

Importance of food allergy in atopic dermatitis

Oehling A, Resano A, Sanz ML, Fernández Benítez M. Importance of food allergy in atopic dermatitis.

Allergy 1998; 53: (Suppl 46): 139–142. © Munksgaard 1998.

A. Oehling, A. Resano, M. L. Sanz, M. Fernández Benítez

Department of Allergology and Clinical Immunology, University Clinic, Faculty of Medicine, University of Navarre, Spain

Dr A. Oehling
Department of Allergology and Clinical Immunology
University Clinic
Faculty of Medicine
University of Navarre
Spain

In several papers previously published and in agreement with many authors, we have reiterated the importance of food sensitization in triggering the skin manifestations of atopic dermatitis. This is a sensitization in which IgE- and IgG4-mediated anaphylactic mechanisms are involved, as well as mechanisms mediated by cellular immunity. In the papers mentioned before, the cause-and-effect relation and its verification by means of *in vivo* and *in vitro* allergologic diagnosis of the reaction mediated by hypersensitivity to some food were present in 60.9–77% of the patients. On the other hand, we must take into account the fact that most of these patients presented not only skin manifestations, but also accompanying rhinitis and asthma, very often of pollen-sensitization origin, with which sensitization to house-dust mites is obviously associated.

This is why, although we have already emphasized these well-known aspects in several papers, we decided to perform a new study and a 3-year follow-up on patients diagnosed with atopic dermatitis, making a thorough *in vivo* and *in vitro* allergologic study by means of the existing techniques for immunoallergologic study of food allergy. As we said before, we also intended to perform a long follow-up, considering the causal food factor and the appropriate drug therapy.

Studies performed

In this last study, 74 patients diagnosed with atopic dermatitis were selected, aged 9–46 years (90% of

whom were under 16 years of age), 56% males and 43% females. The diagnosis of food allergy was mainly based on a clear cause-and-effect relation between the food and the triggering of the symptomatology or its aggravation. Intradermal skin tests were performed with 12 groups of food allergens used by us on a routine basis as well as with the foods involved according to the anamnesis (milk, eggs, fish, shellfish, nuts, wheat, fruits, legumes, and cacao). The food antigens were prepared in our laboratory by the Frugoni-Hansen method and at 1/100 concentration of the extract obtained. The patients were also tested against 13 groups of airborne antigens from Ifidesa Aristegui (Bilbao, Spain) (mites, dander, pollens, and mold spores). All the patients underwent total and antigen-specific serum IgE determinations for food and airborne allergens by means of the CAP System and the histamine-release test, of which we have much experience in food allergy.

As far as the clinical evolution is concerned, the score followed can be seen in Table 1. For the treatment, once the diagnosis was given, the foods involved were taken out of the diet. The medication used was ketotifen, antihistaminics, and corticosteroids, usually only topical administration. Unfortunately, double-blind, placebo-controlled food challenge tests could not be performed, since the ethics committee of our clinic does not allow them and most patients would not sign the informed consent form.

In the course of the disease, repeated ingestion of the causal food took place occasionally, always with

Table 1. Clinical follow-up score

0	Negative. Clinical symptomatology similar to the one referred when diagnosed, with no decrease of pharmacological treatment required.
1	Fair: Slight clinical improvement in comparison with previous revision although use of topical corticosteroids is necessary due to skin relapses.
2	Good. Clear improvement of the clinical symptomatology with no active lesions. No need of corticosteroid treatment.
3	Very good: Asymptomatic.

positive test results. Finally, performance of patch tests was not considered appropriate, considering the results of the *in vitro* tests, and since, apart from the cellular immunity mechanisms involved, we consider that humoral immunity mechanisms through IgE and IgG4 play a very important role.

Results

We observed that out of the 74 patients diagnosed with atopic dermatitis, a high percentage (79.7%) presented other associated allergologic disorders: 17.5% of them were diagnosed with rhinitis and 62.2% with bronchial asthma.

After the allergologic study performed both *in vivo* and *in vitro*, we found the following sensitizations to airborne allergens: mite (*Dermatophagoides pteronyssinus*) in 25 patients (34%) and grass pollen in 18 patients (24.3%). We found a clinical history indicative of food allergy and confirmed by means of skin tests and/or *in vitro* tests in 64.9% of the patients studied. Regarding the food antigens, milk (36.5%) and egg (35.1%) were the most frequently involved allergens in the triggering of the skin manifestations, followed by fish (21.6%) and nuts (6.8%) (Table 2).

The treatment followed by the patients is summarized in Table 3. Obviously, in those cases where there was sensitization to food antigens, an exclusion diet was established (52 patients; 70.3%). Although no statistical significance was found, the

Table 2. Frequency of food allergens involved (%)

No food allergy.	35.1%	
Food allergy:		
Milk	36.5	} 64.9%
Egg	35.1	
Fish	21.6	
Nuts	6.8	
Crustaceans	2.7	
Wheat	2.7	
Legumes	1.3	
Tomato	1.3	
Mustard	1.3	
Snail	1.3	

need for topical corticosteroids due to aggravation of the skin manifestations, and the use of anti-histaminics tend to be less in this group of patients than in patients where the causal food origin was not proven.

The clinical evolution of the patients became distinctly satisfactory after year 1 of treatment; in the follow-up after 1 year of treatment, we observed that 77.3% of the patients were in groups 2 and 3, as can be seen in Table 4. Nevertheless, it is in year 2 that the improvement became more marked (88.2%), and it remained stable in the subsequent reviews, since the patients did not report important relapses. Also to be highlighted is the gradual increase of group 3 (asymptomatic patients), which was significantly greater after year 3 of treatment ($\chi^2 = 58.08$; $P < 0.001$). As can be seen in Tables 5 and 6, the evolution followed by the patients with food allergy was more favorable than that of patients for whom this disorder was not proven. Nevertheless, in the first 18 months, the difference was not significant, although it reached a very high clinical significance after 3 years of treatment and follow-up ($\chi^2 = 54.02$; $P < 0.000$) (Fig. 1); thus, 71.4% of the patients diagnosed with atopic dermatitis and food allergy felt asymptomatic after 3 years, whereas only 20% of the patients with atopic dermatitis where the

Table 3. Treatment followed after allergologic study

	No exclusion diet (n=22)	With exclusion diet (n=52)
Corticosteroids	10 (45.5%)	17 (32.7%)
Antihistaminics	14 (63.6%)	25 (48.1%)

Ketotifene. 67 patients (90.5%).

Antibiotic: 21 patients (28.8%).

Table 4. Clinical evolution after 3 years of treatment in patients diagnosed with atopic dermatitis (%)

	6 Months	1 Year	18 Months	2 Years	30 Months	3 Years
0 (Negative)	5.8	1.5	1.7	0	0	0
1 (Fair)	37.7	21.2	15.5	11.8	11.1	13.2
2 (Good)	49.3	47	55.2	43.1	35.6	28.9
3 (very good)	7.2	30.3	27.6	45.1	53.3	57.9

Table 5. Clinical evolution after 3 years of treatment in patients diagnosed with atopic dermatitis with no food allergy (%)

	6 Months	1 Year	18 Months	2 Years	30 Months	3 Years
0 (Negative)	9.1	4.5	4.5	0	0	0
1 (Fair)	31.8	15.8	24.1	16.7	18.2	20
2 (Good)	59.1	53.4	50	50	54.5	60
3 (Very good)	0	26.3	21.4	33.3	27.3	20

food cause-and-effect relation was not found presented remission of their skin manifestations.

Discussion

As for the reliability of the *in vitro* allergologic diagnostic techniques, from our experience, we can conclude that the histamine-release test is more sensitive than antigen-specific IgE determination.

Surprisingly, nowadays, diagnosis by immunologic techniques is not performed routinely in accordance with its usefulness. In this study, we can see that in 79.7% of the subjects there is another disorder associated, represented by 17.5% of the patients with rhinitis and by 62.2% with bronchial asthma. From the etiopathogenetic point of view, sensitization to the house-dust mite was the most frequently found (34% of the patients), followed by that to grass pollen (24.3%). Obviously, sensitization to the mite *D. pteronyssinus* is greater in patients with an associated disorder of rhinitis or bronchial asthma.

Regarding the food causal factor, as can be seen in Table 2, sensitization could be proven by means of the mentioned techniques and with a positive clinical history in 64.9% of the patients. Surprisingly, milk and egg are the most frequent foods in Spain triggering atopic dermatitis, and the clinical history shows that intolerance of these foods usually starts in the lactation period and persists even in a group of adults. On the other hand, because of the very great consumption of fish in Spain, sensitization to it represents an important figure, affecting 21.6% of the patients. Table 2 specifies the foods involved in the triggering of the

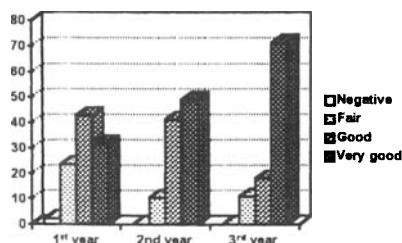


Fig. 1. Clinical evolution in patients diagnosed with atopic dermatitis with food allergy (percentage).

Table 6. Clinical evolution after 3 years of treatment in patients diagnosed with atopic dermatitis with food allergy (%)

	6 Months	1 Year	18 Months	2 Years	30 Months	3 Years
0 (Negative)	8.2	2.1	0	0	0	0
1 (Fair)	38.8	23.4	13.6	10.3	8.8	10.7
2 (Good)	42.9	42.6	56.8	41	29.4	17.9
3 (Very good)	10.2	31.9	29.5	48.7	61.8	71.4

skin manifestations in our patients and the percentages found.

What we have previously shown is complemented by the treatment followed by the patients, which is summarized in Table 3. There we can see that the patients who followed an exclusion diet of the causal food importantly reduced treatment with corticosteroids and antihistaminics. Regarding the clinical evolution (Table 4), we can note that removal of the responsible food and the suitable medication shows, already in year 1 of treatment, a favorable evolution, which gradually increases over the years, especially in year 3, where the need for treatment with topical corticosteroids was reduced to 13.2% of the patients. The percentage increase in group 3 is progressive and stable in time, and, as can be seen in Table 6, it is much more important in the group of patients with atopic dermatitis and food allergy. The clinical evolution of these patients is noticeably more favorable, with 71.4% feeling asymptomatic after 3 years. The group of patients with no evident cause of food allergy (Table 5) also had a satisfactory evolution, since only 20% presented important skin manifestations; the main difference is that the improvement of these patients did not reach complete remission of the symptomatology, even though they were following the suitable medical treatment. Therefore, we confirm that although after 18 months the evolution of both groups was similar, it was after 3 years that the difference reached a high degree of significance, since the allergologic study performed allowed us to detect the existence of a food allergen directly involved in the etiopathogenesis of the disease.

References

- González de la Reguera I, Iñigo JF, Oehling A. The importance of food sensitization in atopic dermatitis. *Dermatologica* 1971;143:288-91.
- Oehling A, Jerez J. Etiopatogenia de la dermatitis atópica. *Allergol Immunopathol (Madr)* 1975;3:23-8.
- Oehling A, Jerez J. Aktuelle Betrachtungen zur Ätiologie und Pathogenese der Dermatitis atopica. *Derm Mschr* 1975;161:104-7.
- Madamba A, Subirá María L, Oehling A. Etiopathogenesis

- of atopic dermatitis in children. *Allergol Immunopathol (Madr)* 1980;8:579-86.
5. Sampson HA. Role of immediate food hypersensitivity in the pathogenesis of atopic dermatitis. *J Allergy Clin Immunol* 1983;71:473-80.
 6. Rajka G. Atopic dermatitis. London: WB Saunders, 1975.
 7. Atherton DJ. The role of foods in atopic eczema. *Clin Exp Dermatol* 1983;8:227-32.
 8. Oehling A, Subirá ML. Comparative study of antigen extracts for diagnosis by way of the different extraction methods. Their analytic and biologic evaluation. *Allergy Asthma* 1965;11:301-6.
 9. Trento H, Oehling A, Ona J. Effects of immunotherapy on histamine release: a study in allergy to *Dermatophagoides pteronyssinus* and house dust. *Allergol Immunopathol (Madr)* 1982;10:295-300.
 10. Oehling A, Ona J, Wierna G, Sanz ML, Castillo J. The inhibition effect of ketotifen on *in vitro* histamine release in allergic patients. *Allergol Immunopathol (Madr)* 1985;13:475-85.
 11. Oehling A, Fernández M, Córdoba H, Sanz ML. Skin manifestations and immunological parameters in childhood food allergy. *J Investig Allergol Clin Immunol* 1997;7: 155-9.
 12. Oehling A. Evolución del diagnóstico alergológico a alimentos. *Rev Esp Alergol Immunol Clin* 1996;11 Suppl 2:40-2.
 13. García BE, Sanz ML, Fernández M, Diéguez I, Oehling A. Value of IgG4 antibodies against food in atopic dermatitis. *Allergol Immunopathol (Madr)* 1990;18:197-201.
 14. Sanz ML, Prieto I, Oehling A. The histamine release test as an important complement to the diagnosis of allergic diseases. *Allergy Clin Immunol News* 1995;7:56-61.