

Role of maternal diet and mode of infant feeding in prevention of atopic dermatitis in high risk infants

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Ever since the first description of atopic eczema mentioned in the introduction of this supplement, we have come a long way towards understanding its clinical characteristics, contributing and precipitating factors, diagnosis, and management. It is clear that hereditary predisposition is an important underlying factor. In addition, both dietary and environmental allergens may initiate the disorder and contribute to its persistence.

The heavy burden of atopic illness in terms of physical and emotional costs has led to attempts at prevention. It is clear that exclusive breast feeding affords partial protection. However, the undoubted occurrence of serious atopic disease even among the exclusively breast-fed infants has prompted us to postulate that sensitization to food antigens may occur *in utero* as well as via breast milk after birth (1). In view of these considerations, we have conducted several studies to evaluate the role of maternal diet during pregnancy and lactation.

High-risk subjects

Attempts at prevention are best applied selectively to those individuals who are at high risk of developing atopic eczema. The World Health Organisation has outlined the major criteria that should be satisfied when a screening program is put into operation. These include low level of risk and discomfort, few false positive and false negative results, effective early treatment or prevention, adequate medical facilities, and reasonable cost-benefit ratio. Three methods of identification of subjects at high risk of developing atopic eczema have proven to be useful.

Family history

Presence of an affected first-degree relative (parent(s), sibling (s)) indicates an atopic background. A family history of allergy is elicited in about 70 % of all patients with atopy. Biparental history is a stronger predisposing factor than uniparental history.

Cord blood IgE concentration

The regulation of reaginic antibodies by maternal influences and age of exposure has been extensively studied. The fetus is capable of synthesizing IgE from the 11th week of gestation and it is attractive to suggest that newborn infants who subsequently become symptomatic may already show a tendency to produce IgE in greater amounts than non-atopic subjects. Thus one might find higher cord blood IgE in infants who subsequently become atopic. Indeed, this possibility has been investigated and the data do indicate that high and low IgE response is already coded at birth. For example, it was found that 70 % of infants with positive family history for atopy and high cord blood IgE showed evidence of atopy by 24 months of age (2). Our data show that cord blood IgE is a strong predictor of atopic eczema in young infants, irrespective of family history (3). However, there is a significant influence of infant feeding.

The predictive value of cord blood IgE in the development of atopic disease was evaluated by us in a prospective study of two groups of infants (3). Cord blood IgE greater than 0.7 U/ml carried a high risk (72.6% and 58.4%,

Table 1

T-cell subpopulations in infants with and without family history of atopy

Group	% of cells		
	T4-positive	T8-positive	T4/T8
Negative history			
healthy	51±3.2*	28±4 ^a	1.9±0.21 ^c
symptomatic	47±3.7	20±1.9 ^b	2.6±0.33 ^d
Positive history			
healthy	45±4.1	25±2.0 ^a	2.0±0.25 ^c
symptomatic	49±3.5	17±2.5 ^b	2.8±0.51 ^d

* Mean±S.E.M.
Values with different superscript letters are significantly different.

respectively, in the groups with and without family history) and cord blood IgE concentration less than 0.7 U/ml carried low risk (13.4% and 1.1%, respectively, in the groups with or without family history).

Suppressor T cells

The production of IgE is regulated by the balance of T helper and suppressor cells. IgE underlies the genesis of many of the manifestations of atopic disease. Thus it is logical to consider using the number and function of T cell subsets as an index of high risk. Strannegård et al. (4) found reduced proportion of rosette-forming T lymphocytes in 233 atopic

Table 2

Confounding variables influencing the scientific validity of studies of the association between breast feeding and atopic disease

Prospective versus retrospective
Duration and exclusive nature of breast feeding
Definition of disease
Time of introduction of solids
Small number of subjects
Drop-out rate
Social demographic characteristics
Attendance at day care facility
Environmental control (smoking, dust, pets)
Compliance
Blinding
Lack of supportive immunological data
Statistical analysis

children compared with 59 controls. The discrepancy between results in later studies may be due in part to methodologic differences. For instance, techniques that do not permit detection of low avidity binding of sheep red blood cells may not show differences between atopic and control patients. Our prospective studies showed that reduction in CD8+ T cells preceded the development of atopic eczema in infants irrespective of the presence or absence of family history (5) (Table 1).

Infant feeding and eczema

Breast feeding may partially protect the high risk infant from developing eczema. This is

Table 3

Influence of maternal antigen avoidance and mode of feeding on incidence of atopic eczema in infants

Groups	n	Eczema present	No Eczema	Statistical analysis (Fisher's Exact Probability Test)		
Group I. Maternal food antigen avoidance	55	17	38	$p = 0.0046$		
I (BF) Breast-fed	35	5	30			
I (FF) Formula-fed	20	12	8			
Group II. Control	54	24	30			
II (BF) Breast-fed	36	11	25	$p = 0.0503$		
II (FF) Formula-fed	18	13	5			
				$p = 0.7864$		
				$p = 0.6933$		

Table 4

Influence of maternal antigen avoidance and mode of feeding on severity and extent of atopic eczema in high-risk infants

Group 1	Breast-fed	Formula-fed
Maternal antigen avoidance (n = 55)	20 ± 3 ^a (n = 35)	32 ± 3 ^b (n = 20)
Control (n = 54)	29 ± 4 ^b (n = 36)	46 ± 5 ^c (n = 18)

The results are expressed as mean ± S.E.M. of eczema score. Values designated with a different superscript letter differed significantly from one another on Student's t-test analysis, a vs c, $P < 0.01$; b vs c, $P < 0.05$.

because atopic eczema may be precipitated or aggravated by foods to which the infant is sensitised. The possible mechanisms for the protective effect of human milk include reduced exposure to sensitising food proteins such as beta-lactoglobulin, anti-infective properties that reduce the incidence of infections, and increased maturation of intestinal barrier. In our prospective studies, we observed a significant beneficial effect of exclusive breast feeding for at least 3–4 months on subsequent occurrence of eczema (3, 6). This protective effect of breast feeding against atopic disease has been seen in a number of prospective studies (2, 7). Some investigations, largely retrospective, were unable to demonstrate any beneficial effect of breast feeding on incidence of atopic disease. For example, one report concluded that breast feeding and delayed introduction of solid foods do not protect against subsequent atopic eczema. An important drawback of this study, however, is the fact that it was a retrospective

Table 6

Environmental engineering

Pregnancy	Avoid allergenic foods
Infancy	Prolonged breast feeding
	Delay solid foods
	Reduce exposure to inhalants
	Reduce risk of infection
	Eliminate parental smoking

investigation in which the parents of children aged 1 month to 20 years were interviewed regarding feeding history, family history and demographic data. Obviously the reliability of such a history long after the events had taken place would be questionable. Furthermore, many of the negative studies examined general population samples rather than children from atopic families. The important aspects of study design and analysis have been described elsewhere (Table 2) (8).

Maternal dietary precautions during pregnancy and lactation

Several clinical observations, largely anecdotal, and the demonstration of food antigens in breast milk and amniotic fluid, led to the logical suggestion that maternal antigen avoidance during pregnancy and lactation would reduce the risk of atopic eczema during infancy (1). We have reported the results of a prospective study of maternal antigen avoidance during pregnancy and lactation on the incidence and severity of atopic eczema in infants at high risk of developing the disorder (9). A group of 121

Table 5

Presence of dietary antigens in breast milk

	Number of mothers tested	β -lactoglobulin	Casein	Ovalbumin	Any Antigen
Antigen avoidance advice	20	3	2	1	3*
Control	16	12	7	10	15*

* Chi square test, $\chi^2 = 22.0$, $P < 0.01$.

women with a history of a previous child with atopic disease were randomly allocated during the next pregnancy to antigen avoidance or control groups. Dietary advice consisted of almost complete exclusion of milk and dairy products, egg, fish, beef and peanut throughout pregnancy and lactation. A total of 109 completed the study. Maternal antigen avoidance was associated with reduced occurrence of atopic eczema and the skin involvement was less extensive and milder. The maternal antigen avoidance and control groups were found to be matched for several confounding variables that may influence compliance, choice of the mode of infant feeding, the development of atopic eczema, and follow-up. Maternal antigen avoidance was associated with reduced occurrence of atopic eczema (Table 3). Among the 55 in Group I who completed the trial of antigen avoidance, 27 infants developed atopic eczema, 5 of 35 were breast-fed and 12 out of 20 who were formula-fed. Among the offspring of 54 control mothers in Group II given no dietary restrictions, eczema was observed in 24 infants, 11 of 36 breast-fed and 13 of 18 formula-fed. The incidence of atopic eczema was significantly reduced in Group I, mainly among the breast-fed group. Fewer exclusively breast-fed infants developed eczema compared with formula-fed infants both in Group I and Group II. For the entire group of breast-fed infants, the incidence of eczema was significantly less compared with the formula-fed group. The beneficial preventive effect of breast feeding was more marked when combined with maternal antigen avoidance. The extent of atopic eczema as estimated by an objective scoring system was significantly less in the antigen avoidance group (Table 4). The breast-fed infants had a lower score compared with formula-fed babies both in Group I and Group II. One or more food antigens were detected in breast milk samples obtained from 3 of 20 mothers in Group II controls (Table 5). These differences are significant statistically. Thus, avoidance of common dietary allergens during pregnancy and lactation enhanced the preventive beneficial effect of exclusive breast feeding on the incidence of atopic eczema among infants at high risk.

Environmental engineering for the prevention of atopic disease

Since food allergy may contribute to the development of atopic disease (eczema, asthma, others) attempts at prevention have employed exclusive breast feeding, hypoallergenic formula, and maternal dietary restrictions during pregnancy and lactation. Many studies have found a reduction, but not elimination, of atopic eczema among high-risk infants fed exclusively on the breast. Study design differences (8), particularly disregard of confounding variables (Table 2) may be responsible for differences in the results of various studies. The apparent "failure" of even exclusive breast feeding to entirely prevent atopic symptoms may be attributed to several factors. One, sensitization may have occurred *in utero* so that it is already too late at birth to entirely prevent atopic disease. Two, food antigens may be passed into human milk and cause allergic symptoms among the breast-fed group. The latter possibility has been suggested by the detection of such antigens in human milk and by the amelioration of colic-like symptoms and of eczema in infants by antigens avoidance by mothers during lactation.

Several variables may influence the outcome of trials of maternal food avoidance in prevention of allergic disease. This may explain the apparent discrepancy between the results of our studies (9) and those observed by the Linköping group. The Swedish study began dietary precautions in the third trimester of pregnancy, long after the fetus is capable of becoming sensitized. Secondly, only two foods, egg and milk, were avoided. Finally, a casein hydrolysate was fed to the mothers and it is possible that some batches of the preparation may contain sensitizing molecules. A plan of environmental engineering is suggested for reducing the risk of sensitization and thereby that of atopic disease (Table 6). It would be prudent to begin maternal dietary preventive measures during pregnancy and continue them after birth for the first 4–6 months of life. Thus, the maximum benefit may be expected to accrue from avoidance of certain foods during the antenatal period, fol-

lowed by exclusive breast feeding (with continuing precautions related to mother's diet). Mothers who decide not to breast feed should use a protein hydrolysate formula to feed their at-risk infants (10).

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