects of food on his skin disease'. It intends to obtain information about any acute local or generalized symptoms caused by a large panel of food items, as well as their influence on itch or worsening of atopic dermatitis. We structure our anamnesis as follows: the first important division is judging the effects of (a) food of animal origin, and of (b) food of vegetable origin.

(a) *Relevant food of animal origin*: Questions are asked about occurrence of symptoms after consumption of milk, egg, fish, meat, poultry and seafood (such as Crustacea).

(b) *Food of vegetable origin*: Several categories are discussed with the patient: nuts and seeds; fruits and vegetables (arranged in groups according to botanical family); herbs and spices; grain products, and drinks, such as wine, beer, tea, cola.

Panel of Food Items for Testing

The panel of food items for skin tests and specific IgE measurements should include:

(a) *The well-known food allergens* from both animal and vegetable origin: *cow's milk, egg, fish, meat, seafood (shrimp); peanut, soy, wheat* (the wellknown food allergens in childhood are italicized), and the 'classic parapollen' allergens: nuts, apple, celery and potato.

(b) *More items of those food families showing extensive cross-sensitivity*: Papilionaceae, Umbelliferae, Solanaceae, in order to obtain a clearer view on their clinical importance.

(c) *Food items that may serve as 'alimentary alternatives'*: For example, fruit not belonging to the Rosaceae (citrus, banana, grape, melon, etc.); maize, rice, buckwheat to use in case of wheat allergy; herbs and spices not belonging to the Umbelliferous plant family. In case of widespread vegetable food sensitivity our goal is to have tested at least one edible variant of the different botanical families (Compositae, Liliaceae, Cruciferae, Chenopodiaceae). The selection is based on the usual Dutch diet. Special attention to deviant food habits is necessary in dealing with patients from other cultures.

(d) *The food items the patient regards as (possibly) harmful*.

An Overview

The synopsis should comprise the results of anamnestic data, results of skin tests and specific IgE measurements. Finally, this overview can serve to register the effects of oral challenge tests.

Table 1. Clinical symptoms in 6 adult patients with cow's milk allergy (5 females, 1 male; mean age of onset 26 years)

Clinical symptom	Frequency
Worsening of atopic eczema	6
Oral allergy	6
Urticaria, angioedema	6
Vomiting, diarrhea	2
Rhinitis, asthma	2
Anaphylaxis	3
Atopy: positive skin tests to common inhalants	6
'Complex' food allergy (> 3 items positive)	5

Results

Food of Animal Origin

It was interesting to observe that in adult patients, cow's milk can still be an important causative allergen and is sometimes even clinically a recently acquired food allergy. Since 1989, we have observed 6 patients (5 females, 1 male) with atopic dermatitis, whose signs of cow's milk allergy became apparent for the first time in adolescence [8]. All 6 had been able to tolerate cow's milk in childhood, without any apparent influence on their usually mild atopic dermatitis. However, between the age of 20 and 30 years these patients became aware of adverse effects of cow's milk. Apart from worsening of atopic dermatitis, consumption of cow's milk caused oral pruritus, swelling of lips and tongue, urticaria and angioedema, vomiting, diarrhea, rhinitis and asthma and in three signs of anaphylaxis (table 1).

All 6 patients were atopic as judged by positive skin tests to common inhalants; in 4, multiple positive skin tests were found to other food allergens, mainly of vegetable origin. All 6 had positive skin tests and/or high specific IgE for whole cow's milk. Skin prick tests with Na-caseinate powder and commercially obtained extracts of β -lactoglobulin and α -lactalbumin revealed positive reactions to casein protein and generally much weaker or negative reactions to whey proteins (table 2). Five had high specific IgE levels to casein (class V–VI in the Pharmacia CAP system). One had a rather low level, but in all 6 patients the casein antibody level exceeded the level for α -lactalbumin or β -lactoglobulin (table 3). The data suggest that in this 'late-onset' cow's milk allergy the main sensitizing protein is casein and that probably casein-containing food items are most hazardous for these patients. Elimination diets proved reasonably success-

Table 2. Skin test results in 6 adult patients with cow's milk allergy (5 females, 1 male; mean age of onset 26 years)

Patient No.	Whole cow's milk ¹	Casein ²	α -Lactalbumin ³	β -Lactoglobulin ³
1	+	+++	-	-
2	++	+++	+	+
3	+	+++	-	-
4	n.d.	+	+	-
5	++	+++	-	++
6	n.d.	++	-	-

n.d. = Not done.

¹Prick test Diephuis (patients 1, 3) and Bencard (patients 2, 5).

²Scratch patch test with Na-caseinate powder in saline.

³Prick test ARTU Biologicals NV, Lelystad.

Table 3. Serological tests in 6 adult patients with cow's milk allergy (kU/l in Pharmacia CAP system) (5 females, 1 male; mean age of onset 26 years)

Patient No.	Total IgE	Specific IgE (CAP classes in parentheses)			
		whole cow's milk	casein	α -lactalbumin	β -lactoglobulin
1	663	56 (V)	73 (V)	<0.35	<0.35
2	18,168	92 (V)	>100 (VI)	58 (V)	80 (V)
3	9,256	99 (V)	>100 (VI)	RAST 3+	RAST 1+
4	18,774	n.d.	91 (V)	9 (III)	1.5 (II)
5	96	0.7 (II)	0.9 (II)	<0.35	<0.35
6	4,464	20 (IV)	80 (V)	<0.35	<0.35

n.d. = Not done; RAST = radioallergosorbent test done by the Central Laboratory of the Red Cross Blood Transfusion Service, Amsterdam.

ful both in controlling the acute symptomatology and the atopic dermatitis. Onset of cow's milk allergy in adult life as well as the predominant sensitization to casein has been described by others [9–12].

Food of Vegetable Origin

Our impression that birch and/or mugwort pollen sensitization and the consequent multisensitization to vegetable food is seen especially in patients with

Table 4. Pollen and food allergy in 45 patients with a severe form of atopic dermatitis (A CAP value of 3 kU/l serum is used to discriminate between positive and negative patients)

Category	n	%	Category	n	%
Pollen-positive	28	62	Pollen-negative	17	38
Grass	28	62			
Birch	21	47			
Mugwort	7	17			
Food ¹ -positive	19	70	Food ¹ -positive	2	12

¹Egg, Cow's milk, peanut, hazelnut, potato, wheat, celery, soy.

severe atopic dermatitis, was confirmed by analyzing the data of 45 patients receiving in-hospital treatment for their eczema [13]. Taking into account CAP values > 3 kU/l, 62% of these patients were sensitized to grass pollen, 47% to birch and 17% to mugwort pollen. Sensitization to food was found in 21 patients (46%), and was almost exclusively seen in the 'pollen-positive' group (table 4). In the patients with 'isolated' grass pollen allergy, raised specific IgE values for food were found in only 4 subjects: 3 were sensitized to food of animal origin, and only 1 was sensitized to food of vegetable origin. This is in agreement with the well-known fact that sensitization to food of vegetable origin is related to birch and mugwort pollen allergies. The prevalence of atopic disease, and especially of pollen allergy, is increasing, probably because of atmospheric pollution [14, 15]. Pollutants damage the epithelium of the respiratory tract, thus increasing the permeability for allergens. In animal studies, suspended particles (aerosols) such as present in diesel exhaust may act as adjuvant in promoting the IgE response. Hay fever in the UK has increased 4-fold over the past 30 years [16].

The increased prevalence of pollen allergy and the consequent multisensitization to food of vegetable origin, may account for the increasing number of patients we see with difficult to treat forms of atopic dermatitis. However, it never becomes quite clear if we are to regard this 'pollen-related' food allergy merely as a sign of broader expression of atopy, and only serving as an explanation for the so often mentioned oral allergy symptomatology, or if we have to consider vegetable-food allergy to be a real cause in the pathogenesis of the atopic dermatitis. Results of open (bulk) challenge tests at the end of a period of hospital observation were disappointing (often negative), and the results of diets unrewarding, even when we selected the food items for challenge tests carefully and according to the guidelines mentioned above.

The debate is still not settled. Did we select the right food items and did we create the desired conditions for our challenge tests? Or should we have serious doubts about the influence of vegetable-food allergens on atopic dermatitis. Tryptase and ECP measurements have been described as potential useful monitoring parameters in the effects of oral food challenges, especially in atopic dermatitis, and might help to distinguish between relevant and irrelevant positive skin tests and RAST's for food allergens [17, 18]. Though of great interest, food allergy as cause of atopic dermatitis in adult patients remains a controversial subject.

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