

FOOD ALLERGY IN ATOPIC DERMATITIS: EXPERIMENTAL OBSERVATIONS

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Abstract. Results of an investigation of 134 subjects with atopic dermatitis and 29 controls are described. The investigation involved: 1) an allergological enquiry into each patient's medical history, with particular reference to consumption of eggs, milk and fish; 2) a total IgE assay; 3) RAST with egg, milk, cod; 4) a challenge test. Recording of medical histories revealed the existence of clinical sensitivity to egg, milk and cod in respectively 21, 17 and 7 of the 134 subjects with atopic dermatitis, but in none of the controls. In the atopic subjects, RAST demonstrated egg, milk and cod antibodies in 37, 28 and 14 cases respectively, while of the controls only 2 had antibodies—and then in minimal amounts. The maximum incidence of egg and milk antibodies was demonstrated in the initial 3 years of life. Clinical sensitization to cod manifests itself in the form of attacks (urticaria, angi-oedema, vomiting) showing significant correlation between clinical history, results of RAST and the response to challenge, while in the case of sensitivity to eggs and, even less evidently, to milk, the symptoms are more often referred to as "exacerbation of the dermatosis" and the results of RAST, of challenging and the clinical history tend to be contradictory.

Key words: Dermatitis, atopic; Food sensitivity, RAST.

According to old literature data (1), any connection between sensitization and exposure to well defined antigens on the one hand and the clinical course of atopic dermatitis on the other is difficult to establish.

The discovery of immunoglobulin E and the demonstration of its role as a carrier of serum reaginic activity (3, 4) opened up a new era in the study of allergic phenomena. In fact, the advent of the radioallergosorbent test (8) made possible the identification and quantitative determination of circulating antibodies of the reagin type.

The aim of the work reported here was to re-examine, using the recently introduced radioimmunologic techniques, the role of the more common food allergens (egg-white, milk, fish) in the pathogenesis of atopic dermatitis.

MATERIAL AND METHODS

134 subjects with atopic dermatitis were investigated. Of these, 118 (82 males) were under 12, and 16 (2 males) were 13 to 42 years of age. In addition the study included 29 subjects aged 1 to 20 years with non-atopic disorders characterized by high plasma levels of IgE (papular urticaria, Dühring disease, parasitoses, Schoenlein-Henoch purpura).

The investigation included:

(a) careful recording of family and personal history of allergies;

(b) radioimmunological assay of IgE using kit Phadebas IgE-test (Pharmacia, Uppsala);

(c) radioimmunological assay of specific IgE against egg albumin, milk and fish (cod) using the kit Phadebas-RAST (Pharmacia, Uppsala). The results of this test were expressed in conventional terms as class 0 (negative) for sera whose radioactivity was less than that of reference serum D, class I (borderline positive) whose radioactivity fell between that of the reference sera D and C; class II (definitely positive) with values between sera C and B; class III (strongly positive) with values between sera B and A; class IV (very strongly positive) with values above that for serum A;

(d) antigen challenge, carried out only in hospitalized patients and in the absence of any history of severe anaphylactoid reactions.

RESULTS

History

Of 134 subjects with atopic dermatitis, 21 reported clinical sensitization to eggs, 17 to milk and 7 to

Table 1. *Clinical pictures of food sensitivity*

	Egg	Milk	Cod
Pruritus and exacerbation of the dermatosis	15	8	0
Abdominal cramps, vomiting, diarrhoea	4	6	1
Acute urticaria	0	3	6
Skin rash	2	0	0

Table II. Results of RAST

	RAST class				
	0	I	II	III	IV
Egg	97	19	14	1	3
Milk	106	18	6	3	1
Cod	120	6	4	3	1

cod; none of the 29 controls reported a clinical history of food allergy. The types of clinical pictures are listed in Table I.

Total IgE

High levels were demonstrated in 89 of 134 subjects examined and most evidently in those with severe or complicated forms of atopic dermatitis. The mean level for 78 RAST-negative subjects was 339 u/ml as against 3038 μ /ml for 56 RAST-positive subjects and 2735 μ /ml for 29 controls.

Radioallergosorbent test

The results of RAST for 134 subjects are summarized in Table II.

Of the allergens examined, egg-white proved the most active as regards circulating antibody responses, with specific antibodies demonstrated in 37 of 134 subjects (definitely positive 18, borderline positive 19). The age distribution for egg-white antibodies is indicated in Table III.

As regards milk, the antibodies were demonstrated in 28 cases; in 10 definitely and in 18 at borderline levels. Of the allergens in question, milk was the one to produce humoral immune reactions at the earliest stage. Definite positive response was obtained in a baby aged 5 months. The age distribution for milk antibodies is indicated in Table IV.

Cod antibodies were demonstrated in 8 cases in

Table IV. Age distribution for milk antibodies

RAST class	Years												
	1	2	3	4	5	6	7	8	9	10	11	12	>12
IV					1								
III	1										1		1
II	1	1	2							1			1
I	1	6	4	1	1			2		2			1
0	5	25	23	11	8	4	4	3	4	3	2	1	13

definite amounts and in 6 cases in borderline amounts. The age distribution for cod antibodies is indicated in Table V.

Challenge test

The challenge test was positive in 10 of 11 cases of abdominal reactions (negative in 1 case of milk sensitivity) and in all 9 cases of acute urticaria; it was even positive in 3 cases of exacerbation of the dermatosis (2 cases of egg-sensitivity with IgE antibodies classes III and IV, 1 case of milk-sensitivity with IgE antibodies class IV).

DISCUSSION

On overall examination the results of the radioallergosorbent test called for comment. First of all, except for two doubtful positive (class I) and in spite of the rather elevated mean IgE level (2735 u/ml), no egg-white, milk or cod antibodies were demonstrated in the 29 controls. This contrasts sharply with the situation in the atopic subjects, among whom antibodies to one or more allergens were demonstrated in many cases (56 of 134).

Thus we are dealing here with the old problem of establishing the significance of these antibodies in the pathogenesis of atopic dermatitis. High total

Table III. Age distribution for egg-white antibodies

RAST class	Years												
	1	2	3	4	5	6	7	8	9	10	11	12	>12
IV	1	1	1										
III		1											
II	4	5	1		1		1			1			1
I		9	2	1		1		1	2				3
0	2	20	21	10	7	4	7	4	3	4	2	1	12

Table V. Age distribution for cod antibodies

RAST class	Years												
	1	2	3	4	5	6	7	8	9	10	11	12	>12
IV					1								
III			1						1				
II		2	1	1									
I		2	1	1			1						1
0	5	33	26	14	5	1	6	5	2	5	2		16

Table VI. *Abdominal cramps, vomiting, diarrhoea and results of RAST*

	RAST class				
	0	I	II	III	IV
Egg (4 cases)		1	2	1	
Milk (6 cases)		5		1	
Cod (1 case)			1		

IgE levels and the demonstration of specific serum reagins suggest that they play a prominent role in the causation of this disease but this role still remains to be demonstrated and, in fact, literature data (1, 7, 5) deny that the sensitizing allergens are an important factor in atopic dermatitis. Recently Schur (6) while approaching the problem in the light of new techniques for demonstration of free reagins in the serum, reported 5 cases of clinical sensitization to egg-white, maintaining that the antigen-antibody reaction may induce exacerbation of atopic dermatitis. More recently oral provocation test with milk was performed in 81 children with atopic dermatitis (2): in 15 of the 81 children an exacerbation of the dermatitis was seen.

Our findings thus provide grounds for certain conclusions. In the presence of a clinical history of abdominal reactions (abdominal cramps, vomiting, diarrhoea) or urticaria, it is possible to demonstrate in the atopic subjects the presence of specific antibodies, though in varying amounts, as is indicated in Tables VI and VII. The converse, however, is not true, inasmuch as we demonstrated the presence of egg, milk and cod antibodies in very large amounts in absence of abdominal or urticarial reactions or, in fact without any symptoms or signs whatsoever, as indicated in Table VIII.

On the other hand, when the history is one of exacerbation of the dermatosis, the immunological situation varies from the presence of large amounts

Table VIII. *No symptoms (challenge test: negative) and results of RAST*

	RAST class				
	0	I	II	III	IV
Egg (133 cases)	89	16	6		2
Milk (117 cases)	102	13	2		
Cod (127 cases)	120	5	1	1	

Table IX. *Pruritus and exacerbation of the dermatosis and results of RAST*

	RAST class				
	0	I	II	III	IV
Egg (15 cases)	7	2	5		1 ^a
Milk (8 cases)	4		2	1 ^a	1 ^a
Cod (0 cases)					

^a Challenge test: positive.

of antibodies (class IV) to their complete absence (class 0), as indicated in Table IX.

These tabulated results suggest that a true, objectively demonstrable exacerbation of pruritus and manifestations of eczema may be produced (after 24–48 h) by large amounts of antibodies. However, in the other 2 cases with specific egg-white antibodies class IV, the clinical history was negative and so was the result of challenging. These data suggest that exposure to egg allergens in subjects with large amounts of specific antibodies is not necessarily associated with exacerbation of the clinical picture of eczema.

These findings do not support the hypothesis that sensitization to egg, milk or cod is an important etiopathogenetic factor in the appearance and clinical evolution of atopic dermatitis.

To conclude, therefore, atopic dermatitis does not seem attributable to specific sensitization by definite allergens but seems to be characterized by excessive production of reagins, not always responsible for the clinical manifestations and the cause of exacerbation of the dermatosis.

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Table VII. *Acute urticaria and results of RAST*

	RAST class				
	0	I	II	III	IV
Egg (0 cases)					
Milk (3 cases)			2	1	
Cod (6 cases)		1	2	2	1

REFERENCES

1. Champion, R. H. & Parish, W. E.: Atopic dermatitis. In Textbook of Dermatology. (ed.) A. Rook, D. S. Wilkinson, F. J. G. Ebling), 229 pp. Blackwell Scientific Publications, Oxford and Edinburgh, 1968.
2. Hammar, H.: Provocation with cow's milk and cereals in atopic dermatitis. *Acta Dermatovener (Stockholm)* 57: 159, 1977.
3. Ishizaka, K., Ishizaka, T. & Hornbrook, M. M.: Identification of gamma-E-antibodies as a carrier of reaginic activity. *J Immunol* 99: 1187, 1967.
4. Johansson, S. G. O.: Raised levels of a new immunoglobulin class (IgND) in asthma. *Lancet* ii: 951, 1967.
5. Rajka, G.: Atopic Dermatitis, 65 pp. W. B. Saunders, Co., London, Philadelphia, Toronto, 1975.
6. Schur, S., Hyde, J. S. & Wypich, J. I.: Egg-white sensitivity and atopic eczema. Abstracts of American Academy of Allergy. *J Allergy Clin Immunol* 53: 88, 1974.
7. Solomon, L. M. & Bearman, H.: Atopic dermatitis. *Am J Med Sci* 252: 478, 1966.
8. Wide, L., Bennich, H. & Johansson, S. G. O.: Diagnosis of allergy by an in vitro test for allergen antibodies. *Lancet* ii: 1105, 1967.

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