Acta Dermatovener (Stockholm) Suppl. 92: 99–102, 1980

# DIETARY ANTIGEN AVOIDANCE IN THE TREATMENT OF ATOPIC DERMATITIS

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*Abstract.* There is now good evidence that food allergy is an important aetiological factor in atopic dermatitis and that dietary antigen avoidance is a helpful form of therapy, particularly in younger children. Allergy history, prick tests and the RAST are of limited value in identifying the allergies present in individual children. A systematic practical approach to allergy diagnosis is currently under evaluation.

*Key words:* Dermatitis; Atopic; Food sensitivity; RAST

The role of food allergy in the aetiology of atopic dermatitis has received little attention from dermatologists, paediatricians and immunologists alike in recent years. Relatively few children give a clear history of exacerbation of their dermatitis by foods. Although prick tests to food antigens are frequently positive, avoidance of the test food frequently produces no noticeable improvement. For these reasons, antigen exclusion diets have for some time been unfashionable in the treatment of atopic dermatitis. The conviction that benefit results from the avoidance of certain foods, especially cows' milk and eggs, is nevertheless a common phenomenon among the parents of children with atopic dermatitis. Dietary treatment has been advocated by allergists, particularly in Scandinavia and in the USA, though little objective evidence of its therapeutic value has appeared in the literature. The finding, that exclusive breast feeding can reduce the incidence of atopic dermatitis in predisposed infants (2), certainly adds support to the concept that this disease might be a consequence of sensitization to food antigens occurring during early life. However, the mechanism by which such an effect is achieved has not been established, and avoidance of cows' milk protein per se may not be the most important factor.

There was a clear need for a properly controlled study of the effect of dietary antigen avoidance in atopic dermatitis. In designing such a study we decided to concentrate attention on children under 9 years, though we excluded those below 2 years for ethical reasons. We selected, empirically, a diet excluding eggs and cows' milk primarily, but also chicken and beef because these share some common proteins. A major problem was to create an appropriate control regime against which to test the antigen avoidance diet. Rigid exclusion of certain foods in a diet administered in the child's home requires the full co-operation of the parents and cannot be achieved without their full understanding. The maintenance of 'blind' conditions was overcome by the use of a 'sham' diet. Eggs, cows' milk, chicken and beef were avoided in *both* the 'trial' diet and the control diet. A milk 'substitute' was given during both periods, consisting of a dried soya preparation during the 'trial' diet, and a mixture of dried cows' milk and egg during the control diet. Although these milk substitutes tasted different, both had a flavour unfamiliar to the patients and their parents; they were not informed of the nature of the milk substitutes. We invited 36 children to take part in the 12 week study; all had typical atopic dermatitis and at least one positive prick test to a standard battery. Each diet was given for a 4-week period with an intervening 4-week period when the children resumed their usual diet. The order of allocation of the diets was randomised and unknown to the dermatologists making the clinical assessments. The results of this trial have been published in detail (1). Significantly greater clinical improvement was observed during the trial diet period than during the control period. 12 out of the 20 children completing the study experienced really worthwhile benefit from antigen avoidance; we have follow-up data for 11 of these. Seven of these 11 still find dietary antigen avoidance helpful 2 years later. All have tried reintroducing the excluded foods. Reintroduction of eggs led to exacerbation of eczema in all of these 7 children who continue to be on diets, and cows' milk reintroduction caused exacerbations in 6 of these 7. The majority can

| | Prick tests to milk and egg antigens | |
|---|---|---|
| | + | - |
| Response to antigen avoidance | 6 | 6 |
| No response to antigen avoidance | 5 | 2 |

*Fig. 1.* Numbers of patients having positive prick tests (weal >2 mm) to at least one of 5 egg and cows' milk preparations before dietary egg and cows' milk avoidance, according to subsequent clinical response.

now eat beef and chicken with impunity. Of the 4 who have discontinued antigen avoidance, one is now free of dermatitis altogether and the other 3 can now tolerate all the previously excluded foods.

It is often suggested that these diets are too difficult for patients and their parents. Of the 36 children entering the study 9 were excluded from analysis for non-adherence to diet, but in only 2 of these did this occur during the trial diet; if there is clinical response to dietary treatment the difficulties are cheerfully borne by the child and parents.

A further aim of this study was to assess whether a careful history, prick tests and the RAST could identify those children most likely to benefit from dietary treatment. At entry to the trial we sought a history of symptomatic food allergy. Only 4 of the 20 completing patients gave a history of cutaneous reactions to foods and in only 1, possibly 2, was this an eczematous reaction. There was no association between positive prick tests to 5 egg and cows' milk preparations (whole egg, egg yolk, egg white, β-lactoglobulin, α-lactalbumin) and response to dietary avoidance (Fig. 1). We also did the RAST, using 5 egg and cows' milk antigens: ovalbumin,

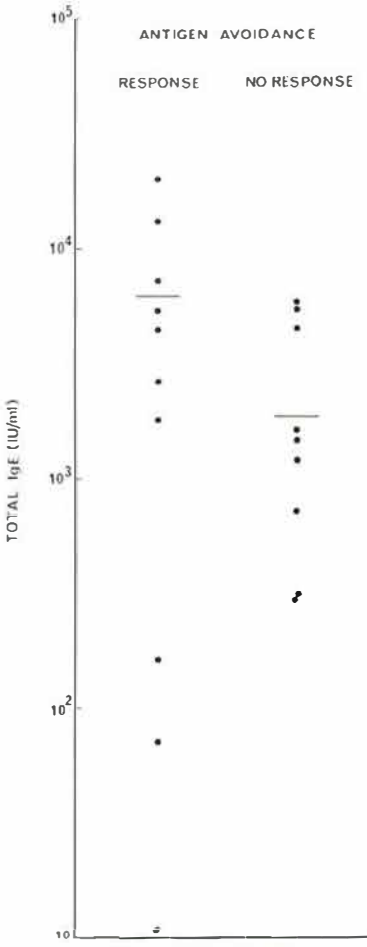


*Fig. 3.* Serum total IgE levels before antigen avoidance according to subsequent clinical response.

bovine serum albumin, β-lactoglobulin, bovine gamma-globulin and α-lactalbumin. All except one patient had at least one positive test. There were more positives in those patients who showed a good clinical response to antigen avoidance (Fig. 2); as anticipated, the mean serum IgE was also some-

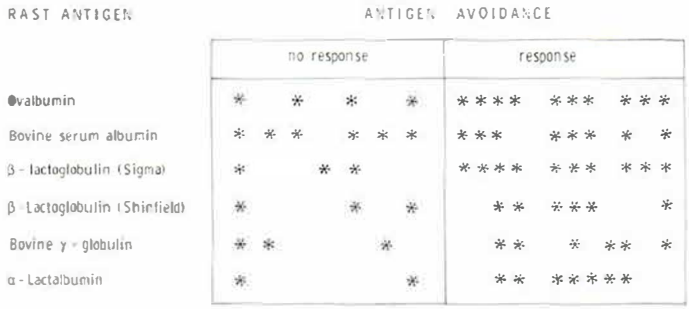


*Fig. 2.* Positive RAST (*) to egg and cows' milk antigens before dietary egg and cows' milk avoidance, according to subsequent clinical response. Vertical columns show results for individual patients. The assay uses microcrystalline cellulose particles; binding exceeding 1.6× cord serum value is taken to indicate positivity.

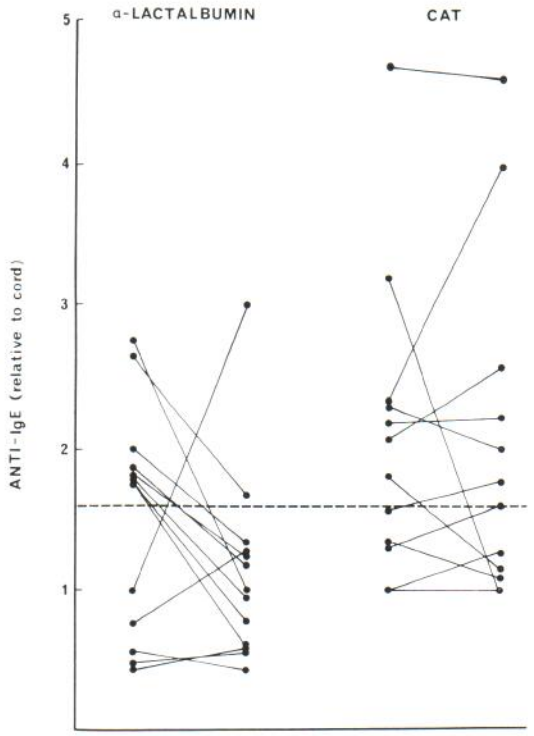


*Fig. 4.* Serum levels of specific IgE to α-lactalbumin and cat dander in a RAST assay using microcrystalline cellulose particles. The broken horizontal line indicates our laboratory threshold for positive binding. Values are shown both before a and after 4 weeks' dietary egg and cows' milk avoidance in individual patients.

what higher in this group (5 280 IU/ml compared to 1 872 IU/ml, Fig. 3); neither of these differences reached statistical significance.

The specific IgE antibody assays were performed on sera collected at the start and finish of the first dietary period, whether 'trial' or control; in 13 patients this was the 'trial' diet period. In Fig. 4 the changes occurring in the serum levels of specific IgE to α-lactalbumin during this 4-week period are compared with those to cat dander. Sharp decreases in specific IgE to α-lactalbumin occurred in 8 of the 13 patients, and in 7 of these the test would have been reported as having changed from positive to negative. These changes approached statistical significance in the paired 'T' test (log transformed data, $0.05 < p < 0.1$). The changes in serum levels of specific IgE to cat dander show no discernible trend. In a few patients large and unexplained changes in specific IgE levels to both antigens were seen. These data suggest that avoidance of an allergen can induce appreciable changes in serum levels of specific IgE antibody in a surprisingly short period of time.

Thus, neither history, prick test nor the RAST would have enabled us to identify those children most likely to benefit from dietary avoidance of egg and cows' milk antigens. We considered that the evidence was strong for benefit from such a diet. The problems remained the selection of children for such treatment, and the identification of the relevant dietary allergens upon which to base antigen avoidance diets in the individual case. Clearly we had only considered a few foods in this initial study; presumably other food allergies were present, particularly in those children who did not show dramatic responses to avoidance of cows' milk, egg, beef and chicken alone. We decided that the absence of more sophisticated tests for allergy diagnosis would force us to elucidate the individual patient's allergies on a basis of trail and error. This process would necessarily be laborious and timeconsuming for patient, parents, doctor and dietitian.

We have gained the impression that younger children are more likely to experience worthwhile benefit from dietary antigen avoidance, though the reasons for this are unclear. It is suggested that allergy to airborne allergens becomes increasingly important in the eczematous child with advancing age. Furthermore, the administration of demanding diets is accompanied by fewer problems in the pre-school child. We have now concentrated our attention on this group for a further study. Although the progress of this study is still at an early stage I would like to describe briefly what happens to these patients in our hospital. The opportunity to investigate the child's food allergies in more detail is offered to parents of pre-school children if the response to general measures, ordinary topical treatment and a standard egg and cows' milk avoidance diet is judged inadequate. The patient then progresses through 3 distinct phases. Initially he is

Table I. '*Oligo-antigenic*' *diets*

| 1 | 2 |
|---|---|
| Lamb | Turkey |
| Rice, rice flour etc. | Potato, potato flour |
| Carrots, swede | Cabbage, Brussels sprouts |
| Goats' milk | Soya 'milk' |
| Apricots | Peaches |

put on what we have optimistically called an 'oligo-antigenic' diet. There are 2 such diets, each entirely different (Table I). Diet 1 is given first, for a period of 4 weeks. If marked improvement occurs, the patient will be able to progress to the second phase in which foods are re-introduced on a scheduled basis. If marked improvement does not occur, the patient is given diet 2 for a 4 week period, to rule out the possibility of allergy to any constituent of diet 1. If a child does not benefit from either diet, food allergy is unlikely to be a major aetiological factor in his particular case. During the reintroduction phase one new food is tried each week. The food is given on 4 successive days, a very small quantity on the first day, then a larger quantity on the next 3 days. If no adverse reaction is noted during these 4 days or during the 3 subsequent days, this food can be added to the basic diet and eaten freely. If any reaction is noted, particularly a cutaneous reaction, the parents note the details in a special diary and the food is not given again. There are of course special problems with certain foods containing several constituents, such as bread, which may include wheat, soya, yeast and often also milk and pork fat. With such foods we specify particular recipes or commercial brands whose contents are known, and reintroduction is not attempted until each constituent has already itself been successfully reintroduced. At the end of several months, each patient should have identified a list of foods to which allergy is suspected. We are keen to attempt confirmation of these allergies by double-blind challenges; this is the purpose of the third phase. H. J. Heinz & Co. have very kindly made up suitable preparations for these challenges. There are 2 'carriers', one savoury, based on carrots and lentils, and one sweet, based on apricots and rice. The carriers themselves are used for the control challenges and a variety of foods such as wheat, egg, milk, chicken and pork are added to these in such a way that identifiable alteration is minimised. For each 'true' challenge a control challenge is given. One challenge is given each week, in hospital; the order is randomly allocated by the dietitian. Each challenge is given over 7 successive days, a small quantity only being given on the first day. Insufficient data are available at this stage to justify discussion here, but we believe that successful allergy diagnosis can be achieved using these methods. One hopes, though, that better understanding of the immunopathogenesis of atopic dermatitis will lead to a more fluent approach to the identification and treatment of patients' allergies.

## REFERENCES

1. Atherton, D. J., Sewell, M., Soothill, J. F., Wells, R. S. & Chilvers, C. E. D.: A double-blind controlled cross-over trial of an antigen avoidance diet in atopic eczema. Lancet *i:* 401, 1978.
2. Matthew, D. J., Taylor, B., Norman, A. P., Turner, M. W. & Soothill, J. F.: Prevention of eczema. Lancet *i:* 321, 1977.

## DISCUSSION

*Rook* (Cambridge). Q: Children when they first start to feed themselves are not very good at getting food into their mouths—they get it all over their hands and all over their faces. What is your view as to the importance of contact urticaria to foods as a mechanism by which foods exacerbate eczema in small children?

A: I believe that this does happen. Similarly, when food and other antigens exacerbate eczema following systemic absorption, the initial lesion may always be urticarial. Eczematisation might then follow if scratching occurs.

### Concluding remark

*By Kjell Aas*

I would like to finish off this session with what I believe to be very important. We must be aware that technical details play an important role in establishing allergy. The RAST classes 1 and 2 are often non-specific. One can have non-specific reactions also to skin tests. When using a commercial extract in a given concentration one can have 30–50 % reactions which are called positive, but if one dilutes that extract twenty times, it will then give a 95 % correlation. Furthermore, we must not forget the nature and the natural causes of this disease. It is fluctuating and multifactorial, so we need very strictly controlled trials without compromise.