Few food diets in the treatment of atopic eczema

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SUMMARY Sixty six children with severe atopic eczema were treated with highly restricted ('few food') diets followed, if they improved, by serial reintroduction of excluded foods. Twenty four patients (36%) improved considerably during the few food phase of the diet. Fifteen of these (23% of the study group) maintained this improvement on dietary treatment, of whom three abandoned the diet after periods ranging from six to 10 months, despite continued benefit, because they found the dietary restrictions too arduous. Thus 12 out of 66 children (18%) with severe eczema experienced prolonged and useful benefit from this dietary manoeuvre. Double blind food challenges performed in 10 patients failed to establish that parental identification of provoking foods is reliable. A search for historical and in vitro predictors of diet responsiveness was unsuccessful in this series.

A number of studies, both uncontrolled¹⁻³ and controlled,^{4,5} have examined the therapeutic effect of 'simple' empirical diets excluding a few foods (cows' milk and egg in particular) in atopic eczema.

We are aware of seven published studies of highly restricted diets in the treatment of atopic eczema. Three of these deal with 'oligoantigenic' or 'few food' diets. Hathaway and Warner described problems of compliance in 40 children whose eczema improved on milk and egg exclusion ($n=7$), few food diets ($n=30$) or 'elemental' diets ($n=3$).⁶ However, it is not clear what proportion of all those treated with diets, these 40 diet responsive children represent. Graham *et al* treated 26 children with a moderately restricted diet for two weeks followed by a few food diet for a final week.⁷ Twenty two children completed the dietary protocol of whom 18 showed benefit, and 16 of these experienced some benefit from the few food phase of the diet. Armstrong *et al* used a similar protocol to assess a group of eczematous adults and children, starting with a simple exclusion diet followed, if improvement did not occur, by a few food diet.⁸ Of 28 children who did not benefit from a simple exclusion diet, 12 proceeded to a few food diet and two of these 12 improved. The study by Juto *et al* deals exclusively with infants under 16 months and the effect of delayed sequential weaning in this group.⁹

The other three studies assessed the therapeutic effect of 'elemental' (theoretically antigen free) diets; one placebo controlled study in adults¹⁰

showed no benefit while another open and uncontrolled study suggested improvement in five out of six adults on an elemental diet.¹¹ Hill and Lynch reported improvement in eight out of 10 eczematous children in an uncontrolled study of an elemental feed (Vivonex).¹²

No published study to date has examined the effect of few food diets in a large number of children with atopic eczema. We have used such diets to treat 66 children of varying ages with atopic eczema severe enough to justify such a disruptive measure. Our aims were: (i) to assess the therapeutic value of such diets, (ii) to identify the most frequent provoking foods by serial reintroduction, (iii) to confirm that improvement and deterioration in eczema was genuinely food related by administering double blind placebo controlled food challenges, (iv) to evaluate parental history, skin prick tests, and IgE antibodies as tests for the identification of provoking foods and, finally (v) to seek out any identifiable characteristics of diet responsive patients.

Patients and methods

Sixty six children (mean age 4.2 years, range 0.6–16.8 years; 36 boys) were selected from the dermatology outpatient clinic at the Hospital for Sick Children, Great Ormond Street during the period from late 1983 to early 1985. All had severe atopic eczema inadequately controlled by standard topical treatment and families who were judged to

be capable of managing complex dietary manipulations. Sixty children (91%) had first degree relatives with atopic disease. Thirty two children were from social classes I and II, 26 from social class III, and eight from social classes IV and V. Twenty eight children (42%) had had at least one hospital admission for eczema. Fifty nine children (91%) were woken by itching on more than 50% of nights if the mean of the best and worst months of the latest six months was taken. Thirty five children (53%) had undergone previous dietary treatment for their eczema and in 13 this was said to have been beneficial. Thirty four children (52%) were already excluding one or more foods at the start of the study.

Parents were questioned as to the history of the disease in their child, observed dietary and environmental factors, and previous treatments. Where both the child's compliance and the severity of the eczema allowed, children were skin prick tested with extracts of cows' milk, egg, dog fur, cat fur, house dust mite, and Timothy grass pollen (Bencard). Blood was taken to measure circulating IgE antibodies using a modification of the radioallergosorbent test (RAST) technique described by Ceska *et al*¹³ and antigens obtained from Sigma Chemical Co (ovalbumin and β lactoglobulin) and Bencard (house dust mite, cat fur, and Timothy grass pollen). Gastrointestinal permeability, a possible marker of food allergic disease,¹⁴ was measured using the lactulose: rhamnose excretion ratio before and after the few food phase of the diet.

Each child was prescribed an individual few food diet after discussion with the parents. Dietary constituents were selected according to the following criteria: (i) foods generally regarded as commonly exacerbating atopic eczema were excluded, (ii) foods implicated on history in the exacerbation of

the individual child's eczema were excluded, (iii) foods frequently eaten by the child were excluded, (iv) the diet was nutritionally adequate for the period concerned and, (v) the diet was judged by the parents, dietitian, and doctor to be as strict as the child could tolerate and palatable enough to ensure compliance. The diets therefore varied in strictness and constitution from child to child (diets A, B, and C in table 1 give an indication of the degree of this variation). The mean (SD) number of foods in the few food phase was 8.76 (3.76) with a range from one food (a casein hydrolysate for an infant aged 7 months) to 19 foods.

Eczema severity was assessed by a single clinician (MGP) before and after the few food phase of the diet. A modification of the visual score system used by Atherton *et al* was completed⁴: the body surface was divided into 20 areas (10 anterior and 10 posterior); for each area, the degree of redness, surface damage, and lichenification were assessed using firstly a numerical scale of severity (0 to 3) and, secondly, a figure expressing the percentage of the area concerned affected by the characteristic being assessed. These two figures were multiplied together and the products for all three characteristics for all 20 areas were added to give an overall score of severity. Twenty children had their visual eczema score assessed by one clinician (MGP) on two occasions not less than an hour apart as an indication of the variability of this measurement; the coefficient of variation calculated from these duplicate scores was 5.1%. Parents kept diary cards on which itch, redness, and sleep disturbance were each scored daily (0, 1, 2, 3 in order of increasing severity) and the amount of treatment used was documented. Dietary mistakes—that is excluded foods eaten in error—were also recorded on the diary card.

The median duration of the initial phase of the

Table 1 Examples of the kind of diet prescribed

A	B	C
Lamb	Rabbit	Venison
Rice*	Potato	Duck
		Rice*
Casein hydrolysate†	Brassicas (cabbage, cauliflower, sprouts, broccoli)	Potato and/or buckwheat, sago, yam
	Peaches, apricots, grapes, raisins	Parsnips, carrots, cucumbers, courgettes
	Olive oil	Dates, guava, lychee
		Sunflower oil
		Sugar

These examples indicate the range of few food diets used in order of decreasing strictness. Note frequent use of uncommon foods to which children were unlikely to have been previously exposed.

*Included additive and malt free 'rice krispies' produced by Kellogg Co Great Britain, Manchester.

†Nutramigen, Bristol-Myers.

Fig 1 Protocol for few food diet, serial reintroduction of foods and double blind placebo controlled food challenge.

diet was 26 days (range 19–44 days, the longer duration resulting from a desire on some occasions to see whether a mild initial improvement would increase with time). At the end of this phase the doctor judged whether sufficient improvement had occurred to justify continuing dietary treatment (fig 1). This decision was a clinical one (to which visual score chart and diary card data were contributory but not fundamental) and judged whether improvement had occurred of such a degree as to justify continuing with what is a very difficult and protracted form of treatment.

Children who were not judged to have improved adequately either discontinued dietary treatment or proceeded to a second diet, similar in type but with entirely different constituents. Diet responsive children continued, with parental agreement, to the serial reintroduction of individual foods at weekly intervals. Foods being introduced were initially taken in small quantities to minimise the chance of an unexpected severe allergic reaction but from the second day in full helpings at least once a day. If the child's eczema remained apparently unaffected by the introduction of a food it was incorporated into the diet. If a deterioration occurred that progressed during exposure to the food and improved on its withdrawal, the food was judged to exacerbate the eczema and withdrawn. Sometimes a number of reintroductions and withdrawal periods were neces-

sary to establish whether a food was exacerbating or innocuous.

In children who successfully completed the food reintroduction phase, double blind, placebo controlled food challenges were performed, (i) to confirm that the child's eczema improved and deteriorated in response to dietary manipulation and (ii) to validate parental identification of exacerbating foods.

A food identified by parents as exacerbating was disguised in a mixture with an innocuous food ('active') and the effect was compared with that of the innocuous food alone ('placebo'). Active and placebo components of the challenge were confirmed to be indistinguishable from one another by a group of 10 adult volunteers. Each mixture was taken daily in the same quantity and form, and for the same period as had been necessary to produce exacerbation on open introduction. When benzoic acid and tartrazine were tested, doses of 50 mg/day and 20 mg/day respectively (these doses being of the same order of magnitude as the daily intake of a normal child in the United Kingdom) were concealed in opaque capsules (Elanco). The order of active and placebo challenges was randomised and there was a one week wash out period between the active and the placebo periods.

Eczema was assessed by visual score chart before and after each challenge period and diary cards were

kept by parents throughout the challenge period. Both parent and doctor indicated which they thought to be the exacerbating component before the mixtures were decoded.

Data from questionnaires, and from in vivo and in vitro testing, were evaluated as predictors of diet responsiveness.

Informed consent was obtained from all parents and approval for the study was obtained from the hospital's standing committee on ethical practice.

Results

OUTCOME OF FEW FOOD DIETARY TREATMENT (fig 2)

Forty three children performed one few food diet, 20 performed two, and two patients performed three. Children failed to complete the few food phase of the diet on five occasions; three of these were second diets in children who had already completed a first diet without benefit; one was a first diet in which chicken pox supervened and this child subsequently successfully completed a diet; one was a first diet in an infant who was cared for by an extended family in which it proved impossible to obtain compliance by all family members. Therefore

Fig 2 Outcome of dietary treatment (number starting few food diet=66).

65 out of 66 children completed at least one few food diet.

Thirty children (46%) were felt by the parents to have improved sufficiently to justify continuing to food reintroduction, but the doctor concurred with this opinion in only 24 cases (36%) (in no case where the doctor thought sufficient improvement had occurred did the parents disagree). Only in the 24 cases in whom the doctor judged sufficient improvement to have occurred was a reintroductions phase considered. In four of this group of 24, however, coincident factors were thought by the doctor or parents, or both, to be important: two were admitted to hospital for intensive topical treatment because of exacerbations of their eczema during part of the few food phase of the diet and in two other children a change of washing powder and seasonal factors respectively were thought to have contributed significantly to the improvement.

Twenty children (30%) therefore proceeded to the reintroductions phase. In five of these 20 children the eczema deteriorated during the first one to three months of the reintroductions phase. Renewed exclusion of foods they had reintroduced produced no benefit; it was therefore not possible to ascribe their deterioration to dietary factors. These children therefore withdrew from the study leaving 15 children (23%) who maintained worthwhile improvement on dietary treatment. Three of this group of 15, however, abandoned dietary treatment despite persisting improvement after periods ranging from six to 10 months. These children and their families found the diets too burdensome despite their beneficial effects. A review of the historical and test data for these three children did not identify any distinguishing features; in particular they were not older than the children who persisted with dietary treatment.

Therefore, ultimately, 12 of 66 children (18%) persisted with dietary treatment with long term benefit. At the end of the study the mean duration of dietary treatment in these children was 47.9 weeks (range 26.4-71.1 weeks).

OPEN REINTRODUCTION OF FOODS

The 15 children who improved on dietary treatment had reintroduced without deterioration a mean of 15.3 foods each by the end of the study (range 6-37). The overall rate of successful food reintroduction was one food per three weeks (range one food in seven weeks to one food in one and a half weeks).

The foods most often judged to exacerbate atopic eczema on open reintroduction are listed in table 2.

Table 2 Proportion of times individual foods reintroduced were identified as causing a deterioration in eczema

Food	Exacerbations/total reintroductions	Food	Exacerbations/total reintroductions
Meat/poultry/fish		Vegetables	
Lamb	2/11	Pea/runner bean	3/10
Beef	6/13	Carrot/parsnip	3/10
Pork	3/13	Brassicas	1/11
Rabbit	0/3	Tomato*	6/9
Chicken*	6/12	Onion/leek	3/5
Turkey	1/5	Courgette/cucumber	0/1
Cod*	4/8	Potato	1/8
Mackerel	1/1	Lentil	1/1
Plaice	3/4		
Milks and soya		Fruit	
Cows' milk*	10/14	Apple/pear	3/13
Goats' milk*	6/11	Apricot/peach	1/10
Sheeps' milk	1/5	Plum/nectarine	0/2
Soya 'milk' formula*	5/7	Grape/raisin	2/7
		Orange*	6/11
		Banana*	8/12
		Pineapple	3/7
		Blackcurrant	2/4
		Melon	0/2
Eggs		Additives	
Hens' egg*	6/9	Colourings/ preservatives	6/14
Grains/yeast/malt		Other	
Wheat*	7/13	Sugar	0/7
Corn	5/12	Chocolate ('plain')	2/5
Oats	4/13	Tea	0/4
Rice	1/8		
Rye	0/2		
Yeast	1/7		
Malt	0/6		

*Foods reintroduced by seven or more children and identified as exacerbating eczema on 50% or more of these reintroductions.

DOUBLE BLIND, PLACEBO CONTROLLED FOOD CHALLENGES

Ten of the 15 diet responsive patients completed double blind food challenges. The active and placebo components of these challenges are shown in table 3.

When the child had completed both active and placebo parts of the double blind challenge, parents and doctor each indicated which they thought had been the 'active' period; parents and doctor each identified the active period incorrectly on five occasions and correctly on five occasions. Parents and doctor were in agreement with each other in eight of these decisions.

Visual eczema scores were analysed both comparing the end of the active period with the end of the placebo period and also comparing the change from the beginning to the end of the active period with the analogous change in the placebo period. Diary card scores for itch, redness, sleep disturbance, steroid usage, and emollients were each analysed as follows: (1) the score for each variable for the whole of the active period was compared with the placebo period (paired *t* test). (2) The change in score for each variable from the start (first two days) to the

finish (last two days) of the active period was compared with the same change in the placebo period (paired *t* test). There was no significant difference between active and placebo periods on any of these analyses.

During the interval between open introduction and double blind challenge there is a theoretical risk that the child's response to the food will alter. The mean interval from the identification of an exacerbating food on open introduction to double blind challenge was 45.4 days (range 16–181 days). There was no significant difference in the duration of this

Table 3 Constituents of double blind food challenges (n=10)

No of patients	Active component	Placebo component
4	Cows' milk	Goats' milk
2	Cows' milk	'Nutramigen'
1	Cows' milk	Soya 'milk'
2	Benzoic acid and tartrazine	Calcium gluconate
1	Benzoic acid	Calcium gluconate

interval between the double blind challenges in which the active component was correctly identified, whether by doctor or patient, and those in which it was incorrectly identified ($p>0.01$, Mann-Whitney U test in both analyses).

CHARACTERISTICS OF DIET RESPONSIVE PATIENTS

Data for the 15 diet responsive patients were compared with that for 41 unequivocally unresponsive patients. Excluded from this analysis were the child who did not complete a diet, the four children in whom concurrent non-dietary factors may have been responsible for the improvement, and the five children whose eczema deteriorated early in the reintroduitory period without an apparent dietary cause. No significant differences were found with the exception of positive associations between response to diet and positive IgE antibody to ovalbumin, and larger number of 'slow' (occurring more than two hours after ingestion) cutaneous reactions to foods reported on history (t test, $p<0.05$ in both

cases, table 4). The number of analyses performed was such that two results significant at the 5% level would be expected to occur by chance.

PREDICTORS OF EXACERBATING FOODS

No useful assessment could be made of the predictive value of skin prick tests and IgE antibody tests (RASTs) in the identification of exacerbating foods, as the double blind challenge trial failed to validate the exacerbating effect of these foods.

VISUAL SCORE CHART AND DIARY CARD DATA

In the diet responsive group over the few food phase of the diet, the visual scores showed a mean improvement of 32.4% (range, 62.4% improvement to 1.3% deterioration) and the cumulative diary card symptom score (itch, redness, and sleep disturbance combined) showed a mean improvement of 20.9% (range, 57.9% improvement to 39.6% deterioration) if the first and last seven days of the few food phase of the diet were compared. Paradoxical deterioration in one or other measurement occurred in three children; two showed an appreciable improvement in visual score but a deterioration in symptom score; one child had a visual score that was marginally worse (1.3%) with a 31% improvement in symptom score.

Topical steroid usage increased slightly and emollient use decreased during the few food phase, in neither case being significantly different from the changes in treatment in diet unresponsive patients.

Discussion

These data suggest that few food diets are of limited benefit to children with severe atopic eczema. Although it may be argued that our sample was selected for diet unresponsiveness (as 54% continued to have severe eczema despite past dietary treatments), the response to the present dietary protocol was not in fact better in children who had not previously experienced dietary treatment than in those who had (table 4).

Our few food diets were of varied composition but excluded foods identified, from previous reports, as exacerbating eczema and observed as exacerbating eczema in the individual child concerned. Comparison of the two outcome groups (diet responsive and diet unresponsive) does not suggest that, within the range of diets used in this study, extremely strict or prolonged diets are more effective than shorter less strict diets (table 4).

Of particular interest in the present study was the identification of a group of four children whose improvement could be ascribed to non-dietary factors and a further five children who deteriorated

Table 4 Data compared in diet responsive and diet unresponsive patients

Personal data:	Age. Sex. Age at onset of eczema. Severity of eczema (judged by visual score) at start of few food diet.
Environmental factors:	Breast feeding (history of/duration of) History of seasonal fluctuation of eczema. Presence of dog or cat in home with relevant skin prick test/IgE antibody positive.
Dietary factors:	History of inhalent allergy. Previous dietary treatment with or without benefit. Milk and egg already excluded at start of diet. History of food induced exacerbation of eczema. Number of reported 'immediate' (within two hours of ingestion) reactions to foods cutaneous and non-cutaneous). Number of reported 'slow' (more than two hours after ingestion) reactions to foods (cutaneous* and non-cutaneous). Reported reactions to non-foods (immediate and slow; cutaneous and non-cutaneous). Duration of few food phase of diet. Number of foods allowed in few food phase of diet.
In vivo and in vitro test data:	Skin prick test to foods/inhalants. Presence of IgE antibodies to: Ovalbumin* β lactoglobulin House dust mite Cat fur Timothy grass pollen Gastrointestinal permeability to oligosaccharides at start of diet. Change in gastrointestinal permeability with diet.

*Significant difference between diet responsive and diet unresponsive groups ($p<0.05$).

in the first one to three months after improving on the few food diet without dietary factors appearing to be responsible for their deterioration. These children, if they had been classified as diet responsive, would have increased our diet responsive group by 38%; clearly careful review of coincident non-dietary factors and follow up to confirm that improvement is maintained should be part of any future dietary study of this type.

Three children in the group judged to have shown considerable improvement in fact showed a deterioration in one of the indices of severity, in the presence of an appreciable improvement in the other. These cases emphasise the difficulty of quantifying the severity of this condition. Diary card symptom scores may be affected by extraneous factors (for example, sleep disturbance due to intercurrent illness), and both the weight allocated to individual symptoms and the periods at the beginning and end of the few foods phase of the diet for which cumulative scores are calculated (in this study seven days) are arbitrary. Visual scores at the time of consultation may not invariably reflect a symptomatic improvement—long standing lichenification is unlikely to change measurably over three weeks and erythema may be exacerbated transiently by ambient irritants, temperature, or emotion. For these reasons decisions as to dietary outcome on the basis of preset numerical criteria may misallocate patients.

The poor response rate in this study meant that our double blind trial was small. Furthermore, the interval between open reintroduction and double blind challenge was long in some cases and theoretically an alteration of the effect of the active food (or indeed of the placebo) might have occurred during this interval. However, the results as they stand have two implications. Firstly, parental identification of provoking foods in atopic eczema is unreliable, presumably because of the fluctuating nature of the disease and the multiplicity of confounding influences (environmental, emotional, etc.). Secondly, the results do not demonstrate exacerbation of these children's eczema by foods. Therefore, by implication, the improvement observed, on an open uncontrolled basis during the few food phase of the diet, cannot be ascribed with any confidence to food exclusion.

It is of interest that, though analysed differently, the double blind trial described in the study of Armstrong *et al* also showed correct identification of the active component in only half of the challenges.⁸ In this context, Wilson and Silverman's demonstration that asthmatic children may respond to allergenic foods, not by simple bronchospasm, but by an increase in bronchial lability rendering them more

susceptible to a second agent, may be relevant.¹⁵ Should a similar two stage mechanism occur in atopic eczema, simple provocation tests of the kind used in these studies would not necessarily identify it.

The list of foods implicated on open introduction (table 2) therefore remains unvalidated. The similarity to the foods implicated by the patients in Hathaway and Warner's study⁶ and in the study of Armstrong *et al*⁸ is of note, however, as is the frequent implication of soya which, though used as a placebo agent in milk and egg exclusion studies in the past,^{4,5} may now be viewed as an unsatisfactory choice for such a role.

Numerous comparisons of historical and test data for diet responsive and diet unresponsive patients showed only two weak associations with diet responsiveness; however, as stated above, the number of analyses performed was such that two results significant at the 5% level would be expected to occur by chance. Neither association would have usefully improved the response rate if used as the criterion for dietary treatment in our study group. Of particular interest was the absence of any association between increased intestinal permeability and response to diet and the absence of a significant change in permeability over the dietary period in children whose eczema improved considerably on dietary treatment; though increased permeability has been shown to occur in childhood atopic eczema¹⁶ and in association with food induced hypersensitivity reactions of probable IgE mediated type,¹⁴ it does not appear to usefully predict response to exclusion diets of the type we have assessed.

'Simple' empirical diets such as that studied by Atherton *et al* are a well established part of the treatment of childhood atopic eczema.⁴ Further work is needed to clarify the role of elemental diets in a controlled fashion in larger numbers of children with extreme eczema than have been studied hitherto. Given the burden, both emotional and financial, of the few food diet, the eagerness (well illustrated in our study) of parents to pursue such diets even when the benefits are marginal, and our failure to achieve even a small response group validated by double blind challenge, it would seem prudent to restrict the use of such diets unless and until further evidence is forthcoming.

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