

Maternal abstention from cow milk and egg in allergy risk pregnancies

Effect on antibody production in the mother and the newborn

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To study the possibility of intrauterine sensitization, 212 women were enrolled on a voluntary basis into a prospective, randomized study, comparing the effects of an elimination diet and normal food during late pregnancy. The diet group took no cow milk and no egg from week 28 to delivery, and extra calcium and casein hydrolysate (Nutramigen®) supplement was given to fill the nutritional needs of mother and child. The control group took normal food, including approximately 1/2 liter of milk/day and 3-5 eggs/week. All families had a history of allergy in mother, father, or sibling. Maternal weight gain during pregnancy was significantly lower in the diet group. Birth weights showed no significant difference between the two main groups, but smokers in the elimination diet group had significantly smaller babies. IgE antibodies to cow milk and egg were significantly higher in atopic than in non-atopic women before the trial. The diet caused a significant fall in IgG-antibodies to cow milk and egg in both atopic and non-atopic subjects. Cord blood IgE determination revealed no significant difference between the groups. No IgE antibodies to cow milk or egg were detected in any of the cord sera. The participating babies are being followed up until 18 months of age.

Key words: cord blood IgE; cord blood IgG; intrauterine sensitization.

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The human fetus is able to synthesize IgE long before birth, as has been demonstrated in fetal lung and liver cells from the 11th week of gestation (16), and the placenta prevents the passage of IgE antibodies from mother to child (7, 12, 15). Thus, provided fetomaternal blood admixture has not occurred at delivery, IgE antibodies in cord sera should be of fetal origin.

There is substantial evidence that IgE elevation at term is of value in the prediction of allergy (1, 3, 4, 15). Specific IgE antibodies not present in corresponding maternal sera have been reported in a few cases (1, 15), possibly indicating intrauterine sensitization.

Besides constituting a potent barrier to protect the fetus, the placenta provides a route of active transport of protective immunoglobulins from mother to offspring. Therefore at term, the serum

IgG level is higher in the baby than in the mother. Although fetal synthesis of IgG has been found from the 21st week of gestation (18), the bulk of cord IgG probably derives from the mother.

The intrauterine environment also greatly reduces the exposure of the fetus to, for instance, inhalant allergens. The fetomaternal blood circulation in the placenta might, however, constitute a pathway for the transport of intact or break-down products of food proteins. Such proteins are normally present in the serum of healthy adults after a meal (17).

In a fetus with a genetical predisposition to allergy, even minute quantities of allergen might induce sensitization. It has been shown in animal studies that a small dose of antigen is more likely to sensitize than a large dose (9).

It has been suggested that maternal elimination

of certain highly allergenic foods in pregnancy could be a way of preventing allergy. In a previous, non-randomized study (8), such measures as avoidance of smoking, pets and certain dietary factors including cow milk and egg, had no effect on the IgE concentration of the neonates. Even if this does not preclude a lower allergy risk during infancy as a result of the diet, some doubt arose about possible positive effects of diet. Dietary manipulation during pregnancy might expose mother and baby to the risk of malnourishment and should not be recommended unless proven effective.

The aims of the present study were:

- a) to study the effect of maternal abstention from cow milk and egg in late pregnancy on total IgE and food specific IgE and IgG antibodies in cord blood of the babies.
- b) to study maternal IgE and IgG antibody levels during pregnancy in relation to maternal diet and to maternal atopy.
- c) to evaluate for mother and child the nutritional aspects of a maternal dietary regimen by studying maternal weight gain in pregnancy and birth weight of the babies.

This paper will present the results during pregnancy and at birth. The sizes of the studied groups were selected on the basis of previous knowledge of the allergy risk in babies with positive family history (12). Data from a follow-up of all babies until 18 months of age are needed to give definite statistical proof of a possible difference between the groups.

MATERIAL AND METHODS

Patient characteristics

During one year, starting in November 1982, the midwives asked all pregnant women attending the well-mother-clinics in the Linköping area about their personal and family history of allergy: atopic eczema, allergic rhinitis, or asthma in the woman herself, in her husband and in her previous children. In families with a history of allergy in one or more members, the midwife informed the woman about the purpose of the study, and gave her written information. All interested women were

interviewed over the phone by one of the authors (K.F.M.). When the allergic history had been confirmed by telephone and the woman had accepted to participate, she was randomly assigned to either "diet group" or "non-diet group". In the phone interview, information about avoidance of smoking and pets, and recommendation to breast feed was given to *all* women. Women allocated to the diet group were informed, together with their husbands, about the diet at an informal meeting with the dietician, one specially trained nurse and one of the authors (K.F.M.).

The existence of "atopy" in the mother was confirmed by positive skin prick test (SPT) and/or specific serum IgE-antibodies. "Non-atopic" mothers had a negative history, negative SPT and/or negative RAST, and IgE below 120 kU/l (19). A further classification of data could thus be obtained according to maternal atopy/non-atopy. Four groups of mothers were formed: D_A = diet mothers, atopic ($n = 42$); ND_A = non-diet mothers, atopic ($n = 49$); D_{NA} = diet mothers, non-atopic ($n = 22$); and ND_{NA} = non-diet mothers, non-atopic ($n = 26$). Only mothers following the allocation were included in these four groups. Mothers with confounding data (e.g. positive SPT with negative history) were not accepted in this classification.

Dietary regimen

A strict cow milk- and egg-free diet was instituted from week 28 to delivery. A detailed history was taken by the dietician of meals and snacks taken by each woman, and an individual menu was proposed including a list of commercially available milk- and egg-free products. Apart from two to three complete meals (comprising meat/fish, vegetables and fruits) and 1–2 snacks a day, food was supplemented with 1 dl (= approximately 65 g) of casein hydrolysate (Nutramigen® dissolved in water or juice) and 0.25 g of calcium-phosphate (containing 50 mg Ca^{2+}) a day, giving a total amount of approx. 1200 mg (= 30 mmol) calcium daily. About half of the women took the recommended dose of Nutramigen, $\frac{1}{4}$ took lesser amounts, while the remainder could not take Nutramigen as they disliked the taste. When less than 1 dl of Nutramigen was taken, the calcium-

phosphate was increased as well as the meal size. During the diet period several phone calls from the nurse and dietician encouraged the participating women to maintain the diet. The dietician devoted at least 3 h of information to each women.

Blood sampling

Venous blood was drawn from the mothers at weeks 25 and 35 of pregnancy and at the delivery. One blood sample was drawn from the fathers. Serum IgE levels were determined in mothers and fathers, while IgE antibody levels to beta-lactoglobulin, ovalbumin and ovomucoid were determined in maternal blood at week 25 (i.e. before diet) and at delivery. Cord blood was obtained from the cut cord after careful wiping. It was collected in 195 of 210 babies, and in another six babies venous blood was drawn during the first week (these 6 sera are included in the results of cord blood IgE, Table 4). Samples were left to clot at room temperature for at least 2 h (at most 108 h), and after centrifugation sera were frozen in aliquots of 1–2 ml at -20°C for later, parallel analyses.

METHODS

The IgE level in the sera of mothers and fathers was determined by Phadebas IgE PRIST® (Pharmacia Diagnostics AB, Uppsala, Sweden), performed according to the manufacturer's recommendations and with a lowest detectable level of 2.5 kU/l. The concentration of IgE in the cord blood was analysed by a previously described extra-sensitive PRIST method (9), with minor modifications, resulting in a lowest detectable level of 0.125 kU/l.

Specific IgE was determined by Phadebas IgE RAST® (Pharmacia Diagnostics AB, Uppsala, Sweden) either according to the manufacturer's recommendations or, when analysing cord sera, in an extra-sensitive application with continuous shaking during a prolonged (20 h) first incubation. The modified procedure had a lowest detectable limit of 0.15 PRU (Phadebas Rast Unit). RAST disks with ovomucoid were prepared by coupling ovomucoid (Sigma, St Louis, USA) to CNBr activated paper, 1 µg/disc. Other allergen discs were

obtained from Pharmacia Diagnostics AB, Uppsala Sweden.

IgG antibodies to egg and milk proteins were measured by ELISA (6). Beta-lactoglobulin, ovalbumin and ovomucoid (Sigma, St Louis, USA) were coated on microtiterplates (Nunc, Roskilde, Denmark) at a concentration of 10 µg/ml, 100 µl/well. Samples, diluted 1/100, were compared to a reference standard curve and results were expressed as Arbitrary Units (U) per ml.

Total IgA content of cord serum samples was tested by ELISA (6). Rabbit anti-human IgA (Pharmacia Diagnostics AB, Uppsala, Sweden) was coated on microtiterplates as previously described for the analysis of IgG. Detection was performed by the same antibody (rabbit anti-human IgA) conjugated to alkaline phosphatase. The reference was an Immunoglobulin Standard Set (Boehringer Ingelheim GmbH, Stockholm, Sweden) and results were expressed in µg/ml.

When a cord serum had an IgE concentration above 0.5 kU/l and the corresponding maternal serum contained detectable amounts ($\text{PRU} > 0.2$) of specific IgE to any of six tested allergens (dog, cat, birch, timothy, milk, egg), the cord blood was analysed for the presence of antibodies to this major maternal allergen in order to detect maternal blood admixture.

When performing calculations, values less than the lowest detectable limit were calculated = lowest detectable limit.

After delivery, all parents were offered skin prick test (SPT), and 314 accepted (13). SPT was performed by double pricks, with Pharmalgen 10,000 and 100,000 BU/ml (birch, timothy, dog, cat, mould, house dust mite), to milk and egg with Dome-Hollister-Stier extracts 1:20 and with histamine chloride, 1 and 10 mg/ml as well as diluent.

Ethics and statistics

Informed consent was given by all participating parents and the study was approved by the Human Research Ethics Committee, Linköping.

Statistical calculations were performed with Sign-test, Student's t-test (one-tailed), and Rank Sum test.

RESULTS

Subjects' compliance

Three women of the 212 who initially accepted participation denied further participation already before delivery, and their babies were not subjected to cord blood collection or further follow-up. All three had been allocated to the diet group. The remaining 209 women had 210 babies (one pair of twins). Twenty-two women interrupted the diet, usually during the first week of diet, but completed the study. Seven women did not accept allocation to the non-diet group, and for ethical reasons obtained the same information on the diet as women primarily allocated to the diet.

Results will be given for the women randomized to diet (D_{rand} , $n = 101$) and non-diet (ND_{rand} , $n = 108$). For comparison, the results of the groups D_{true} , $n = 79$, and ND_{true} , $n = 101$ will be given, representing the women of each group who actually followed the allocation (diet or non-diet).

Family score of allergy

At the first telephone interview, an estimate of the family history for allergy (atopic eczema, allergic rhinitis or asthma) was done by a scoring system, where 0 = non-allergy, 1 = probable allergy and 2 = obvious allergy in mother, father or sibling. Obvious allergy was defined as convincing history confirmed by previous positive skin prick test

and/or positive RAST, or, in the case of atopic dermatitis, by the diagnosis of a dermatologist or pediatric allergist. A convincing history of birch pollen allergy confirmed by adverse reaction to fresh, but not prepared, stone fruits was also accepted as obvious allergy even without previous testing. Probable allergy was defined by a less convincing history and/or history not confirmed or denied by previous laboratory tests (skin prick tests, IgE, RAST). The family score was the sum of the points of the family members, with a highest score of 6 (Table 1).

After delivery further classification based on the results of IgE-tests and skin prick tests in parents was performed. The scoring system was then reevaluated, using $IgE \geq 120$ U/ml (19) and/or skin wheal diameter ≥ 3 mm as cut-off limit for positive test as a complement to the case history (Table 1).

Maternal IgG antibody levels

The mean maternal serum IgG antibody levels to beta-lactoglobulin, ovalbumin and ovomucoid at week 25 (open bars) and at delivery (hatched bars) are shown in Fig. 1 a–c respectively. According to the Sign test, a significant number of mothers were displaying reduced levels of all the three food-specific IgG antibodies after the elimination diet. For ovalbumin there were also significantly diminished values in the non-diet group, which might indicate inadvertant avoidance of egg. Atopic mothers had significantly higher anti-ovomucoid

Table 1
Family allergy score according to A) first telephone interview B) interviews, IgE and skin prick tests in mothers and fathers

Group	No.	Family score				<i>P</i> ^c
		A		B		
		Mean	Mean + 1SD	Mean	Mean + 1SD	
ND _{rand} ^a	108	2.6	3.7	2.4	3.6	NS
D _{rand} ^b	101	2.6	3.7	2.5	3.7	
ND _{true} ^c	101	2.5	3.7	2.4	3.6	
D _{true} ^d	79	2.8	3.9	2.5	3.7	NS

^aRandomized to non-diet; ^brandomized to diet; ^crandomized to non-diet, and not taking diet; ^drandomized to diet and taking diet; ^eStudent's t-test.

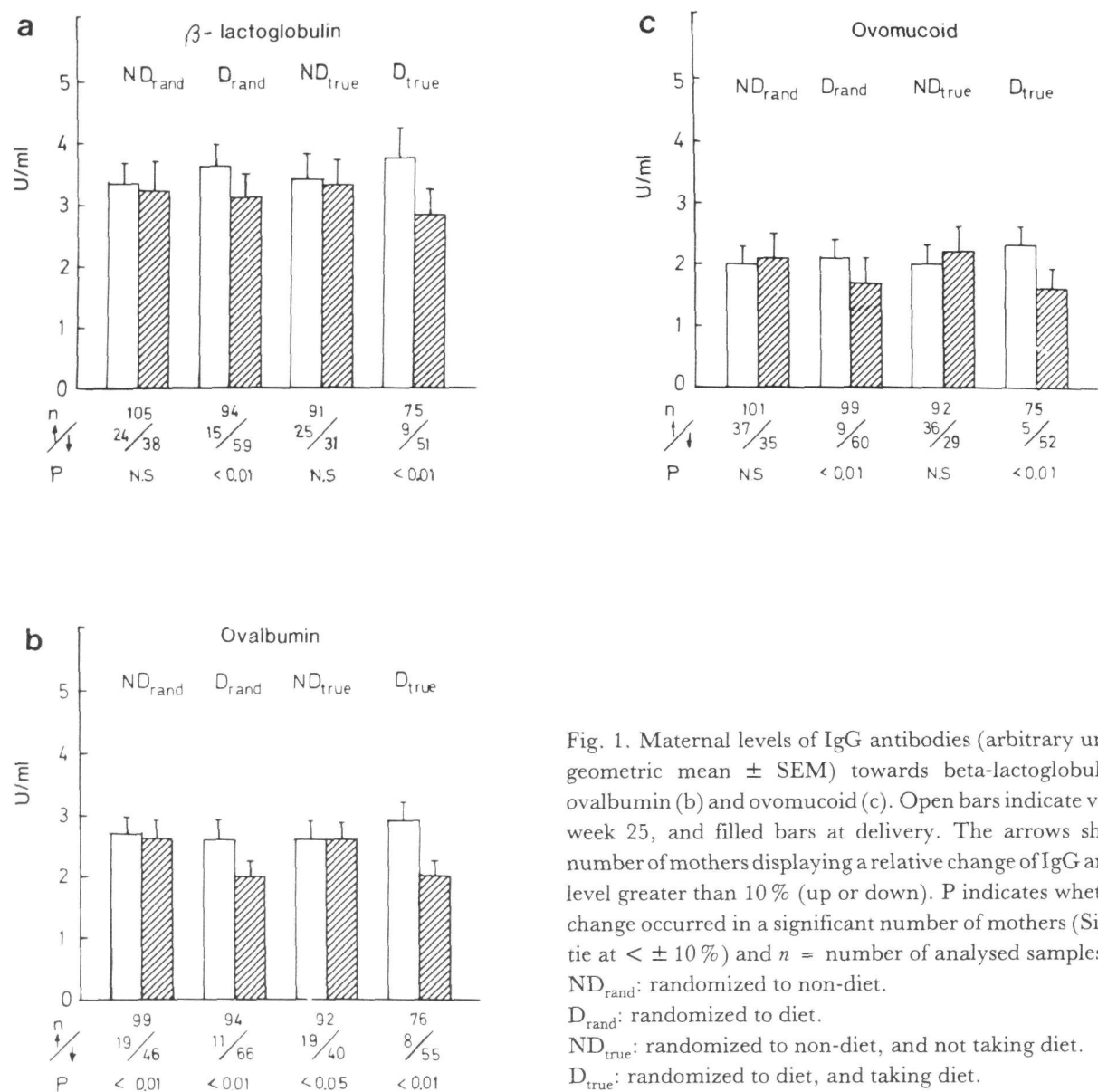


Fig. 1. Maternal levels of IgG antibodies (arbitrary units/ml; geometric mean $\pm$ SEM) towards beta-lactoglobulin (a), ovalbumin (b) and ovomucoid (c). Open bars indicate values at week 25, and filled bars at delivery. The arrows show the number of mothers displaying a relative change of IgG antibody level greater than 10% (up or down). P indicates whether the change occurred in a significant number of mothers (Sign test, tie at $< \pm 10\%$) and n = number of analysed samples. ND_{rand}: randomized to non-diet. D_{rand}: randomized to diet. ND_{true}: randomized to non-diet, and not taking diet. D_{true}: randomized to diet, and taking diet.

and anti-ovalbumin levels of IgG than non-atopic mothers, whereas anti-beta-lactoglobulin levels were not significantly different. However, elimination diet reduced the antibody levels to all three food antigens in a significant number of mothers,

irrespective of their classification (atopic or non-atopic) (Fig. 2 a-c).

Maternal weight gain in pregnancy

The average weight gain was about 20% (Table 2). However, the mothers on diet had a significantly lower increase during pregnancy than the mothers on normal food. This difference was naturally most apparent when comparing the “true” groups.

Some data are missing due to rapid labour not allowing a weight check before delivery, but comparable data are available in all groups (ND_{rand} 78.7%, D_{rand} 78.2%, ND_{true} 79.2% and D_{true} 74.7%).

Table 2

Relative maternal weight gain in percent during pregnancy

Group	No ^a	Weight gain (%)		P ^b
		Mean	Mean + 1SD	
ND _{rand}	85	22.3	30.1	< 0.005
D _{rand}	79	19.3	25.9	
ND _{true}	80	22.4	30.3	< 0.0025
D _{true}	59	18.6	24.8	

^aSome data missing due to rapid labour; ^bStudent's t-test.

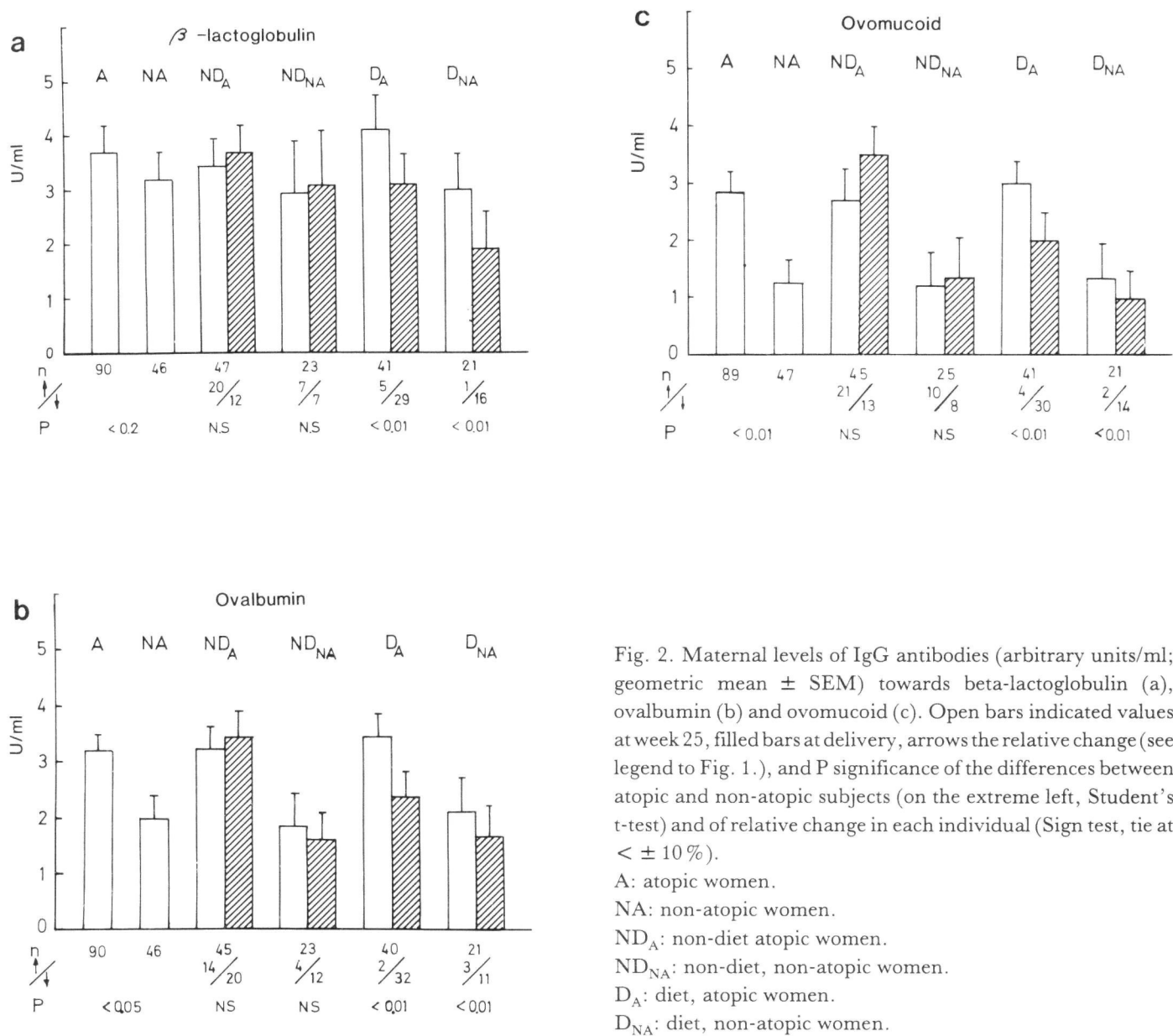


Fig. 2. Maternal levels of IgG antibodies (arbitrary units/ml; geometric mean $\pm$ SEM) towards beta-lactoglobulin (a), ovalbumin (b) and ovomucoid (c). Open bars indicated values at week 25, filled bars at delivery, arrows the relative change (see legend to Fig. 1.), and P significance of the differences between atopic and non-atopic subjects (on the extreme left, Student's t-test) and of relative change in each individual (Sign test, tie at $\leq \pm 10\%$).

Birth weight

Despite the discrepancy in weight gain of diet and non-diet mothers, there was no significant difference between the birth weights of the corresponding babies (Table 3A). Three babies were born before 36 weeks of gestational age, and had a birth weight of less than 2500 g (1530, 1680 and 1600 g respectively). The corresponding maternal diagnoses were: premature labour (week 31) in the first, and placental insufficiency due to pre-eclampsia in the remaining two. These three were all in the diet group, but the maternal diet was not considered as a contributing factor to the complications of these mothers.

When adding the information of maternal smoking habits and sex of the baby, the difference

between daughters of smoking and non-smoking mothers in the diet group is statistically significant (Rank Sum test, Table 3B). The mean parity among the non-smoking diet mothers was 1.8 ± 0.6 (mean $\pm$ SD), while it was 2.0 ± 1 among the smoking diet mothers. Thus, the higher birth weight among the daughters of non-smoking diet mothers could not be explained by higher maternal parity.

Apgar score at birth

There were no significant differences in Apgar score between the groups.

At 1 min the babies of the ND_{rand} group had an Apgar score of 8.7 ± 1.0 (mean $\pm$ SD), while the score of the D_{rand} babies was 8.9 ± 0.7 (NS).

Cord blood total IgE

There were no significant differences between the cord blood IgE concentration in the groups, either when geometric mean, or median values were compared (Table 4A). Likewise, when we excluded samples suspected of admixture of maternal blood, no significant differences were detected between the groups (Table 4B). It was previously suggested (8) that detectable IgA antibody levels in cord blood would indicate fetomaternal blood admixture, and detectable IgA levels were found only in samples with IgE antibody levels above 1 kU/l. In the present study, however, detectable levels of IgA (> 0.3 µg/ml) were found both in samples with high

and low IgE (even below < 0.125 kU/l), which might be explained by difference in sensitivity of the methods used. With the methods used here, determination of IgA in cord blood does not seem to be a reliable tool for distinguishing fetomaternal blood mixing, and only cord blood samples comprising specific IgE antibodies to a major maternal allergen (Table 4B) were excluded.

IgE antibodies in cord sera

In all cord sera, the level of IgE antibodies to beta-lactoglobulin, ovomucoid and ovalbumin was below the extended detection limit (i.e. 0.15 PRU).

IgG antibodies in cord sera

The mean IgG antibody levels to beta-lactoglobulin, ovalbumin and ovomucoid in cord sera are shown after grouping according to the mother's food intake alone (Fig. 3), and food intake and presence or absence of atopy (Fig. 4).

As expected, the levels of food specific IgG in cord sera were higher than the corresponding maternal levels (compare Fig. 3 with Fig. 1, and Fig. 4 with Fig. 2), though no statistically significant differences were found. The mean level in neonates was 114 %, 117 % and 118 % of the corresponding maternal level (for antibodies towards

Table 3 A
Birth weight of the babies (g)

Group	No.	Birth weights (g)		P*
		Mean	± 1SD	
Mothers not taking diet (all babies full term)	124	3557	431	NS
Mothers taking diet:				
all babies	86	3476	603	
full term babies	83	3544	494	

P* Student's t-test

Table 3 B

Mean birth weight (MW) of the babies in relation to maternal diet in pregnancy, maternal smoking, and sex of baby

Maternal characteristic	Male			Female		
	No.	Median	MW ± SD	No.	Median	MW ± SD
Non-diet mothers	77	3580	3588 ± 460	47	3495	3504 ± 378
Diet mothers:						
all babies	50	3635	3594 ± 543	36	3325	3313 ± 650
full term babies only	49	3650	3633 ± 473	34	3335	3416 ± 502
Non-smoking, non-diet mothers	66	3555	3585 ± 475	36	3535	3535 ± 317
Non-smoking, diet mothers:						
all babies	47	3620	3566 ± 530	29	3580	3387 ± 696
full term babies only	46	3635	3607 ± 454	27	3610	3522 ± 497*
Smoking, non-diet mothers	11	3600	3604 ± 375	11	3140	3403 ± 538
Smoking, diet mothers	3	3670	4033 ± 691	7	2880	3007 ± 268*

*P < 0.05, Rank Sum test.

beta-lactoglobulin, ovalbumin and ovomucoid respectively).

Further, there were no significant differences between babies of diet mothers and babies of non-diet mothers. However, the babies of atopic mothers had higher IgG levels than babies of non-atopic mothers (apart from beta-lactoglobulin in the non-diet group), whether the mother had been on a diet or not. This is in accordance with the findings in the corresponding maternal sera.

DISCUSSION

Manipulation of maternal food intake in pregnancy has been suggested as a means of preventing allergy, since dietary constituents might pass the placenta and sensitize or induce tolerance in the fetus (10). Another possibility, not yet fully elucidated, is the passage of anti-idiotypic antibodies of IgG subclass from mother to fetus (14). Such an antibody, being the mirror picture of a true anti-

gen, could possibly induce antibody production in the immunologically only partially competent fetus.

In this randomized continuing study, the results at birth have not demonstrated any effect of maternal elimination of cow milk and egg in late pregnancy on cord blood IgE of the baby, thus confirming the preliminary reports (8) from a previous non-randomized study.

There is no absolute guarantee that the participating mothers on diet fulfilled the obligation of the diet during the whole period. However, since all mothers were informed that continued participation in the study was allowed in spite of a break in diet, we believe that our group classification (D_{true} and ND_{true}) is correct. The significant fall in maternal IgG to food antigens in the diet group but not in the non-diet group, seems reasonable to explain by compliance to diet or non-diet.

The choice of week 28 as starting point of the diet can be questioned, since the fetus has been shown

Table 4 A
Cord blood IgE (kU/l) in the babies. All analysed samples

Group	No.	Median	Geom.mean	Mean + 1SD	Mean + 2SD	P*	Samples over detection limit
ND _{rand}	101	0.13	0.25	0.65	1.72	NS	54
D _{rand}	100	0.15	0.26	0.79	2.38		57
ND _{true}	94	0.14	0.25	0.69	1.86	NS	53
D _{true}	79	0.15	0.27	0.88	2.87		45

*Student's t-test

Table 4 B
Five samples excluded due to suspected admixture of maternal blood

Group	No.	Median	Geom.mean	Mean + 1SD	Mean + 2SD	P*	Samples over detection limit
ND _{rand}	99	0.13	0.23	0.57	1.39	NS	52
D _{rand}	97	0.15	0.23	0.56	1.34		54
ND _{true}	92	0.14	0.24	0.59	1.42	NS	51
D _{true}	76	0.13	0.22	0.54	1.33		42

*Student's t-test

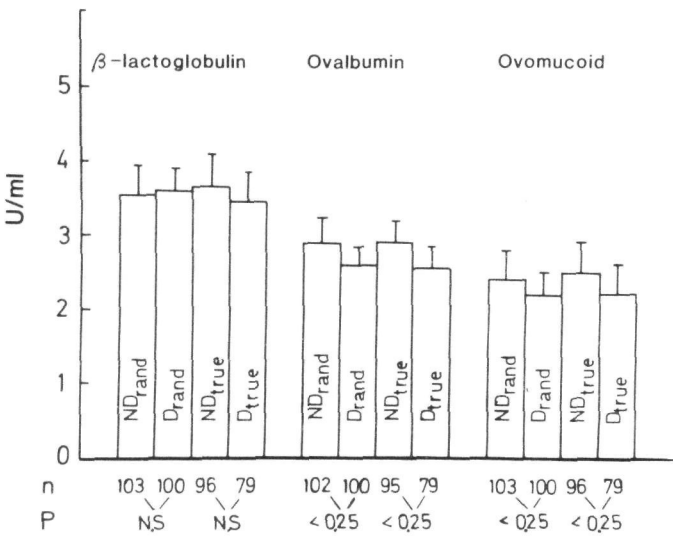


Fig. 3. Cord blood IgG antibody levels to betalactoglobulin, ovalbumin and ovomucoid (arbitrary units; geometric mean $\pm$ SEM). The groups are named according to maternal group classification (for example see Fig. 1). “n” states the number of analysed samples, and P the significance of differences between indicated groups (Student’s t-test).

to be able to synthesize IgE from the 11th week of gestation (16). Elevated IgE levels in the newborn, however, have not been reported before term (15). The main reasons for selecting the third trimester were ethical, nutritional and practical. Dietary regimen earlier in pregnancy could possibly, if the mother did not follow the advice of the dietician, lead to malnourishment of the fetus. Naturally occurring abortions and malformations might by the family be associated with the maternal diet, although a causal relationship is unlikely. Furthermore, due to the natural malaise and fatigue experienced by most women in early pregnancy, it would have been even more difficult for them to endure an extended period of exclusion diet.

Since totally egg- and milk-free food is more expensive, more time-consuming to prepare and limits the choice, the observed dropping out of 25 of 108 women randomized to diet is not surprising. Among the drop-outs, family allergy score was slightly lower (2.2 ± 0.9 , mean $\pm$ SD, compare Table 1B, NS). Also, smoking was more common among the drop-outs ($7/25 = 28\%$ compared to 12.7% in the D_{true} sample and $27/212 = 12.7\%$ in the whole group). However, since 22/25 women dropping out of diet were still subjected to follow-up and the results of the groups D_{rand} and D_{true}

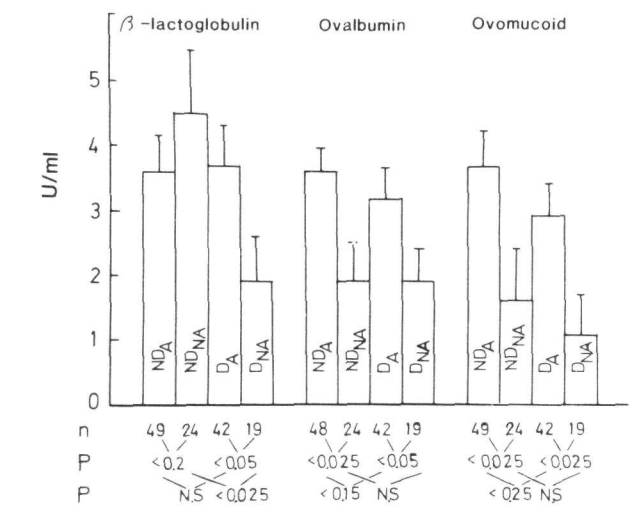


Fig. 4. Cord blood IgG antibody levels to betalactoglobulin, ovalbumin and ovomucoid (arbitrary units; geometric mean $\pm$ SEM). Groups are named according to maternal group classification (please see Fig. 2). “n” indicates number of analysed samples, and P whether there is any significant difference (Student’s t-test) between groups connected by lines.

are similar, the dropping out should not affect the conclusions drawn.

Only cow milk and egg were excluded since they are the most common foods causing IgE-mediated allergy in early infancy in Sweden (5). This probably reflects both the antigenicity and the relatively high intake of these foods in the Scandinavian countries. Individual mothers avoided also fresh stone fruits or vegetables which they could not take themselves. Other foods like fish, nuts, oranges, tomatoes, strawberries were allowed, although the mothers were advised to take moderate amounts.

In spite of the limited dietary restrictions imposed on the mothers, the professional advice and substitutes offered by the dietician and the supervision by midwives of optimal prenatal care, there was a significantly lower birth weight in diet babies when the mother was a smoker (Table 3B).

Evidently, a future beneficial effect of maternal diet in pregnancy in families at risk of allergy can not be excluded by estimation of cord blood IgE only, even if IgE has previously shown to be of good predictive value (1, 3, 4, 15). The consequences of the maternal fall in IgG-antibodies (Fig. 1a–c, 2a–c) to food antigens are not known, although it has been previously reported (2) that low levels of IgG antibodies to beta-lactoglobulin

in the mother increased the risk of cow milk allergy in the baby (at least if the baby was formula fed). Clinical follow-up of these babies and further analysis of IgE and IgG antibodies in the babies will hopefully give an answer to the question of whether dietary regimen in pregnancy should be advocated or not. In the meantime, whenever dietary restrictions are recommended to a pregnant woman, professional help from a dietician is urgently needed since elimination of any basic food requires supplementation by an equivalent substitute.

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REFERENCES

1. Businco, L., Marchetti, F., Pellegrini, G. & Perlini, R.: Predictive value of cord blood IgE levels in "at risk" newborns and influence of type of feeding. *Clin. Allergy* 13, 503-508, 1983.
2. Casimir, G., Gossart, B., Vis, H. L. & Duchateau, J.: Antibody against beta-lactoglobulin (IgG) and cow's milk allergy. *J. Allergy Clin. Immunol.* 75, 207, 1985.
3. Chandra, R. K., Puri, S. & Cheema, P. S.: Predictive value of cord blood IgE in the development of atopic disease and the role of breast feeding in it's prevention. *Clin. Allergy* 15, 517-522, 1985.
4. Croner, S., Kjellman, N-I. M., Eriksson, B. & Roth, A.: IgE-screening in 1701 newborn infants and the development of atopic disease during infancy. *Arch. Dis. Child.* 57, 364-368, 1982.
5. Dannaeus, A., Johansson, S. G. O. & Foucard, T.: Clinical and immunological aspects of food allergy in childhood. II. Development of allergic symptoms and humoral immune response to foods in infants of atopic mothers during the first 24 months of life. *Acta Paediatr. Scand.* 67, 497-504, 1978.
6. Engvall, E. & Perlman, P.: Enzyme-linked immunosorbent assay (Elisa) III. Quantification of specific antibodies by enzyme-labelled anti-immunoglobulin in antigen-coated tubes. *J. Immunol.* 109, 129-135, 1972.
7. Hamburger, R. N.: Development and inheritance of IgE and allergy. *Allergol. Immunopathol. Suppl.* II, 101-106, 1974.
8. Hamburger, R. N., Heller, S., Mellon, M. H., O'Connor, R. D. & Zeiger, R. S.: Current status of the clinical and immunological consequences of a prototype allergic disease prevention program. *Ann. Allergy* 51, 281-290, 1983.
9. Hemady, Z., Blomberg, F., Gellis, S. & Rocklin, R. E.: IgE production *in vitro* by human blood mononuclear cells: a comparison between atopic and non-atopic subjects. *J. Allergy Clin. Immunol.* 71, 324-330, 1983.
10. Jarrett, E. E. E. & Stewart D. C.: Rat IgE production. I. Effect of dose of antigen on primary and secondary reaginic antibody responses. *Immunology*, 27, 365-377, 1974.
11. Jarrett, E. E. E. & Hall, E.: The development of IgE-suppressive immunocompetence in young animals; influence of exposure to antigen in the presence or absence of maternal immunity. *Immunology* 53, 365-373, 1984.
12. Kjellman, N-I. M. & Johansson, S. G. O.: IgE and allergy in newborns and infants with a family history of atopic disease. *Acta Paediatr. Scand.* 65, 601-607, 1976.
13. Kjellman, N-I. M., Dreborg, S., Fälth-Magnusson, K.: Skin prick test with Phazet™ compared with allergen extracts, serum IgE and history in 314 adults (submitted).
14. Melander, L., Carlsson, B., Hanson, L.-Å.: Secretory IgA and IgM antibodies to E-coli 0 and poliovirus I antigens occur in amniotic fluid, meconium and saliva from newborns. A neonatal immune response without antigenic exposure - a result of anti-idiotypic induction? *Clin. Exp. Immunol.* 63, 555-561, 1986.
15. Michel, F. B., Bousquet, J., Greillier, P., Robinet-Levy, M. & Coulomb Y.: Comparison of cord blood IgE concentrations and maternal allergy for the prediction of atopic disease in infancy. *J. Allergy Clin. Immunol.* 65, 422-430, 1980.
16. Miller, D. L., Hirvonen, T. & Gitlin, D.: Synthesis of IgE by the human conceptus. *J. Allergy Clin. Immunol.* 52, 182-188, 1973.
17. Paganelli R., Matricardi, P. M. & Aiuti, F.: Interactions of food antigen-antibody complexes in health and disease. *Clin. Rev. Allergy* 2, 69-78, 1984.
18. van Furth, R., Schuit H. R. E., Hijmans W.: The immunological development of the human fetus. *J. Exp. Med.* 122, 1173-1188, 1965.
19. Zetterström, O. & Johansson, S. G. O.: IgE concentrations measured by PRIST® in serum of healthy adults and in patients with respiratory allergy. *Allergy* 36, 537-547, 1981.

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