

Diet and atopic eczema in children

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The relationship between food hypersensitivity and atopic eczema continues to be discussed. Infants with atopic eczema have a high frequency of positive immediate skin-reactions to foodstuffs (1) and of high levels of food specific IgE as measured by RAST (2). Moreover they are often affected by other cutaneous and non-cutaneous symptoms dependent on food hypersensitivity (3). Finally there are many reported open studies (4-7) and at least 2 placebo-controlled studies (8, 9) suggesting a relevant and positive role for "elimination diets" in the treatment of many infants and children affected by atopic eczema. Nevertheless there are no absolute criteria to predict the clinical effects of an elimination diet for any particular patients, and other factors (such as climate, skin infections, emotional stress) are known to influence the clinical expression of the disease. So there is as yet a large area of debate concerning the true role of food hypersensitivity in causing atopic eczema and it is still unclear whether all or only a portion of patients can improve with elimination diet.

Is atopic eczema related to diet? The total parenteral nutrition evidence

To test the hypothesis that food hypersensitivity plays a major role in atopic eczema, we decided to feed 9 selected patients with total parenteral nutrition (TPN). Clinical data regarding the 9 cases are shown in Table 1. All the patients were affected by long lasting diffuse eczema and had previously undergone "food exclusion" diet with no apparent benefit. TPN consisted of Freamine, a dextrose and electro-

lyte solution in standard concentrations. Each patient was given 60-75 Kcal/kg/die and 1g/kg of amino acids. TPN was maintained for 15-34 days in 8 patients, while one girl refused it after 9 days. In another girl, TPN was stopped after 14 days because of fever and a pain in the arm where the catheter had been inserted. After an average of 11 days, while still receiving parenteral nutrition, the patients were challenged with one food every 3 days.

The eczema score improved significantly in all but one of the patients after 8-17 days of TPN (Fig. 1) as did peripheral eosinophil count (Fig. 2).

Complete improvement during TPN with tolerance of many foods after this period

Four patients were able to tolerate all foods with only the exclusion of eggs, milk and dairy products. Moreover these children remained symptom-free after eating previously non-tolerated foods to which they had also positive skin tests (for instance gluten, soy, tomato or pork).

Complete improvement during TPN but worsening of eczema with food challenge

Three children improved; 2 of them presented multiple reactions (milk, any kind of meat, rice and/or foods rich in histamine).

Only partial, unsatisfactory improvement of clinical score during TPN

In this single patient, the eosinophil count normalized as in cases with the optimal improve-

Table 1

Features of 9 patients with atopic eczema who underwent TPN

Total cases	9
M/F	4/5
Age (years)	2.3-15.1
IgE > 1/3 SD	8
Eosinophil count	620-2980/mm ³
No improvement during egg- and milk-protein-free diet	9
No improvement during strict elimination diet (six-food diet)	9
Deterioration during six-food diet	2
Steroid dependence (local and/or systemic)	9
Some features of cortisonism	3

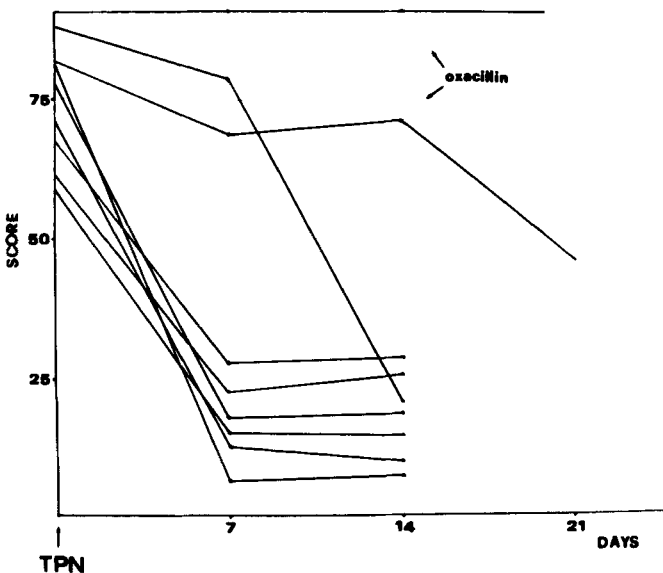
ment during TPN. We cannot exclude that a superinfection prevented the eczema from completely healing. In fact, the clinical score improved after antibiotic therapy. This child can partially tolerate a diet without egg and milk and presents frequently worsening of his eczema which is readily responsive to antibiotic (antistaphylococcal) treatment.

No improvement

In this single case, the eosinophil count remained very high. Antibiotic therapy did not

show any benefit and no worsening at food challenges was observed. The IgE in this case was elevated (1788 μ /ml).

These data support the hypothesis that dietary antigens contribute to childhood and juvenile "intractable" eczema, even when the patient does not improve during an elimination diet. In fact the benefit of total avoidance of foodstuff was evident in 8 of the 9 patients, and eosinophil count normalization was in favour of this benefit. We stress that some patients were able to tolerate previously non-tolerated foods after TPN. We can hypothesize that a period of total starvation and the consequent suppression of local anaphylaxis plays a favourable role in breaking the vicious cycle between the mucosal histamine production, abnormal absorption of macromolecules and food hypersensitivity. As one of our patients shows, we cannot affirm that an elimination diet is ineffective in the treatment of a child with atopic eczema without excluding bacterial superinfection (10, 11). TPN efficacy in the treatment of severe atopic eczema merely points to the primary role of food hypersensitivity in the aetiopathogenesis of atopic eczema and obviously cannot be suggested for routine therapy. In selected severe cases highly dependent on steroid therapy, TPN can be useful not only for temporary relief from



Eczema score (11) before and after TPN in 9 patients.

symptoms, but also in restoring tolerance to some foods. A TPN trial is useful in understanding whether or not an individual case might benefit from an elimination diet.

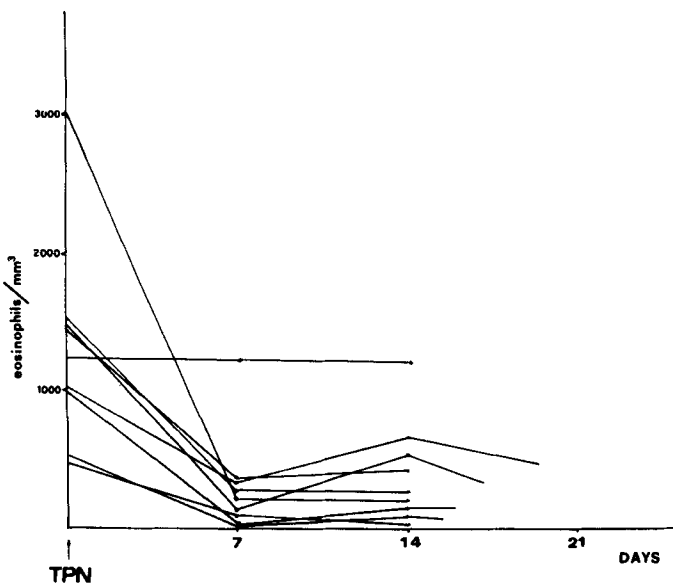
Some guidelines for prescribing a diet

The case of the breast-fed child with atopic eczema

There is some evidence that atopic eczema in breast-fed infants could be related to food antigens in the mother's diet (12). Egg and milk proteins are considered the most frequently implicated, but controlled trials have shown that the exclusion of these proteins from the mother's diet is effective only in a minority of cases (13).

Twenty-four exclusively breast-fed infants, attending our clinic for atopic dermatitis were selected because of their high score symptoms. An egg- and milk-protein-free diet was initially prescribed for the mothers. If any improvement in eczema score was noted after 15 days, gluten was also excluded from the mother's diet for a minimum 7-day period. When a satisfactory clinical response was observed (score improvement > 30%) the suspected food was reintroduced into the mother's diet

as a challenge. At the end of the study, on the basis of significant improvement of the dermatitis and pruritus during the mother's elimination diet and of a prompt relapse during challenge, atopic eczema was considered to be related to the mother's diet in 13 of 24 infants (8 cases to egg and milk, only 5 to egg, milk and gluten). The remaining 11 infants did not show any improvement during the study. Skin prick test (SPT) (Lofarma) and RAST to ovalbumin and/or cow's milk proteins were positive in 9 of the 24 infants, while IgE to gluten was demonstrated in only 3 cases. We did not observe any association between response to diet, and the presence or absence of positive immediate SPT or raised serum levels of IgE antibodies to milk, egg and gluten antigen. Of some interest, however, was the observation of the positive SPT with mother's milk in 4 infants. In these infants, the SPT with mother's milk was negative during the mother's exclusion diet. From our experience, we can confirm that the mother's diet can influence the clinical expression of an atopic dermatitis in an exclusively breast-fed infant. Each food antigen consumed by the mother can be "*a priori*" faulted: the egg and milk protein-free diet may be useful in some cases, but the



Eosinophil count before and after TPN in 9 patients affected by atopic eczema.

nonresponder infants may also benefit from a more restricted maternal diet. We suggest that gluten should be considered as a major antigen in these cases (especially if it is significant in the mother's diet), but theoretically any other food antigen would be suspect. We must be aware of the risk of a restricted maternal diet. Most breast-fed infants with atopic dermatitis can be treated without any restriction in the maternal diet. We should only address this approach in severe selected cases, while we have no reliable test to identify the children that will benefit from a maternal elimination diet. Gluten or other food antigens may be suspected if any improvement can be observed during an egg and milk protein-free mother's diet, but the benefit/cost ratio of such a restricted mother's diet must be carefully evaluated in each case. Anyway if no clinical improvement is observed in 2 weeks, the mother's diet should be stopped.

The age of symptom-onset as a guide to the diet

Many studies have demonstrated that egg and cow's milk protein are the most common food antigens implicated in the aetiology of diet dependent atopic dermatitis in children (5, 8, 14). In a previous study, we suggested that the ratio of milk to egg hypersensitivity decreases with the increasing age of patient at the onset of atopic eczema (5). Milk proteins are implicated in cases starting before 6 months and only rarely after this age, while egg proteins are related to symptoms in the majority of infants presenting atopic eczema after 6 months. Our more recent experience confirms these data. Moreover we have observed that gluten hypersensitivity is frequently implicated in aetiopathogenesis of late-onset atopic eczema. In 7 of 22 selected patients of atopic eczema with onset between 8 months and 4 years (10 more than 1 year old) and who improved with elimination diet, gluten sensitivity (having excluded coeliac disease and Duhring dermatitis) was demonstrated. Only 2 of the 7 had detectable levels of IgE (SPT and RAST) to gluten.

Two of these seven cases were sensitive to gluten only, whereas in the remaining 5, other food hypersensitivities were found (egg, tomato and milk). Other food antigens (including fish, tomato, soya, chicken, etc.) can occasionally be implicated in the late-onset diet-dependent atopic eczema (14). It is rare that only an elemental diet (15) or the TPN (as we have suggested) can be tolerated. In our experience, infants with severe atopic dermatitis while exclusively breast-fed and non-responding to the egg, milk- and gluten-free maternal diet, fall into this category.

The possible role of histamine-rich or histamine-releasing foods in food-dependent atopic eczema

The first step in a food allergic reaction is the absorption of food antigens through the intestinal mucosa. There is some evidence that in patients with atopic eczema, the antigen entry is increased (16, 17). Moreover, some animal experiments have demonstrated that mucosal anaphylaxis initiated by one antigen, results in the increased entry of other antigens given simultaneously (18, 19). This partially explains a possible mechanism for multiple food hypersensitivity. Other factors, such as an increased mucosal histamine level independent of local anaphylaxis (as in the case of food-dependent, exercise-induced anaphylaxis (16-18)) can increase the intestinal mucosa permeability of antigen entry with consequent abnormal reactions to food. So, particular foods may only worsen the eczema under very specific conditions. We suggest that some foods rich in histamine (fermented cheeses, dry sausage) or which can release histamine at the intestinal mucosa level (e.g. chocolate, tomato, strawberry) play a major role in increasing intestinal permeability and thus in worsening atopic eczema in many cases after the first year of life. We have observed more than one case in which gluten and tomatoes provoked atopic eczema only when eaten together, while no symptoms appeared if these foods were separately consumed. Other similar

cases in our experience implicate gluten and Parmisan (fermented cheese) or egg- and tomato-dependent atopic eczema. Moreover in 15 cases of our selected group of 22 children with late-onset food-dependent atopic eczema, we repeatedly observed worsening of symptoms after the ingestion of foods with a high histamine content, or foods able to trigger histamine release. We would like to stress that chronic, moderate, atopic eczema can improve with a diet free of histamine-releasing foods.

A word of caution

Although there is sufficient data to establish a definitive role for dietary treatment in atopic dermatitis we have to address this treatment for selected cases. In fact most patients with this disease can be treated in a symptomatic way and often spontaneously improve after the first year of life. In our out-patient clinic for allergic diseases we prescribed elimination diet in about to 30% of the 627 cases seen in the last 2 years. The candidates for elimination diet are probably fewer in a non-specialised out-patient clinic. Dietary therapy is just one of the many approaches that must be considered for the individual patient and should be considered when simpler treatments alone have failed to provide adequate improvement. In any case, whenever an elimination diet is given, the nutritional adequacy must be controlled (especially regarding the calcium content). The diet should be stopped if no benefit is apparent (and if superinfection has been excluded) within 4 weeks. Even when the diet is successful, an attempt should be made to withdraw dietary treatment after a period not exceeding one year, especially in infants with simple cow's milk hypersensitivity. Finally we must be aware that the child with atopic eczema on an elimination diet may be at risk of potentially lethal anaphylactic reactions at challenge, even if SPT or RAST tests are negative (23).

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