

Treatment of infantile atopic dermatitis with a strict elimination diet

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Summary

Of twenty-one infants with atopic dermatitis, twenty were treated with a strict elimination diet for a period of up to 6 weeks. Seven infants healed and twelve improved. The infants who healed were less than 6 months old and had had a short duration of dermatitis. For one infant the skin condition was unchanged. Another infant was breast-fed throughout the period with dermatitis. Blood eosinophilia and/or elevated serum IgE commonly found on admission decreased significantly ($P < 0.01$) during the diet period. On challenge with cows' milk, twelve infants were considered as intolerant. At the age of 2 years the dermatitis had cleared in all but four children. Of these four children, two were still cows' milk intolerant. Another two infants were also cows' milk intolerant, but without dermatitis.

Introduction

Atopic dermatitis is a common skin disease during infancy and often appears as the first clinical sign of atopy. Elevated serum IgE and blood eosinophilia are common laboratory findings (Berg & Johansson, 1969; Church, Kleban & Bellanti, 1976; de Graciansky, 1966). Early studies demonstrated that atopic dermatitis could be improved by elimination diets (Kesten, 1954; Rowe & Rowe, 1951). Possibly, because of the introduction of topical steroids, these reports of beneficial effect of elimination diets lost interest.

We have studied the effect of a strict elimination diet during a limited period in a group of infants suffering from atopic dermatitis with regard to clinical symptoms, blood eosinophils, serum IgE and IgA. Intolerance to cows' milk was also recorded.

We found that clinical symptoms and laboratory findings were influenced by the diet.

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Patients and methods

The study included a total of twenty-one infants referred for atopic dermatitis from October 1974 to April 1975. The diagnosis was based on the presence of erythema, papules and itch. The lesions were characterized by beginning on the face, with subsequent spreading to the trunk and extremities, but leaving the scalp free. Differentiation between atopic and seborrhoeic dermatitis may be difficult; in this study the distribution of lesions, itch and absence of fat scaling were used as indicators for atopic dermatitis.

The age at onset of dermatitis was 3 weeks to 8 months (median 2 months). At the time of onset two infants were exclusively breast-fed, five mixed-fed and fourteen exclusively cows' milk-fed (see Table 2).

Family history positive for atopic skin disease (eczema or recurrent urticaria) in parents or older siblings was obtained for nine out of the twenty infants. For two infants there was a family history only of asthma or rhinoconjunctivitis. One infant was adopted and therefore had no family history available.

On admission the infants were transferred to the strict elimination diet defined in Table 1, except for one infant who was breast-fed throughout the period with dermatitis. The clinical effect of the diet was evaluated after 2–3 weeks in five cases and after 4 weeks in sixteen cases. A four grade scale was used (healed, improved, unchanged or worse). After 4–6 weeks on the diet the patients were challenged with increasing amounts of cows' milk formula every 2 hr at home or in hospital. The reaction to challenge was evaluated by the parents at home or by staff in the ward. Positive reactions consisted of erythema and/or itch with discomfort within 24 hr.

Infants with positive challenge continued on cows' milk-free diet and were again challenged every 3 months until tolerance appeared. After the period with strict elimination diet and challenge with cows' milk, new foods were introduced at weekly intervals. Egg and fish were recommended to be avoided during the first year of life, even if the infant was free from symptoms.

Patients with negative challenge tests were switched back to an ordinary diet with the exception of fish and egg.

Blood samples were collected on admission and again after the strict elimination diet period, and then subsequently in some patients every 3–4 months. Blood eosinophils were counted in a Fuchs–Rosenthal chamber, serum IgE determined by Pharmacia Phadebas IgE test kits and serum IgA by rocket immunoelectrophoresis.

A baby ointment consisting of vaseline, paraffin and cetanol was used in all

Table 1. Elimination diets

Strict elimination diet to the age of 5 months	Strict elimination diet after the age of 5 months
Casein hydrolysate (Nutramigen®)	Casein hydrolysate (Nutramigen®)
or	or
Soy milk formula	Soy milk formula
and	and
Vitamins	Beef or veal
	Potato
	Corn
	Rice
	Buckwheat
	Vitamins

infants. Topical hydrocortisone was occasionally used on lichenified patches after the effect of the strict elimination diet was evaluated. This was the case in four infants directly after the strict elimination diet and later on in a further five infants. The breast-fed infant received topical hydrocortisone.

Wilcoxon's test for pair differences was used for the statistical analyses.

Results

Clinical course

The dermatitis of the breast-fed infant appeared at the age of 1 month and healed at 8 months. The nursing mother's diet was modified. After the initial period with strict elimination diet the dermatitis healed in seven infants and improved in twelve, and remained unchanged in one infant. At the age of 2 years the dermatitis had cleared in seventeen children.

Intolerance to cow's milk

As shown in Table 2, twelve out of nineteen patients challenged with cows' milk after 4-6 weeks on the strict elimination diet showed positive reactions. Seven patients were challenged in hospital and six of them were considered as positive. The other twelve were challenged at home. One infant was challenged later with a negative result. The breast-fed infant was given cows' milk for the first time at the age of 10 months without any reaction. Of the four children whose dermatitis remained at the age of 2 years, two were still cows' milk tolerant. Of the seventeen children whose dermatitis had cleared at the same age, two were cows' milk intolerant.

Laboratory findings

The course of the dermatitis in relation to diets, blood eosinophils, serum IgE and serum IgA is shown in Figs 1 and 2.

Elevated eosinophil counts, i.e. 400 cells/mm^3 , were commonly found when the patients were first investigated. All four infants with generalized dermatitis had more than $1000 \text{ eosinophils/mm}^3$. One of them was exclusively breast-fed. Only four infants had normal levels. The lowest value was 208 cells/mm^3 and in this patient the dermatitis was mild and localized to the face and neck. Thus there seemed to be a relation between severity of dermatitis and eosinophilia.

The IgE levels varied from very high to values within normal limits. All infants with IgE levels within 2 s.d., i.e. in our laboratory 1-55 u/ml, had elevated eosinophil counts. For one of the infants with generalized dermatitis (A.N.), serum IgE was not available on admission. Later, during the elimination diet, he had the highest levels of all the infants, 3200 u/ml. The other three infants with generalized dermatitis had, on admission, IgE levels of 47, 85 and 1450 u/ml. Apparently, high levels of serum IgE were related to generalized dermatitis.

The IgA levels were evenly distributed from 0.06 to 0.6 g/l, and there was no obvious relation to severity of clinical symptoms.

During the period of strict elimination diet the median values decreased for the eosinophils from 676 to 344 cells/mm^3 , for IgE from 74 to 33 u/ml and for IgA from 0.27 to 0.24 g/l (Fig. 1). The differences were statistically significant for eosinophils and IgE ($P < 0.01$).

In the only infant (M.J.) in whom the dermatitis did not improve during the period

Table 2. Type of feeding in relation to the course of atopic dermatitis in twenty-one infants

Patient	Age at onset	Diet at onset	Duration of dermatitis before ED	Substitute for CM	Challenge with CM	Duration of CM-free diet	Comments
E.T.	3 w.	BM and CM	1 w.	S	Neg.	1.5 m.	
M.J.	3 w.	BM and CM	2 m.	S and N	Pos.	5 m.	
J.A.	3 w.	CM	2 m.	S and N	Neg.	5 m.	No challenge until 5 months on ED
L.L.	1 m.	CM	7 m.	S	Pos.	7 m.	
A.V.	1 m.	BM and CM	3 m.	S	Neg.	1.5 m.	
P.J.	1.5 m.	BM and CM	2 w.	N	Neg.	2 w.	Sensitized to N
T.J.	1.5 m.	BM and CM	2 w.	S and N	Pos.	2 m.	
L.S.	1.5 m.	CM	3.5 m.	S	Neg.	1.5 m.	
A.R.	2 m.	CM	6 m.	S	Pos.	>24 m.	
O.H.	2 m.	CM	2 m.	S	Pos.	>23 m.	
J.M.	2 m.	BM and CM	12 m.	S	Pos.	10 m.	
C.H.	2.5 m.	CM	2 w.	S	Neg.	1 m.	
J.L.	3 m.	BM and CM	1.5 m.	S	Pos.	17 m.	
A.N.	4 m.	BM and CM	2 m.	S and N	Pos.	>24 m.	
Å.S.	4 m.	BM	6 m.	S	Pos.	>7 m.	Diarrhoea of CM
S.O.	4 m.	CM	2 w.	S	Neg.	1 m.	
A.S.	6 m.	CM	6 m.	S	Pos.	>18 m.	
D.H.	6 m.	CM	10 m.	S	Pos.	6 m.	
V.R.	7 m.	CM	1.5 m.	S	Pos.	17 m.	
V.E.	8 m.	CM	1 m.	S	Pos.	6 m.	
L.H.	1 m.	BM	—	—	—	—	Breast-fed during period with dermatitis

Abbreviations: BM = breast-milk; CM = cows' milk; N = Nutramigen®; S = soybean formula; w. = weeks; m. = months; ED = elimination diet.

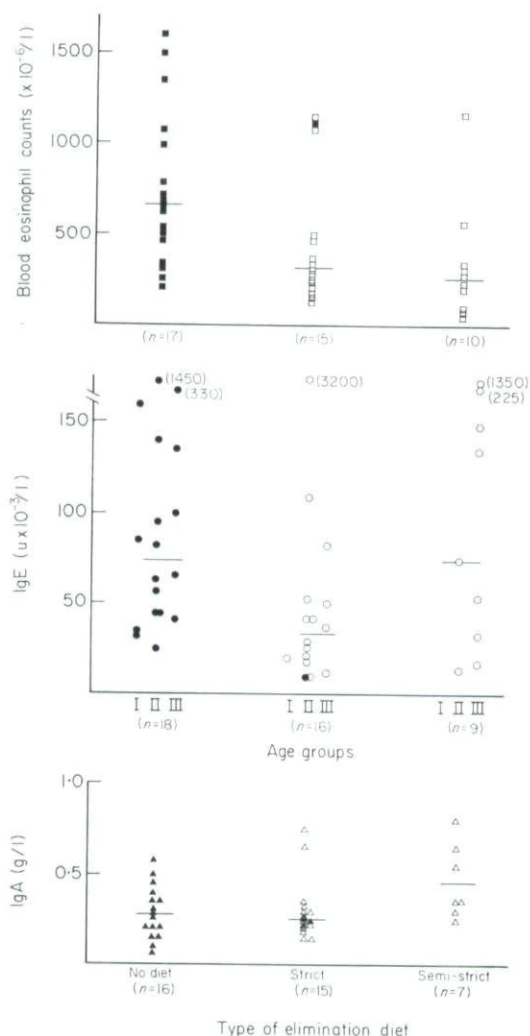


Fig. 1. Blood eosinophil counts (squares), serum IgE (circles) and IgA (triangles) in infants with atopic dermatitis in relation to types of diet: on admission, after period of strict elimination diet and after prolonged period of cows' milk-free diet. The horizontal bars indicate median values. The Roman numerals show different ages: I = 1.5–3 months; II = 3–9 months; III = 9–24 months. (■, ●, ▲) Active dermatitis; (□, ○, △) dermatitis improved or healed.

of strict elimination diet the eosinophils increased from 521 to 1135/mm³, and the IgE decreased from 63 to 10 u/ml.

In five out of seven infants in whom the dermatitis healed after the period of strict elimination diet, blood samples were collected 1–2 months after the return to an ordinary diet with cows' milk. As shown in Fig. 2, the skin remained normal except for one patient, as did the eosinophils, while IgE increased. Patient T.J. became sensitized to Nutramigen, with a relapse of dermatitis some days after the second blood sample was collected. His diet was changed to a soybean formula with an excellent result on the skin condition and an impressive decrease of serum IgE. On challenge with

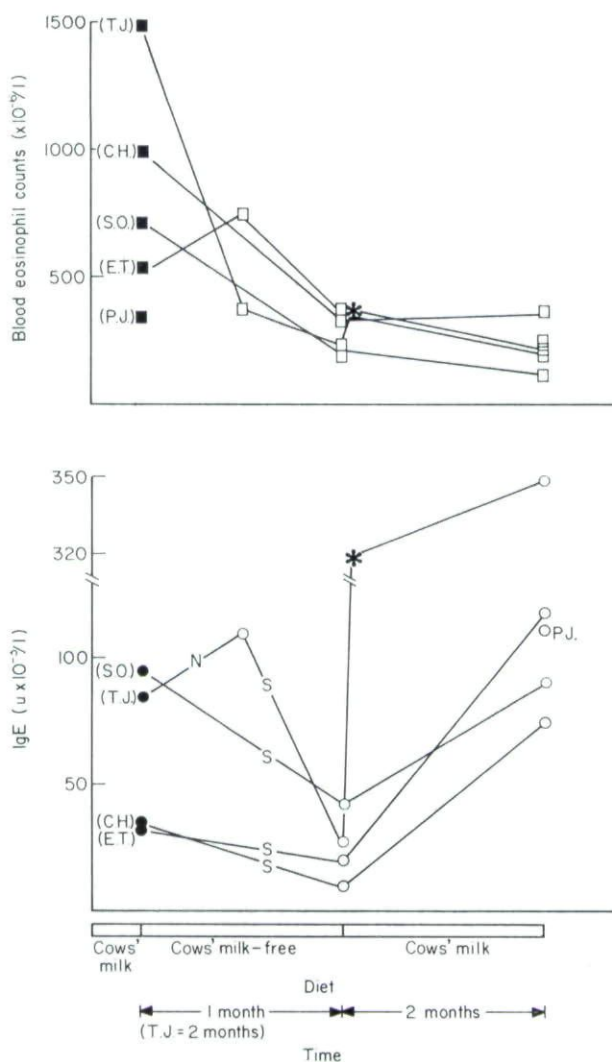


Fig. 2. Blood eosinophil counts (squares) and serum IgE (circles) in five infants with a duration of dermatitis of 2 weeks or less prior to elimination of cows' milk. (■, ●) Active dermatitis; (□, ○) no dermatitis; (*) itch and rash when challenged with either Nutramigen or cows' milk. N = Nutramigen; S = soy milk formula.

cows' milk and Nutramigen he showed positive reactions to both. He refused, however, to continue on the soybean formula and was discharged on cows' milk. The following day he had eruptions of dermatitis which were treated with hydrocortisone. 2 months later he was free from dermatitis but the elevated serum IgE persisted. Up to the age of 2 years he had no other signs of atopy.

In the infants in whom several blood samples were obtained after the period of strict elimination diet, the median for eosinophils continued to decrease to 206 cells/mm³, while IgE and IgA increased to 75 u/ml and 0.35 g/l, respectively (Fig. 1).

Intolerance reactions to foods other than cows' milk

The parents reported skin reactions suggestive of intolerance to fruits in eight, to wheat in three, to egg in four patients and to fish in one patient in a total of eleven patients up to the age of 2 years. The breast-fed infant reacted to fruits, honey and very strongly to egg.

Other possible signs of atopy

At the age of 19 months the boy with the highest IgE values (A.N.) had an attack of asthma which needed treatment in hospital. When admitted the IgE was 1350 u/ml and he had IgE antibodies to pollen, danders, moulds and to egg and fish, but not to milk, which he then had avoided for 13 months. The dermatitis persisted but was mild. Another boy (L.L.) had at the age of 23 months an attack of wheezing accompanied with an upper respiratory tract infection. His IgE was 78 u/ml (2 s.d. 5-75 u/ml at 1-2 years of age) and he had then tolerated cows' milk for 2 weeks without relapse of dermatitis. A girl (Å.S.) developed gastrointestinal symptoms when fed with cows' milk during the period with dermatitis. Her skin healed.

Discussion

The concept that cows' milk plays a role in the pathogenesis of infantile atopic dermatitis is controversial. Grulee & Sanford (1936) reported atopic dermatitis to be seven times more common in artificially fed than exclusively breast-fed infants. Matthew *et al.* (1977) found that infants of allergic parents fed on an allergen-avoidance regimen, i.e. breast milk and avoidance of dairy products, fish and egg up to the age of 6 months, had less eczema than infants in the control group fed on cows' milk. Edgren (1943), however, did not find a higher incidence of atopic dermatitis in cows' milk-fed infants.

The value of elimination diets in the treatment of atopic dermatitis has been questioned. Kesten (1954) reported a beneficial effect of elimination diet in two-thirds of children less than 3 years old, provided the diet was strictly adhered to. In adolescents and adults corroborative evidence of food sensitivity was obtained in 20%. Rowe & Rowe (1951) stated that food allergy should be suspected when the onset of dermatitis was in the first few months of life. On the other hand, Hill (1955) considered that elimination of certain foods sometimes helped babies with eczema, but that this practice should not be carried to an extreme, as was too often done. Norins (1971) reported that diet plays a small role in the care of children with atopic dermatitis.

The evaluation of the effect of an elimination diet and challenge may be subjective. What must be taken into consideration is that as many as twelve out of twenty were found to be intolerant and nineteen out of twenty had a beneficial effect from the diet. The infants who healed after the period with strict elimination diet were less than 6 months old and had had a short duration of dermatitis. This may indicate that the outcome could be more favourable the earlier the elimination diet is instituted. To accurately evaluate the effect of diet control studies where no dietary alterations are made, is needed. In practice this is very difficult, since parents in some way alter the diet when their baby develops dermatitis.

The laboratory findings may support the clinical impressions of beneficial effect of the diet. Both the eosinophils and IgE decreased during the period of strict elimination diet, with subsequent improvement in skin condition. According to Hellerström & Lidman (1956) the blood eosinophils and to Church *et al.* (1976) and Gurevitch,

Heiner & Reisner (1973) the serum IgE are correlated to the severity of the disease. Consequently the decrease would be a result of the improvement in skin condition. However, in four out of the seven infants who healed during the period of strict elimination diet the IgE increased after they returned to the ordinary diet with cows' milk without reappearance of dermatitis. The eosinophils remained normal. Apparently blood eosinophilia is correlated to the presence and severity of dermatitis. The serum IgE in its turn seems in certain individuals during infancy to be influenced by the type of diet. Furthermore, it has recently been shown that even in adults elimination of cows' milk and egg decreases the serum IgE (Crouch, 1977). In a continuing prospective study we have found that infants at the age of 1, 3 and 6 months, who are cows' milk-fed, have significantly higher lymphocyte activity when stimulated with PHA than breast-fed infants. The cows' milk-fed infants also had at 1 month significantly higher number of blood eosinophils (unpublished data). All these data support the view that foreign species proteins, such as cows' milk, especially during infancy, profoundly influence the immunological system. Consequently such an influence could have an important role in the pathogenesis, prevention and treatment of atopic disorders.

We suggest that in infants with atopic dermatitis an early instituted strict elimination of empirically found strongly antigenic foods such as cows' milk, wheat, fish and egg for a limited period is of great value in the treatment and may be in prevention of persisting eczema.

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