

Effect of maternal avoidance of eggs, cow's milk and fish during lactation upon allergic manifestations in infants

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Summary

Atopic/allergic manifestations and skin-prick tests (SPT) to egg white, cow's milk (CM) and fish were evaluated during the first 18 months of life in two matched groups of infants with a family history of atopy/allergy. In one group ($n=65$) the mothers had a diet free from eggs, CM and fish during the first 3 months postpartum, whereas the mothers in the other group ($n=50$) consumed an ordinary diet. The diet of the infants was similar in both groups, i.e. CM was not supplied until 6 months of age, and eggs and fish not until 9 months of age. The incidence of atopic dermatitis was significantly lower in the maternal diet group during the first 6 months postpartum (10.8 and 28%, respectively) but not after that age. Other atopic/allergic manifestations did not differ and the number of positive SPT to egg white, CM or fish at 9 months of age was similar in both groups.

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Introduction

Sensitization to food protein and appearance of immunoglobulin E (IgE) antibodies to food antigens, e.g. egg white and cow's milk (CM), occur early during infancy, even in infants who are exclusively breast fed [1,2]. A diet free from eggs and CM during the third trimester of pregnancy did not diminish the incidence of atopy/allergy in the offspring during the first 18 months of life [3]. The most likely source for the sensitization would thus seem to be passage of small doses of antigen into the breast milk.

The aim of this study was to evaluate the effect of maternal avoidance of eggs, CM and fish during the first 3 months postpartum on the development of atopic/allergic symptoms in the offspring. The sensitization to these nutrients as judged by skin-prick tests (SPT) at 9 months of age was also assessed. The results of determinations of total IgE, IgA and IgG and of IgE and IgG antibodies to food antigens will be presented separately.

Subjects and methods

Patient selection

During a period of 18 months, from August 1984 to

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March 1986, all pregnant women visiting the antenatal clinics of the central hospitals of Skövde and Borås in southwestern Sweden were asked by the midwives about atopy/allergy in their families. In all, 237 families had a history of previous or present atopic dermatitis (AD), allergic rhinoconjunctivitis (ARC) or asthma in the pregnant women, her husband or their children (Table 1). Families that were interested in participating in the study were informed by one of the investigators and the history was confirmed. In addition smoking habits and the presence of furred animals in the families were assessed and only non-smoking families without indoor pet animals were permitted to participate in the study. Families with double heredity ($n=103$), i.e. atopic disease in either both parents, one parent and one sibling or in two siblings, were included at this stage. Families with single heredity were included provided the cord blood IgE (CB-IgE) turned out to be ≥ 0.9 kU/l ($n=12$). During the 18 months follow up period six children with double heredity withdrew from the study because their parents objected to the venepunctures. Thus, 65 infants from Skövde (diet group=D group) and 50 infants from Borås (non-diet group=ND group) completed the study (Table 1).

Diet

The D group comprised the 65 infants in Skövde who

Table 1. Comparability of the maternal groups

	Number of mothers/infants	
	D	ND
Number of pregnant women		
Selected at antenatal clinic	129	108
Fulfilling criteria	95	82
Number of infants		
Fulfilling criteria	67	54
Drop outs	2	4
Completing study	65	50
Double heredity	59	44
Single heredity and CB-IgE ≥ 0.9 kU/l	6	6

completed the study. The mothers had a first consultation with an experienced dietitian during the first 2 weeks of the third trimester of their pregnancy. The dietitian evaluated the dietary habits of the family and gave the mothers information on how to manage with a diet free from eggs, CM and fish that was to be started immediately after delivery and to continue for 3 months. The families were given a list of commercially available products free from eggs, CM and fish products. The mothers diet were supplemented with extra calcium and multivitamins during the diet period. The information was followed up on the obstetric ward and 6 weeks and 3 months after delivery as well as on individual request during the 3-month diet period. The ND group comprised the 50 infants in Borås who completed the study. None of these mothers was lacto-vegetarian and all used CM daily. No particular information regarding the maternal diet was given, and none of the mothers tried prophylactic regimen by herself.

The diet for the infants was the same in both groups. During the first 6 months only breast milk and/or formula based on hydrolysed casein (Nutramigen) was given. After 6 months of age supplementary foods, including CM products, were introduced in all children. Products containing eggs and fish were not introduced until after 9 months of age. Supplemental A-D vitamins were given as recommended in Sweden, i.e. at 6 weeks. The parents recorded any mistakes made with the maternal diet (group D) and the baby diet.

Follow up

All infants were examined neonatally and at 3, 6, 9, 12 and

18 months of age. A history was obtained employing a standardized questionnaire and a physical examination was made focussing particularly on symptoms of atopy/allergy. Weight and length were also recorded. Venous blood was sampled at all visits and the sera were frozen at -20°C and stored for later analysis. In addition, SPT were done at 9 months of age.

In group D there were two additional visits, one for follow-up of the maternal diet and blood sampling at 6 weeks of age and another for blood sampling at 3.5 months, i.e. 2 weeks after cessation of the maternal avoidance diet.

Clinical criteria of atopy/allergy

AD was defined as pruritic, chronic or chronically relapsing, non-infectious dermatitis of typical morphology and distribution based on the suggestions by Hanifin [4]. The diagnosis was verified in all cases by one of the investigators. The eczema was regarded as severe if it was generalized and/or if there was a need for hospitalization, moderate if localized and requiring frequent application of steroid ointments, and mild if no or only mild steroid ointments were needed for 1–3 days.

An episode of bronchial obstruction was accepted as such only if diagnosed by a physician and after examination of the case record by one of us. Three or more episodes of bronchial obstruction was regarded as asthma. ARC was defined as rhinitis and conjunctivitis appearing at least twice after exposition to a particular allergen and not related to infection. Urticaria was defined as allergic if it appeared at least twice within 1 hr after exposure to a particular antigen. Positive exposure to an allergen was defined as an obvious reaction within 1 hr after the exposure on at least two occasions. Serious

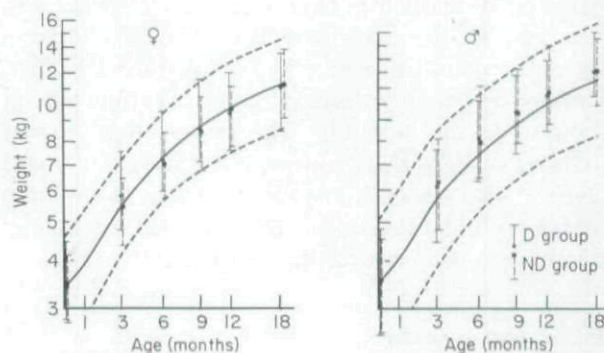


Fig. 1. Weight development in infants of mothers practising antigen avoidance during lactation (●) and infants of mothers not on food restriction (■). The mean, the maximal and the minimal weights are shown for each follow-up examination. The Swedish nomogram (mean weight ± 2 s.d.) is shown.

immediate reactions (e.g. anaphylactic reaction) after contact with a definite allergen was also considered positive.

In order to ensure uniform classification, the records of all the children were evaluated repeatedly and jointly during the study period by the three investigators involved in the clinical assessment.

Laboratory methods

The IgE levels in the cord blood were analysed by a previously described modification of the Phadebas test (IgE PRIST, Pharmacia Diagnostics, Uppsala, Sweden), with a sensitivity of 0.125 kU/l [1].

SPT were performed at 9 months of age as a single test on the volar aspects of the forearms with extracts (egg white, CM and fish) from Dome/Hollister-Stier using 1:20 concentrations (w/v). Histamine dihydrochloride (1 mg/ml) and Coca's solution served as positive and negative controls. The SPT was regarded as positive when the mean diameter of the weal, i.e. half the sum of the largest diameter and its perpendicular, was ≥ 2 mm and the mean diameter of the negative control was < 1 mm.

Statistics

Chi-squared test with Yates' correction was used to test the significance of the difference between the two groups. Fisher's exact test (two-tailed), was used if the table cell was < 5 . Not significant implies $P \geq 0.05$.

Results

Maternal and infant diet

Twelve mothers of group D mistakenly ate food containing very small amounts of milk protein: one of them also ate a fish-containing product. Eight of the mothers failed only once, three mothers twice and one mother three times. The ingested food was one biscuit or slice of crisp bread, margarine or butter on an open sandwich, a piece of sausage or a mouthful of mackerel sauce possibly containing CM protein. No mother ate eggs or any egg-containing products during the diet period.

The weight of 66% of the group D mothers returned to prepregnant levels within 3 months after delivery, to be compared with 20% of the mothers in the ND group ($P < 0.001$).

The duration of breast-feeding was similar in the two groups. Full breast-feeding up to more than 3 months occurred in 39 infants (59%) in group D and in 34 infants (68%) in group ND. Full breast-feeding up to 6 months occurred in 27 D infants (43%) and 18 ND infants (36%).

Table 2. Cumulative incidence (%) of atopic manifestations and adverse reactions to food in two groups of infants with family history of atopy

		Age interval (months)				
		0-3 (%)	0-6 (%)	0-9 (%)	0-12 (%)	0-18 (%)
Symptoms						
Eczema	D	<u>3.1</u>	<u>10.8</u>	16.9	23.1	26.2
	ND	<u>22.0</u>	<u>28.0</u>	30.0	38.0	40.0
Asthma/ bronchial obstruction	D	0	3.1	4.6	7.7	14.0
	ND	0	2.0	4.0	8.0	8.0
Other	D	0	3.1	9.2	13.8	16.9
	ND	0	2.0	4.0	10.0	10.0
Adverse reactions to:						
Eggs	D	0	1.5	1.5	1.5	7.7
	ND	2.0	2.0	2.0	2.0	6.0
CM	D	0	3.1	10.8	10.8	10.8
	ND	4.0	6.0	14.0	14.0	14.0
Fish	D	0	3.1	3.1	3.1	3.1
	ND	0	0	0	2.0	2.0
Totals	D	0	6.0	10.8	10.8	12.3
	ND	6.0	8.0	16.0	18.0	18.0

D = maternal diet for 3 months ($n = 65$), ND = maternal nondiet ($n = 50$). Statistically significant differences between the D and ND groups are underlined.

Eight D babies and 10 ND babies were mistakenly given food off the list but only on one occasion. Two group D infants got breast milk from another mother during their stay in the maternal ward, four were fed a CM-containing formula before the age of 6 months and two consumed egg-containing products and/or fish 2-5 days before the 9-month check. Two of the ND infants were fed a CM-containing formula before 3 months of age and eight infants between 3 months and 6 months.

There was no significant difference in weight gain between the two groups or between the groups and the Swedish weight nomogram (Fig. 1).

Atopic manifestations and adverse reactions

As shown in Table 2 and Fig. 2 the cumulative incidence of children with AD was significantly higher in the ND group at 3 and 6 months ($P = 0.002$ and 0.033 , respectively) but not at 9, 12 and 18 months ($P = 0.151$, 0.125 and

0.169, respectively). During the first 9 months of age openly one of the D group infants had a severe AD to be compared with seven infants in the ND group. The number of children with obstructive bronchitis, asthma, ARC, anaphylactic reaction and urticaria was similar in both groups. The results were not influenced by exclusion of the children exposed to dietary mistakes, involving either themselves or their mothers.

The cumulative incidence (%) of allergic/adverse reactions to eggs, CM or fish are shown in Table 2. The three ND infants considered to react to the maternal consumption of eggs or CM before 3 months of age manifested a rash within 1 hr of breast-feeding. The mothers had previously eaten substantial amounts of the foods during the day. Between 3 and 6 months of age three D infants and one ND infant reacted to maternal consumption of eggs, CM or fish. Between 6 and 9 months of age when CM had been introduced in the babies diet, five D infants and four ND babies reacted to CM. Between 9 and 18 months of age, i.e. after the introduction of eggs and fish, four D and two ND infants reacted to these nutrients. There were no significant differences between the groups at any age interval.

SPT and CB-IgE

Positive SPT to egg white or CM at 9 months of age were noted in 10 D infants and nine ND infants (Table 3). No infant had a positive SPT to fish antigen. In both groups egg white was the dominant allergen.

The CB-IgE levels were similar in both groups. Thus, in babies with double heredity the median values were 0.125

Table 3. Weal diameter (mm) in SPT-positive infants

Infants	Histamine	Allergen	
		Egg white	CM
Diet group (n = 10)			
1	3.0	2.0	—
2	3.5	3.0	—
3	3.5	3.0	—
4	4.0	5.5	—
5	4.5	7.0	2.5
6	4.5	7.0	—
7	4.5	6.0	—
8	6.0	3.0	3.0
9	6.0	7.5	6.0
10	> 10	7.5	—
Non-diet group (n = 9)			
1	3.0	2.0	—
2	3.0	2.0	—
3	3.0	3.0	—
4	3.0	3.0	—
5	3.0	4.0	3.0
6	3.0	4.0	3.0
7	3.0	5.0	—
8	5.0	—	5.0
9	7.0	11.0	—

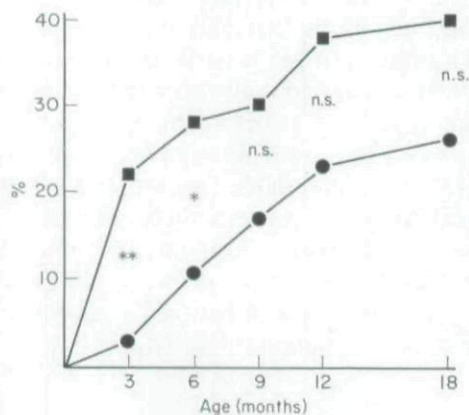


Fig. 2. Cumulative incidence of atopic dermatitis in infants of mothers practising food antigen avoidance during lactation (●) and infants of mothers not on food restriction (■). Not significant (n.s.), $P > 0.05$; significant (*), $0.05 \geq P \geq 0.01$; significant (**), $0.01 > P \geq 0.001$.

kU/l, and elevated levels, i.e. above 0.9 kU/l were seen in three D infants and two ND babies.

Discussion

The incidence and severity of AD was lower for the first 6 months of life in the babies of mothers avoiding eggs, CM and fish during the first 3 months of lactation. From 9 months of age, there was a non-significant tendency to lower AD-rate up to 18 months. It is possible that a larger study population may have shown a beneficial effect of the dietary regimen also after the first 6 months of life.

The dietary regimen did not affect the rate of bronchial obstruction, ARC, urticaria and/or anaphylactic reactions at any age. We find it natural that the AD manifestation of atopy, rather than respiratory symptoms seemed to be influenced by the diet as AD during infancy is often influenced by an IgE-mediated food allergy and can be aggravated by food antigen in the breast milk [5,6].

The lower rate of AD during the first 6 months in the D group could be due to a lower sensitization rate or by

antigen doses that were too low to provoke symptoms. In two recent reports it was suggested that maternal antigen avoidance during pregnancy and during the first months of lactation could reduce the incidence of AD in babies [6,7]. A recent study from our group did not, however, show any effect of maternal avoidance diet during pregnancy [3]. The results of the 1986 reports from Chandra [6] and Zeiger [7], might therefore be explained by an effect of the diet postpartum similar to our findings in this study.

The fact that the two groups of infants were recruited in two different hospitals can be criticized. However, a true randomization would have involved the risk of ND mothers adapting to the diet of the D mothers. We know from clinical experience that many families with pronounced heredity for atopic/allergic diseases enthusiastically try various prophylactic regimens for their potentially allergic infants. We selected therefore, two towns of equal size, localized 60 miles apart in geographically and socioeconomically similar areas. The general hospitals of the towns were equal in size and had similar number of deliveries per year.

Since the season of birth may influence the incidence of allergy [8-11] the studies were started and ended at the same time. We consider the groups of infants are comparable since the same antenatal and postnatal selection criteria were used and they were similar with regard to the distribution of double and single heredity for atopic disease, the proportion of mothers excluded for various reasons, the number of infants not completing the study, the pattern of breast feeding, the number of dietary errors and the distribution of cord blood IgE values.

Since the follow up was not blind (due to the use of matched groups), we tried to eliminate any possible bias by strict uniform classification of atopic/allergic manifestations before the study and by careful discussion of each case record.

The pattern of breast feeding was similar in both groups of infants and to that reported for Swedish infants [12,13]. Despite extensive information to the mothers in the D group and the continuous support of a dietitian, 12 mothers made occasional errors related to their diet. The errors were minor however, and occurred only once in nine mothers, twice in two and three in one mother. All the mistakes occurred when someone else had prepared the food. Such minor mistakes apparently cannot be avoided entirely and we allowed inclusion of the 12 mothers in the final study-group, especially since exclusion of them did not influence the results. In other similar studies such mistakes have been accepted up to four times [5] or not recorded [6,7].

There was no difference between the two groups concerning the clinical reactions to eggs, CM or fish, and

the SPT results were similar in the two groups. We could thus, not show any effect of the maternal diet on the allergy *per se*. Eighteen infants had a positive SPT to egg white, though egg white was not fed to any of them during the first 9 months of life, except for possibly through the breast milk. As all eight ND infants with positive SPT to egg white had been breast fed the likely source for sensitization is small doses of egg white antigen in the breast milk.

In the D group none of the 10 infants with positive SPT to egg white received any egg white through the breast milk during the first 3 months and none of them were given any egg white in their own diet during the first 9 months. However, in nine of them breast-feeding continued after 3 months of age and this could imply a possible route of sensitization. In the tenth infant the route of sensitization is not clear as she was weaned when her mother was still on a hypoallergenic diet. Possible explanations for her sensitization include contact with low doses of antigen during the preparation of food, e.g. by inhalation, an unobserved supply of egg white by mouth or a transplacental transfer of anti-idiotypic antibodies [14]. Although maternal diet did not influence the sensitization to foods as determined at 9 months of age, there may be difference in sensitization before that age.

All of the 37 D mothers with previous atopic/allergic children thought that their babies showed less pronounced or no atopic/allergic manifestations at all compared with their siblings, and four mothers who had borne another infant during the study period used the same diet on their own initiative. Further studies are needed before a general recommendation about maternal antigen avoidance during lactation can be made to families with a history of atopy/allergy. Individual recommendations are, however, feasible in families with pronounced heredity and with previous familial experience of severe atopy/allergy.

In conclusion, a maternal diet devoid of eggs, CM and fish during the first three months of breast feeding seemed to decrease the incidence and severity of AD for the first 6 months of life in infants with a heredity of atopy. The number of other atopic manifestations were, however, similar in both groups, as well as the incidence of sensitization and adverse reactions to eggs, CM or fish.

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