

Factors associated with maternal dietary intake, feeding and weaning practices, and the development of food hypersensitivity in the infant

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Maternal diet during pregnancy and breastfeeding, as well as infant feeding and weaning practices, may play a role in the development of sensitization to food and food hypersensitivity (FHS) and need further investigation. Pregnant women were recruited at 12 wk pregnancy. Information regarding family history of allergy was obtained by means of a questionnaire. A food frequency questionnaire was completed at 36 wk gestation. Information regarding feeding practices and reported symptoms of atopy was obtained during the infants' first 3 yr of life. Children were also skin-prick tested at 1, 2 and 3 yr to a pre-defined panel of food allergens. Food challenges were conducted where possible. Maternal dietary intake during pregnancy, and breast-feeding duration did not influence the development of sensitization to food allergens or FHS, but weaning age (≥ 16 wk) did for sensitization at 1 yr ($p = 0.03$), FHS by 1 yr ($p = 0.02$), sensitization at 3 yr ($p = 0.01$) and FHS by 3 yr ($p = 0.02$). In contrast, children who were not exposed to a certain food allergen before the age of 3–6 months were less likely to become sensitized or develop FHS. Women with a family history of allergic disease were more likely to breastfeed exclusively at 3 months ($p = 0.008$) and avoid peanuts from the infant's diet at 6 months ($p = 0.03$). Maternal dietary intake during pregnancy, and breast-feeding duration did not appear to influence the development of sensitization to food allergens or FHS. Weaning age may affect sensitization to foods and development of FHS. A history of allergic disease has very little impact on maternal dietary, feeding, and weaning practices.

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Background

A small number of studies have investigated maternal dietary intake during pregnancy and its role in the development of allergic disease. These studies included food avoidance during pregnancy (1, 2), the role of fruit and

vegetable intake (3), peanut consumption (4, 5), maternal fat intake and fatty acids (6, 7), and the role of probiotics (8). None of these studies found a conclusive relationship between the factors studied and the development of food hypersensitivity (FHS) or allergic disease.

In the UK, the main study in this area was a cross-sectional study which investigated maternal peanut consumption in relation to development of peanut allergy in the child (4). This study led to the main recommendations of the Committee on Toxicity (COT) report (1998), Department of Health, UK. The COT report recommends that women from atopic families (either the woman herself, the father or a sibling suffer from allergic disease) may wish to avoid peanut during pregnancy and breastfeeding (9). We have previously reported that this information has been misinterpreted by health care professionals and pregnant women (10) and that pregnant women find this information difficult to interpret (11). Interestingly, van Odijk et al. found that some pregnant women in Sweden avoided peanuts during pregnancy for allergy prevention, even though this is not recommended in Sweden. This avoidance of peanut was also unrelated to atopic status of these families (12).

The avoidance of allergenic foods during breastfeeding has also been investigated and a reduction in some manifestations of allergies (mostly eczema) has been reported. However, a number of methodological issues make it difficult to draw any firm conclusions from these studies (13, 14).

Breast-feeding duration and the development of allergic disease or FHS also need further investigation. The American Academy of Pediatrics recommends exclusive breastfeeding for high-risk infants for 6 months (15). Two recent review papers recommended a period of exclusive breastfeeding for 4–6 months (16, 17).

The American Academy of Pediatrics recommends that solid foods should not be introduced into the diet of high-risk infants until 6 months of age, with dairy products delayed until 1 yr, eggs until 2 yr, and peanuts, nuts, and fish until 3 yr of age (15). A European Academy of Allergy and Clinical Immunology task force recommends that solids and cow's milk should not be introduced for the first 4 months (16, 18). The British Dietetic Association (19) recommends weaning from 6 months of age, with those foods more likely to precipitate food allergies introduced singly and with caution.

The above data highlight a lack of clarity regarding maternal dietary intake and feeding and weaning practices in the development of allergic disease and FHS *per se*. It is therefore important to determine if these factors do play a role in the development of FHS.

In addition, it is unclear whether the dietary, feeding, and weaning practices of women with a personal or family history of allergic diseases

differ from those without any personal or family history of allergy. If their diets differ, it may partially explain why children from atopic families are more likely to develop allergic diseases themselves.

A few studies previously looked at the role of family atopy on breast-feeding duration and reported no difference between atopic and non-atopic families (12, 20). Two further studies investigated whether a family history of allergic disease had any effect on weaning practices. van Odijk et al. found no difference between timing of introduction of solids or introduction of highly allergenic foods in the atopic and non-atopic families (12). In contrast, Schoetzau et al. (21) found that mothers of infants with a family risk of eczema had delayed solid food feeding beyond the first 6 months more frequently than mothers of subjects without a family history.

Therefore, the aims of this study were to determine (i) the role of maternal dietary intake, feeding, and weaning practices in the development of sensitization to foods and FHS in the infant and (ii) if maternal dietary intake, feeding, and weaning practices are influenced by a personal or family history of allergy.

Methods

All pregnant mothers with an estimated delivery time between 1st September 2001 and 31st August 2002 were approached at antenatal clinics to participate in this study. Following consent, information regarding family history of allergy (parental or sibling), parental smoking, social class, and household pets was obtained by means of a standardized questionnaire.

A validated food frequency questionnaire (FFQ) was completed (22) by the pregnant women at 36 wk gestation. At 3, 6, and 9 months, as well as 1, 2, and 3 yr, information regarding feeding practices, immunization status, and reported symptoms of atopy were obtained using a standardized questionnaire administered by telephone. Most questions were based on the ISAAC questionnaires (23).

Therefore, in this paper, atopic and non-atopic families are defined based on a reported history of allergic disease using the ISAAC questions (23).

Two members of the research team screened this information and those parents who reported their child having an adverse reaction to a food were contacted. Children with an indicative history were invited to attend the Allergy Centre where a more detailed history was taken to ascertain which foods were implicated in

producing the reported symptoms. Information regarding description of symptoms, time of onset and duration of reaction, quantity of food required to elicit symptoms, and the number of times the reaction had occurred was obtained. In addition they were skin-prick tested to the suspected foods at the time they presented. Children were also skin-prick tested at 1, 2, and 3 yr to a pre-defined panel of food allergens which included milk, egg, wheat, cod, peanut, and sesame.

An allergen skin-test reaction with a mean wheal diameter of at least 3 mm more than the negative control was regarded as positive (24).

Food challenges were conducted with all foods from 6 months of age as described previously (25), except for peanut and sesame, which were conducted once the children were 3 yr old, as it is considered that infants should not be exposed to these foods in the first few years of life (Sampson H, Hill D, Hourihane J, personal communication, 2003). Some were excluded from food challenges because their skin prick test (SPT) diameter was above the 95% positive predictive level.

Analysis of data

All data were double entered by different operators on SPSS versions 10 and 11 and were compared and verified (SPSS Inc, Chicago, IL, USA). Associations between categorical variables were investigated using Fisher's Exact test and summarized using odds ratios. Duration of breastfeeding was investigated using Kaplan-Meier survival functions and comparisons between subgroups made using the Logrank test.

Results

During recruitment, data were obtained from 969 (91% of the total population) (25) families of the birth cohort. The age of the pregnant women ranged from 15 to 44 yr with a mean age of 27 yr and 10 months. The birth cohort comprised 500 boys and 469 girls. Of the 969 families recruited, 806 (83.2%) of the families (mother, father or sibling) and 581 (60%) of the pregnant women reported a history of allergic disease.

Pregnancy

Frequency of intake of the main allergenic foods during pregnancy, as determined by the validated FFQ was available from 937 mothers (Table 1).

Dietary practices were similar for most of the factors investigated. However, pregnant women

Table 1. Reported frequency of intake of main allergenic foods during pregnancy (n = 937)

Food	Never	Moderate	Frequent	Uncertain
Milk	2 (<1)	97 (10)	831 (89)	7 (1)
Wheat	1 (<1)	75 (8)	857 (92)	4 (<1)
White fish	107 (11)	782 (84)	44 (5)	4 (<1)
Shell fish	562 (60)	370 (40)	2 (<1)	3 (<1)
Oily fish	500 (53)	425 (45)	9 (1)	3 (<1)
Peanut	502 (54)	414 (44)	16 (2)	4 (<1)

Values are expressed as n (%).

with a maternal history of atopic disease were more likely to smoke (37.6% vs. 29.4%, $p = 0.01$, OR = 1.45, 95% CI: 1.09–1.91) and to take a multi-mineral supplement (19.4% vs. 13.6%, $p = 0.02$, OR = 1.52, CI: 1.05–2.23) during pregnancy. Pregnant women with a family history of atopy were less likely to stop smoking during pregnancy (31.3% vs. 48.9%, $p = 0.02$, OR = 0.48, 95% CI: 0.24–0.96).

Information on maternal dietary intake during pregnancy and infant sensitization to foods was available on 77.6% (752/969) of the birth cohort at 1 yr and 65.2% (632/969) at 3 yr. At 1 yr, 17 children (25) were sensitized to any of the pre-defined food allergens and 23 children at 3 yr (24). FHS was diagnosed in 39 children by 1 yr and 58 children (77 foods) by 3 yr. This was based on open food challenges and a clear history and/or positive SPT (Table 2 and 3). In this small number of children, frequency of food intake during pregnancy did not appear to influence the development of FHS. For both sensitization and diagnosed FHS, statistical interferences could not be measured due to the small numbers.

A total of 614 mothers (66.2%) breastfed the infant for ≥ 1 wk. These mothers were asked regarding any food avoidance during breastfeeding. In total, 265/614 (43.1%) mothers reported to avoid one or more foods from their diets with 39 mothers avoiding more than one of the main food allergens (Fig. 1). We found no difference

Table 2. Maternal dietary intake during pregnancy and infant's FHS at 1 yr

FHS	Reported frequency of maternal consumption during pregnancy				Total
	Never	Moderate	Frequently	Uncertain	
Milk					
Positive	1 (4)	0 (0)	18 (82)	3 (14)	22
Negative	1 (<1)	97 (11)	813 (89)	3 (<1)	914
Wheat					
Positive	0 (0)	0 (0)	4 (100)	0 (0)	4
Negative	1 (<1)	75 (8)	853 (91)	4 (<1)	933

Values are expressed as n (%).

Table 3. Maternal dietary intake during pregnancy and infant's FHS in the first 3 yr of life

Food hypersensitivity	Maternal reported rate of food consumption during pregnancy				Total
	Never	Moderate	Frequently	Uncertain	
Milk					
Positive	1 (4.0)	2 (8)	20 (80)	2 (8)	25
Negative	1 (<1)	95 (10)	810 (89)	5 (<1)	911
Wheat					
Positive	0	0	4 (100)	0	4
Negative	1 (<1)	75 (80)	853 (91)	4 (<1)	933
Fish					
Positive	0	1 (1000)	0	0	1
Negative	107 (11)	781 (83)	44 (5)	4 (<1)	936
Peanut					
Positive	6 (55)	4 (36)	1 (9)	0	11
Negative	496 (54)	410 (44)	15 (26)	4 (<1)	925

Values are expressed as n (%).

between mothers with and without a history of atopy. Statistical interferences could not be measured due to the small numbers of mothers avoiding each of the major allergens.

Infant feeding practices during the first 3 yr of life

Information regarding infant feeding practices was obtained from 927 (95.7%) mothers at 3 months, 913 (94.2%) mothers at 6 months, 900 (92.9%) at 9 months, 900 (92.9%) at 12 months, 858 (88.5%) at 2 yr, and 891 (92%) at 3 yr.

Feeding practices regarding method of feeding, duration of breastfeeding, introduction of formula feeding are summarized in Table 4. The overall median duration of breastfeeding is 42 days (95% CI: 35–56 days). There is no evidence of a significant difference between

infants born in families with a history of atopy (Logrank test, $p = 0.662$). The median time to introduction of formula feed is 14 days (95% CI: 14–21 days). There is no evidence of a significant difference between infants born in families with a history of atopy (Logrank test, $p = 0.776$). Different types of formulas were used in the infants' diet at different stages. This is summarized in Table 5.

To investigate the role of breastfeeding on the development of sensitization to foods and FHS, the following criteria were considered: exclusive breastfeeding at 3 months, any breastfeeding at 6 and 9 months, any breastfeeding for longer than 9 months and 'ever' breastfed. There was no statistically significant association in terms of sensitization to food allergens or development of FHS at 1 or by 3 yr and breastfeeding practices defined as any of the criteria stated above.

Infant weaning (introduction of solids) during the first 3 yr of life

More than a quarter [27.3% (256/937)] of mothers had introduced solids into the infant's diet by 3 months of age, 82.1% (750/913) before 17 wk (45.6% – 416/913 before 16 wk) and all mothers by 6 months. At 6 months, 61.6% (562/913) of mothers were avoiding some foods from the infant's diet. The corresponding figures for 9, 12, 24, and 36 months were: 58.4% (526/900), 54.1% (487/900), 36.4% (312/858), and 32.1% (286/890). Peanuts, tree nuts, meat, egg, and food additives were the most common foods/ingredients avoided.

The rate of FHS and sensitization to foods were significantly lower in those weaned before 16 wk for sensitization at 1 yr ($p = 0.03$, OR =

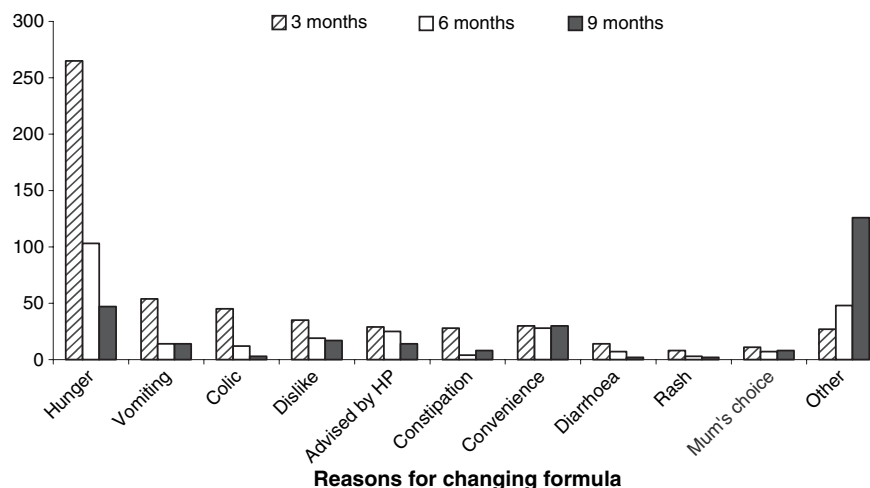


Fig. 1. Reasons for changing infant formulas at 3, 6, and 9 months.

Table 4. Infant feeding practices during the first 3 yr of life

	3 months (n = 927)	6 months (n = 913)	9 months (n = 900)	12 months (n = 900)	2 yr (n = 858)	3 yr (n = 891)
Exclusive breastfeeding	165 (18)	0	0	0	0	0
Exclusively formula feeding	406 (44)	0	0	0	0	0
Mixed feeding	100 (11)	0	0	0	0	0
Breastfed and solids introduced	33 (4)	99 (11)	73 (8)	105 (12)	NA	NA
Formula fed and solids introduced	195 (21)	702 (77)	768 (85)	NA	NA	NA
Mixed feeding and solids introduced	28 (3)	112 (12)	59 (7)	NA	NA	NA

Values are expressed as n (%).

Table 5. Formulas used at 3, 6, and 9 months

Formulas used	3 months (n = 729)*	6 months (n = 814)†	9 months (n = 827)
Whey based	408	274	182
Casein based	347	392	282
Follow-on	0	81	260
Soya	24	24	29
Partial hydrolysate	16	14	12
Extensive hydrolysate	2	3	4
Amino acid	4	4	4
Organic	9	13	12
Other milk, e.g., specialist feeds, formulas bought abroad	5	4	7
Uncertain	3	7	3
Premature formula	3	0	0
Energy dense	1	3	1
Cow's milk	0	2	31

*93 infants were using one or more formula concurrently.

†Seven infants were concurrently using more than one formula.

0.26, CI 0.05–0.94), FHS by 1 yr ($p = 0.02$, OR = 0.41, CI 0.18–0.89), sensitization at 3 yr ($p = 0.01$, OR = 0.33, CI 0.11–0.86) and FHS by 3 yr ($p = 0.02$, OR = 0.51, CI 0.28–0.92) (Table 6).

Exposure to the major allergic foods during the first 3 yr of life

With regards to the avoidance and introduction of the major food allergens, information was obtained prospectively at 3, 6, and 9 months as well as 1, 2, and 3 yr. Exposure to food allergens is defined as those children who were exposed to the food during breastfeeding and the first 3 yr of life (Table 7).

Ideally we wanted to look at whether exposure to the major allergenic foods at different ages had an effect on sensitization and development of FHS to that particular food. As only a small number of children did not have exposure to the major allergenic foods during breastfeeding or in the first 3 yr of life, statistical analysis was not indicated.

At 1 yr, all the children sensitized to a particular food were exposed to the food before the age

Table 6. Infant weaning and its association with sensitization to the pre-defined food allergens and FHS

	Weaning before 16 wk	Weaning after 16 wk	p-value (Fisher's exact test)
1 yr			
Positive SPT	3	14	0.03*
Negative SPT	329	399	
FHS	10	28	0.02*
No FHS	406	468	
3 yr			
Positive SPT	6	21	0.01*
Negative SPT	410	475	
FHS	17	38	0.02*
No FHS	399	458	

SPT, skin prick test; FHS, food hypersensitivity.

*Statistically significant

Table 7. Number of infants with reported exposure to the major allergenic food proteins

Food	6 months (n = 913)	9 months (n = 900)	1 yr (n = 900)	2 yr (n = 858)	3 yr (n = 891)
Cow's milk	912	900	900	858	891
Egg	909	900	900	858	891
Wheat	913	900	900	858	891
Fish	912	899	899	857	891
Peanut	839	854	860	838	884
Tree nut	902	892	895	854	891
Sesame	913	900	900	858	891

of 6 months. All but one child sensitized to cod ($n = 2$), one to peanut ($n = 3$), and another to egg ($n = 14$) were exposed to the food before 3 months. With regards to FHS, all the children diagnosed with FHS at 1 yr were exposed to the food before the age of 6 months. All, but one child with a cod allergy ($n = 1$), and two children with an egg allergy ($n = 16$) were exposed to the food before 3 months.

At 3 yr, all the children sensitized to a particular food were exposed to the food before the age of 6 months. Of the nine children sensitized to egg at 3 yr, eight children were exposed to egg before 3 months. The same applied to six of the

children sensitized to wheat ($n = 8$), one to cod ($n = 3$), seven to peanut ($n = 13$), and six to sesame ($n = 9$).

All the children diagnosed with a FHS by 3 yr were exposed to the food before the age of 6 months. Of the 26 children with a FHS to milk by 3 yr, 25 children were exposed to milk before 3 months. The same applied to 16 of the children with a FHS to egg ($n = 18$), one of the children with a FHS to cod ($n = 1$), six of the children with a peanut allergy ($n = 13$), and three of the children with a sesame allergy ($n = 5$).

In summary, all the children with sensitizations to and the majority of those who developed FHS to a particular food, were exposed to the particular food allergen before 6 months of age as part of their weaning diet.

Infant feeding and weaning practices in relation to a maternal or familial history of atopy

We explored a range of factors relating to feeding and weaning practices at 3, 6, 9, 12, and 24 months between those with a history of atopy and those without. These variables included: breastfeeding history (e.g., duration exclusive or partial), method of feeding (e.g., breast, infant formula, both), time of introduction of solids, foods avoided from the infant's diet, use of commercial baby foods, reported food-related problems, and reported symptoms of allergic disease. Feeding practices were once again compared between the different groups.

Family history of allergic disease vs. no family history. At 3 months, more mothers with a family history of allergic disease were still exclusively breastfeeding (18.2% vs. 9.1%; $p = 0.008$). It was also the mothers from allergic families who were more likely to avoid peanut from the infant's weaning food (36.4% vs. 27.4%; $p = 0.03$). At 6 and 9 months, mothers from atopic families were more likely to report symptoms of allergic disease (not necessarily food related) in the infant [81.5% vs. 66.9%; $p < 0.0001$ (6 months)] and [74.7% vs. 60.5%; $p = 0.001$ (9 months)]. At 12 months no statistically significant differences were found between the two groups. At 24 months, the only significant difference between the groups was the rate of reported food related problems (9.3% vs. 4.1%; $p = 0.04$).

Maternal history of allergy vs. no history. Atopic mothers were more likely to report a food-related problem at 6 (9.5% vs. 8.4%; $p = 0.02$) and 24 months (11% vs. 4.4%, $p = 0.001$). At both 6

and 9 months, atopic mothers reported a significantly higher rate of symptoms of allergic disease [81.8% vs. 74.7%; $p = 0.01$ (6 months) and 77.1% vs. 65.2%; $p = 0.001$ (9 months)] in the infant.

Discussion

This study reports on maternal dietary intake, breastfeeding, and weaning practices of a cohort of women and relates these variables to development of sensitization to foods and FHS in the infant. This study also reports on whether maternal dietary intake, feeding and weaning practices are influenced by a personal or family history of allergy. In this sample of children, maternal dietary intake during pregnancy and breast-feeding duration did not appear to influence the development of sensitization to food allergens or FHS. Interestingly, children weaned at or after 16 wk were more likely to develop FHS and sensitization to foods. In contrast, the data regarding exposure to food allergens and age of weaning on to food allergens showed that children who were exposed to a certain food allergen before the age of 3–6 months were more likely to become sensitized or develop FHS to the particular food at age 1 and 3 yr. Looking at the effect of a family history or personal history of allergic disease, the main findings were that women with a family history of allergic disease were more likely to breast feed exclusively at 3 months and avoid peanuts from the infant's diet at 6 months.

Maternal food intake during pregnancy and breast-feeding duration did not appear to influence the development of sensitization to food allergens or FHS. Five studies indicate that breastfeeding for at least 12 wk prevented some symptoms of allergic disease. Only two studies (26, 27) found that breastfeeding prevented food allergy and only one of these studies (27) diagnosed food allergy by means of food challenges. There are, however, a number of studies in unselected cohorts which have shown that breastfeeding increases the risk of allergic symptoms (28, 29), but none of these looked at the effect of breastfeeding specifically on FHS.

At 3 months, mothers with a family history of allergic disease were more likely to breast feed exclusively. Our data confirms the similar findings by other groups (21, 30) who found that the higher the atopic risk in the family, the greater the mothers' willingness to breastfeed exclusively for the first 4 months of the infant's life. However, we did not find any difference in total

breast-feeding duration between mothers with or without a maternal or familial history of allergic disease, which is in line with findings elsewhere (12, 31). It is often suggested that the conflicting data regarding the protective effect of breast-feeding on the prevention of allergic disease could be due to the fact that perhaps those with the highest degree of atopic heredity will tend to be breastfeeding for the longest period. Our data do not support this hypothesis.

More than 80% of mothers had introduced solids before the infant was 17 wk old, 45.6% before the infant was 16 wk old, and 27.6% before the infant was 12 wk old. All mothers had introduced solids into the infant's diet before 6 months. Weaning age significantly affected the prevalence of sensitization to foods and FHS at 1 yr of age. Surprisingly, children weaned at or after 16 wk were more likely to develop FHS ($p = 0.02$) and sensitization to foods ($p = 0.04$). It is difficult to explain why solid food introduction before 16 wk led to less FHS and sensitization. In contrast, previous studies found that introduction of solids before 3–4 months of age increases the risk of developing allergic disease in unselected (32) and high risk children (33, 34). A recent study (35) showed that weaning after 4 months reduced the prevalence of atopic dermatitis, but delaying introduction of solid foods after 6 months did not provide any additional benefits. More specifically, and in contrast with the above, data regarding exposure to food allergens showed that children who were exposed to a certain food allergen before the age of 3–6 months, were more likely to become sensitized or develop FHS to the particular food at age 1 and 3 yr. This may indicate that although early weaning could lead to tolerization in general, the main allergenic food proteins may behave differently and that age of introduction to these needs special investigation.

We have seen an increase in reported problems of allergic disease, in both the groups with a maternal or family history of allergy. This may highlight an important area of health service provision. The discrepancy between symptoms of allergic disease and diagnosed allergic disease has been reported by a number of studies (36, 37). This study is, however, the only study comparing reported rates in atopic and non-atopic families and mothers. The finding therefore suggests the need for better education and support of these particular groups of parents during pregnancy and the infants' first years of life.

In conclusion, this study is unique as it is an observational study of an unselected population investigating the role of maternal food intake

during pregnancy by means of a validated FFQ. Maternal dietary intake during pregnancy, and breast-feeding duration did not appear to influence the development of sensitization to food allergens or FHS. Weaning age may affect sensitization to foods and development of FHS. A history of allergic disease has very little impact on maternal dietary, feeding, and weaning practices.

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