Risk factors in childhood eczema

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SUMMARY The cumulative rate of childhood eczema during the first three years was studied in a birth cohort of 1265 New Zealand infants. A parental history of eczema was the strongest predictor of rates of childhood eczema but parental asthma was also related to childhood eczema. Children exposed to an early diverse solid-food diet also had increased risks of eczema, but there was no evidence to suggest that breast-feeding practices had any effect on rates of eczema. Analysis of the data suggested that the apparent association between exclusive breast-feeding and reduced rates of eczema reported in previous studies may be because exclusively breast-fed infants were not exposed to early solid feeding rather than to any beneficial effect of breast milk itself.

There have been several studies of the effects of early infant feeding practices on rates of childhood eczema but these have tended to produce inconsistent results. Some studies have produced evidence to suggest that early breast-feeding practices¹⁻³ or the substitution of soy milk⁴⁻⁶ may reduce the risk of eczema, but an equal number⁶⁻¹⁰ have found no beneficial effects for breast-feeding or soy milk substitutes. A possible explanation of published inconsistencies was suggested by a recent study¹⁰ of rates of childhood eczema in a birth cohort of New Zealand children, which found that when parental atopy and early solid feeding practices were taken into account, there was no significant tendency for breast-fed infants to fare better than their bottle-fed peers. These results suggest that what has commonly been attributed to a beneficial effect of breast-feeding may have arisen because exclusively breast-fed infants are not exposed to solid food rather than to any particular benefit of breast milk.

Many studies of the role of parental atopy on childhood eczema have combined such conditions as asthma, eczema, and allergic rhinitis into a single measure of atopy. It seems possible, however, that rates of childhood eczema will vary with the type of atopic response manifested by the child's parent so that children with a family history of eczema may be at greater risk than those with a family history of asthma or other atopic conditions.

We report a further analysis of the rates of eczema in the birth cohort described above. The aims of the analysis were:

(1) To examine the separate effects of parental asthma and eczema on rates of childhood eczema.

(2) To examine the effects of early infant diet on rates of childhood eczema during the first three years of life.

(3) To consider the role of early milk diet in the development of childhood eczema.

Method

The data were collected during the Christchurch Child Development Study in which a birth cohort of 1265 infants born in maternity units in the Christchurch (New Zealand) urban region has been studied at birth, four months, one, two, and three years.

At each stage information on the child's health, social background, diet, and other factors was collected using a structured interview with the child's mother. Information on the child's medical history and diet was supplemented from the following sources.

(1) During the period birth to four months mothers were asked to keep a diary of all of the child's medical attendances and diet at one, two, three, and four months. Compliance with the diary was good, and 85% of mothers returned a record.

(2) Information on the child's early diet was obtained also from a record of attendances to the Plunket community nurse; over 97% of this cohort had contact with the Plunket Society.¹¹

(3) During the period one year to two years, and two to three years, mothers were asked to keep a further diary of their child's health. In this case compliance was only 61%.

(4) When a mother did not return the diary, information was based on maternal recall, often supplemented by a telephone call from the mother to her family doctor to obtain relevant details or by direct contact with the family doctor if the mother gave her signed consent.

This information was used to reconstruct the child's diet during the first four months of life and a history of medical attendances during the first three years of life.

The following classifications were used in the analysis.

(1) Early milk diet was classified into three groups.

Totally bottle-fed infants who had been bottle fed from birth to four months. (Only four of the bottle-fed series received soy milk substitutes and none was fed soy milk from birth).

Complement-fed infants who had received both breast and bottle milks during the first four months.

Totally breast-fed infants who had received only breast milk (with or without the introduction of solid food) during the first four months.

(2) The child's early solid diet was classified according to the number of different types of solid food received, such as cereals, vegetables, dairy products, fruit, meat products, egg.

(3) Parental asthma/eczema. Information was obtained on the history of both asthma and eczema in both of the child's biological parents. (Few children had both parents affected so they were classified into no parent affected and one or both affected.)

(4) Childhood eczema. Information was obtained from the diary kept by the mother, from maternal recall, or directly from the child's doctor. In all cases eczema was defined on the basis of a medical diagnosis or reported diagnosis.¹⁰

RESPONSE RATES

Of the 1265 children enrolled in the research, 1143 remained in the study at three years; this represented 90% of the initial cohort and 96% of the children who were still alive and resident in New Zealand. The numbers in the analysis differ slightly from these numbers owing to small amounts of missing data on childhood medical history.

METHODS OF ANALYSIS

The analysis was based on a series of additive logistic models fitted to the cumulative risks of childhood eczema. In these models the cumulative risk of eczema (measured on the logit scale) was assumed to be a linear function of time and this function was successively refitted introducing the other factors as covariates to examine the extent to which various risk factors and combinations of risk factors influenced

the intercept of the linear model. In effect this method assumed that the cumulative risks of eczema for all risk groups in the analysis had a common slope over time (age) but that the intercept of the function varied from group to group. To test the assumption of parallelism of regression implicit in this model, analysis of deviance¹² was used to test for any significant interaction between time and risk factors.

Results

PARENTAL ASTHMA OR ECZEMA AND CHILDHOOD ECZEMA

Table 1 shows the cumulative risks of childhood eczema over the three-year study period sub-divided by parental asthma and parental eczema. It is apparent from the table that risks of eczema varied quite considerably with the presence or absence of atopy in the child's family: children with a family history of both asthma and eczema had rates of eczema that were between two to three times those of children with no family history of these conditions.

To test for the separate effects of parental asthma and eczema on rates of childhood eczema an additive logistic model was fitted to the data in table 1. This analysis showed that the cumulative risks of childhood eczema varied significantly with both parental asthma ($p < 0.01$) and eczema ($p < 0.0001$). Analysis of deviance of the fitted model showed no significant interaction between age, parental asthma, eczema, and rates of childhood eczema.

Parallel analyses of asthma and eczema in the child's grandparents produced similar but less pronounced results, but the presence of a history of these conditions in the child's grandparents did not significantly increase the prediction of childhood eczema when parental history was taken into account. An analysis of the effects of one or both parents giving a history of asthma and eczema proved to be uninformative owing to the small numbers of children with both parents affected.

Table 1 Cumulative rates % (number studied) of eczema by parental history of eczema and asthma

Parental eczema	Parental asthma	First year	First 2 years	First 3 years
Neither parent	Neither parent	5.9 (791)	13.2 (766)	17.1 (744)
	One or both parents	7.8 (129)	17.1 (123)	20.0 (120)
	Neither parent	9.4 (170)	24.4 (168)	25.8 (167)
One or both parents	One or both parents	16.5 (85)	31.3 (83)	40.2 (82)

Significance of factors: age $p < 0.0001$; parental eczema $p < 0.0001$; parental asthma $p < 0.01$.

Table 2 Cumulative rates % (number studied) of eczema by milk and solid food diet during the first four months

Milk diet	First year				First 2 years				First 3 years			
	Solid food diet (No of different foods)			Total	Solid food diet (No of different foods)			Total	Solid food diet (No of different foods)			Total
	None	1-3	≥4		None	1-3	≥4		None	1-3	≥4	
Bottle only	4.1 (49)	3.7 (188)	5.4 (37)	4.0 (274)	17.4 (46)	13.4 (179)	20.0 (35)	15.0 (260)	19.6 (46)	18.3 (175)	21.9 (32)	19.0 (253)
Breast and bottle	6.3 (143)	8.4 (464)	12.9 (85)	8.5 (692)	13.3 (143)	18.0 (450)	22.6 (84)	17.6 (677)	21.1 (142)	21.5 (438)	25.9 (81)	21.9 (661)
Breast only	6.2 (129)	11.5 (78)	0.0 (2)	8.1 (209)	12.7 (126)	20.0 (75)	0.0 (2)	15.3 (203)	14.8 (122)	21.3 (75)	0.0 (2)	17.1 (199)
Total	5.9 (321)	7.5 (730)	10.5 (124)	7.4 (1175)	13.7 (315)	17.0 (704)	21.5 (121)	16.6 (1140)	18.4 (310)	20.6 (688)	24.3 (115)	20.4 (1113)

Significance of factors: age $p < 0.0001$; number of solid foods $p < 0.01$; milk diet $0.10 < p < 0.20$.

EARLY DIET AND CHILDHOOD ECZEMA

Table 2 shows the cumulative risks of childhood eczema over the three-year study period sub-divided by the child's solid food and milk diet during the first four months. The table shows a small but persistent trend for children exposed to a diverse solid food diet to have greater risks of eczema than other children: children given four or more solid foods during early life had rates of eczema that were roughly 5%–8% higher than children given no solid food; the group exposed to one to three solid foods had results between these extremes. There is no evidence to suggest that rates of eczema were lower in breast-fed children and, in fact, during the first year of life breast-fed infants tended to have a greater risk of eczema.

A logistic model fitted to table 2 showed the presence of a significant ($p < 0.01$) effect for early solid feeding to be associated with increased risks of eczema, but there was no significant effect for the child's milk diet. Analysis of deviance of the fitted model showed no significant interactions between age, solid food diet, milk diet, and childhood eczema.

To examine the effects of solid feeding on any apparent association between exclusive breast-feeding and childhood eczema, table 3 shows a reanalysis of table 2 in which children given an exclusive breast milk diet with no solid food are contrasted with other children. The table shows the presence of a small but consistent tendency for the

exclusively breast-fed series to have less eczema than other children. A logistic model fitted to table 3 showed this difference to be significant ($p < 0.05$).

On the basis of this result one might be tempted to conclude that exclusive breast-feeding conferred some protection against childhood eczema, but as the more comprehensive analysis of table 2 has shown, this benefit arose because the exclusively breast-fed children were not exposed to early solid feeding rather than from any beneficial effect of breast milk.

ADJUSTED RATES OF CHILDHOOD ECZEMA

Since it was possible that parental atopy and childhood diet were related factors and this may have confounded a possible relationship between breast-feeding and rates of childhood eczema, the data were reanalysed using an additive logistic model in which all factors were considered simultaneously. The results of this analysis are summarised in table 4, which shows the adjusted rates of eczema for each level of each factor over the three-year study period. It is apparent from this table that the conclusions of this analysis are essentially the same as those described earlier.

Table 4 Adjusted cumulative rates of eczema % by parental history, solid food diet, and type of milk diet

Measure	Adjusted rates			Significance of factor in model
	0-1 y	0-2 y	0-3 y	
Parental history of eczema				
Neither parent	6.1	13.9	17.5	
One/both parents	11.4	24.2	29.6	$p < 0.0001$
Parental history of asthma				
Neither parent	6.6	14.9	18.8	
One/both parents	11.1	20.3	25.1	$p < 0.005$
Solid food diet				
(No of different foods)				
None	5.7	13.2	16.6	
1-3	7.3	16.4	20.5	
≥4	9.2	20.2	25.0	$p < 0.01$
Milk diet				
Bottle-fed only	6.3	14.3	18.0	
Breast-fed and bottle-fed	7.1	15.9	19.9	
Breast-fed only	7.9	17.6	21.9	$0.10 < p < 0.25$

Table 3 Cumulative rates % (number studied) of eczema by diet in the first four months

Diet	Cumulative rate		
	First year	First 2 years	First 3 years
Exclusively breast-fed	6.2 (129)	12.7 (126)	14.8 (122)
Other	7.6 (1046)	17.1 (1014)	21.1 (991)
Total	7.4 (1175)	16.6 (1140)	20.4 (1113)

Significance of factors: age $p < 0.0001$, diet $p < 0.05$.

(1) A parental history of eczema proved to be the strongest discriminating factor ($p < 0.0001$) in the model, with children having a perental history of this condition having risks of eczema that were roughly twice those of children without family history of the condition.

(2) A family history of asthma played a secondary but none the less significant ($p < 0.005$) part in the condition.

(3) Children who were exposed to an early diverse solid food diet had significantly increased risks of eczema ($p < 0.01$) when the other factors in the model were taken into account.

(4) There was no evidence to support the view that the nature of the child's early milk diet had any detectable effect on risks of eczema.

(5) Analysis of deviance of the fitted model showed no significant interactions between any of the factors in the analysis.

Discussion

The results of this study extend and confirm the findings of a previous study of the prevalence of eczema in this birth cohort. In agreement with the findings of other studies^{3 10} a family history of atopy was the strongest predictor of variations in rates of eczema. Nevertheless, the effects of parental atopy varied: a family history of eczema appeared to be the strongest predictor of childhood eczema and parental asthma played a secondary but none the less significant part. The results suggest that the common tendency to combine various conditions such as asthma, eczema, and allergic rhinitis to produce an index of parental "atopy" is somewhat misleading, since the effects of these conditions on rates of childhood eczema tend to vary with the nature of the atopic condition. This finding is consistent with the conclusions of a discriminant function analysis (B Taylor *et al*, unpublished data), which showed that in terms of parental history, skin prick sensitivity, and IgE levels, children with asthma and eczema form two distinct but overlapping populations.

In confirmation of the previous report exposure to a diverse early solid food diet appeared to increase risks of childhood eczema. This effect persisted when parental asthma/eczema and early milk diet were taken into account and was still present at age 3 years. This suggests that, in some as yet unknown way, early exposure to a diet diverse in potential allergens may predispose children to develop eczema. To some extent this is consistent with the argument proposed by Matthew *et al*² who were of the opinion that early exposure to food antigens may have an adverse effect on the immune mechanisms of the infant and thus

increase the likelihood of subsequent eczema. The argument here differs, however, from that presented by Matthew *et al*, who were concerned primarily with the effects of cows' milk on childhood eczema and paid less attention to other foods. What the results of this and a previous study¹⁰ tend to suggest is that such an effect cannot be attributed to a single allergen such as cows' milk but rather to a whole array of allergens that are roughly summarised by a measure of the diversity of the child's early diet.

There was no evidence to suggest that breast-feeding itself had any beneficial effects on rates of childhood eczema and, indeed, during the first year of life children given cows' milk appeared to have less eczema than their breast-fed peers. Further analysis of the data provided a possible explanation of the reasons for some studies to report benefits for breast-feeding. In particular, when the sample was reclassified so that children receiving an exclusive breast-milk diet (with no solid food) were contrasted with other children, the exclusively breast-fed group had significantly less eczema. Given this result one might have been tempted to conclude that exclusive breast-feeding is associated with a reduction in childhood eczema. A more complete analysis of the data, however, showed that the apparent benefits experienced by the exclusively breast-fed infants were not due to any beneficial effect of breast milk itself but to variations in the solid food diet experienced by the two groups. This suggests that what has been thought to be a beneficial effect arising from breast milk may be because exclusively breast-fed children are not given solid food. This would also account for the inconsistencies in publications on this topic since there are as many reports of beneficial effects for breast-feeding as there are studies that have found no such effect. If the apparent benefits of exclusive breast-feeding are due to variations in solid food diet, then one would expect the findings on the role of breast-feeding in childhood eczema to vary between studies depending on the level of exposure of children in bottle-fed series to solid food. If these conjectures are correct it follows that a substantial amount of evidence on the role of breast-feeding in childhood eczema may require reinterpretation and, in any event, there seems to be a need for further controlled research that pays greater attention to the possible role of early solid feeding practices on childhood eczema.

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