Age at the Introduction of Solid Foods During the First Year and Allergic Sensitization at Age 5 Years

WHAT'S KNOWN ON THIS SUBJECT: The recommendation of exclusive breastfeeding for the first 6 months for the prevention of allergic diseases may lack strong scientific evidence.

WHAT THIS STUDY ADDS: Late introduction of solid foods may increase the risk of allergic sensitization.

abstract

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OBJECTIVE: The goal was to examine the relationship between age at the introduction of solid foods during the first year of life and allergic sensitization in 5-year-old children.

METHODS: We analyzed data from the Finnish Type 1 Diabetes Prediction and Prevention nutrition study, a prospective, birth cohort study. We studied 994 children with HLA-conferred susceptibility to type 1 diabetes mellitus for whom information on breastfeeding, age at the introduction of solid foods, and allergen-specific immunoglobulin E levels at 5 years was available. The association between age at the introduction of solid foods and allergic sensitization was analyzed by using logistic regression.

RESULTS: The median duration of exclusive breastfeeding was 1.8 months (range: 0–10 months). After adjustment for potential confounders, late introduction of potatoes (>4 months), oats (>5 months), rye (>7 months), wheat (>6 months), meat (>5.5 months), fish (>8.2 months), and eggs (>10.5 months) was significantly directly associated with sensitization to food allergens. Late introduction of potatoes, rye, meat, and fish was significantly associated with sensitization to any inhalant allergen. In models that included all solid foods that were significantly related to the end points, eggs, oats, and wheat remained the most important foods related to sensitization to food allergens, whereas potatoes and fish were the most important foods associated with inhalant allergic sensitization. We found no evidence of reverse causality, taking into account parental allergic rhinitis and asthma.

CONCLUSION: Late introduction of solid foods was associated with increased risk of allergic sensitization to food and inhalant allergens. *Pediatrics* 2010;125:50–59

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KEY WORDS

solid foods, allergic sensitization, children, reverse causality, cohort study

ABBREVIATIONS

DIPP—Type 1 Diabetes Prediction and Prevention
IgE—immunoglobulin E

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Current evidence for the recommendation of exclusive breastfeeding for the first 6 months of life and introduction of solid foods thereafter for the prevention of allergic diseases in children is limited.[1–5] Few studies have investigated this topic, and the results reported are inconsistent. In a systematic review of 13 previous studies that met inclusion criteria, 5 studies observed a positive association between early introduction of solid foods and eczema, 1 study found an association with pollen allergy, and others reported no association between early introduction of solid foods and the development of allergic diseases.[2] Some prospective studies supported neither prolonged breastfeeding nor delayed introduction of solid foods for the prevention of allergic diseases in children.[4–7] Conversely, increased risk for atopic dermatitis, eczema, and allergic sensitization (with or without symptoms) has been associated with delayed introduction of egg, milk, cereals, and other solids.[1,3–5,8]

The concept of reverse causality is an important consideration in evaluation of the association between the timing of the introduction of solid foods and the development of allergic diseases in cohort studies.[3,4,7] Families with a family history of allergic diseases or with infants with early signs of allergic outcomes may delay the introduction of solids, a situation that may mask any temporal relationship between the introduction of solid foods and allergic outcomes. In the present study, we aimed to assess the association between age at the introduction of different solid foods during the first year of life and food and inhalant allergic sensitizations in a cohort of 5-year-old children with HLA-conferred susceptibility to type 1 diabetes, taking into account reverse causality.

METHODS

Subjects

Subjects in this analysis were enrolled from the Finnish Type 1 Diabetes Prediction and Prevention (DIPP) nutrition study. The DIPP nutrition study falls within the framework of the larger DIPP study. Both the DIPP study and the DIPP nutrition study have been described elsewhere.[9] Briefly, the DIPP study, which started in 1994, is an ongoing, population-based, prospective, cohort study aimed at exploring possible means to predict and to prevent type 1 diabetes mellitus. All newborn infants with HLA-conferred susceptibility to type 1 diabetes are recruited from the university hospital areas of Turku, Oulu, and Tampere. The nutrition study was initiated within the framework of the DIPP project in Oulu and Tampere in September 1996 and October 1997, respectively. That study aims to examine the effects of maternal diet during pregnancy and lactation in line with the child's diet during infancy and childhood on the development of type 1 diabetes, allergic diseases, and asthma. At the age of 5 years, a questionnaire modified from the International Study of Asthma and Allergies in Childhood questionnaire was administered and a blood sample for measurement of immunoglobulin E (IgE) levels was obtained from each child.

For the present analysis, 1175 consecutively born children were invited to the allergy study between August 1, 1998, and July 31, 2000. Of those, 1067 (91%) participated in the study. Serum IgE measurements were performed for 1018 participants (87% of those invited to the study) with available blood samples. Information on age at the introduction of solid foods and breastfeeding was available for 994 of those children (98%). The study was approved by the ethics committees of the Universities of Oulu and Tampere, and informed consent was obtained from the parents.

Dietary Assessments

The diet of each child was assessed by means of age-specific dietary questionnaires at the ages of 3, 6, and 12 months, with a follow-up form on the age at the introduction of new foods to record the age at the introduction of new foods. The 3-, 6-, and 12-month questionnaires assessed the child's diet from birth until the age of 3 months, after the third month, and after the sixth month, respectively. Each of the age-specific questionnaires inquired about the pattern of breastfeeding, the use of infant formula and cow's milk, the use of vitamin preparations, and the food items the child had received to date. Although the dietary questionnaires were returned to the study center at each specific age after completion, the form on the age at the introduction of new foods was kept and filled in by the families until the age of 2 years; forms were brought to the study center at each visit to be checked by a trained study nurse, and the information was transferred to the database. In addition to the pattern of exclusive breastfeeding, total breastfeeding, and use of cow's milk, we considered the following solid foods, which are common in the Finnish diet, in the present analysis: potatoes, fruits and berries, carrots, cabbages, oats, wheat, rye, meat, fish, and eggs.

IgE Measurements

Specific IgE concentrations were analyzed in samples obtained at the age of 5 years, by using an ImmunoCAP fluoroenzyme immunoassay (Phadia Diagnostics, Uppsala, Sweden). Allergic sensitization was set at ≥0.35 kU/L for the following food and inhalant allergens: egg, cow's milk, fish, wheat, house dust mite, cat, timothy grass, and birch. The food allergens for which we made IgE measurements included the nutritionally important foods in the diet of Finnish children of this age. Clinical symptoms and food tolerance were not evaluated in this study.

Statistical Analyses

We used logistic regression analysis to study the association between age at the introduction of solid foods and allergic sensitization. The end points used were sensitization to any food allergen, egg allergen, cow's milk allergen, wheat allergen, and any inhalant allergen. First, we used unadjusted and adjusted models separately for each dietary variable in relation to the end points (model I). Then, in a backward, stepwise, logistic regression analysis, all dietary variables that were significantly associated with each end point at the unadjusted level were studied together. Cereals first were analyzed together, because they were highly correlated with each other; the significant ones then were studied together with the other foods. The least-significant dietary variables were removed from the model, whereas those that achieved a 5% statistically significant level were adjusted by the potential confounding variables (model II). To study the concept of reverse causality, we used the same analyses (models I and II) for the subgroup of children with parental history of asthma or allergic rhinitis. All adjusted models included the following potential confounders: season of birth, delivery hospital, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, ponderal index, and pets at home during the first year of life. In initial exploratory analyses, age at the introduction of solid foods was not linearly related to the outcomes; therefore, we categorized all of the food variables in thirds. The third categorization was performed to avoid posthoc or outcome-dependent choices of categorization. Most third groups were unequal in size, because the same age was reported for many children. The nearest cutoff point was always used. Statistical significance was defined as a 2-sided P value of $<.05$. SPSS for Windows 15 (SPSS Inc, Chicago, IL) was used for all analyses.

TABLE 1 Distribution of Background Characteristics and Median Duration of Exclusive Breastfeeding

Background Variables	n (%) ($N = 1018$)	Duration of Exclusive Breastfeeding, Median (Range), mo	P[a]
Season of birth			.030
Spring (April to May)	189 (19)	1.8 (0.0–6.0)	
Summer (June to August)	227 (22)	2.0 (0.0–8.0)	
Autumn (September to November)	258 (25)	1.2 (0.0–6.0)	
Winter (December to March)	344 (34)	1.9 (0.0–10.0)	
Gender			.437
Male	551 (54)	1.6 (0.0–10.0)	
Female	467 (46)	1.8 (0.0–8.0)	
No. of siblings at child's birth			.620
0	428 (42)	1.6 (0.0–10.0)	
1	326 (32)	1.8 (0.0–8.0)	
≥2	245 (24)	1.8 (0.0–6.0)	
Missing information	19 (2)	1.8 (0.0–5.0)	
Parental asthma			.655
Yes	126 (12)	1.6 (0.0–6.0)	
No	740 (73)	1.8 (0.0–10.0)	
Missing information	152 (15)	1.5 (0.0–8.0)	
Parental allergic rhinitis			.431
Yes	528 (52)	1.8 (0.0–10.0)	
No	299 (29)	1.8 (0.0–6.0)	
Do not know	40 (4)	1.8 (0.0–5.5)	
Missing information	151 (15)	1.4 (0.0–8.0)	
Maternal age			<.001
<25 y	166 (16)	1.4 (0.0–5.5)	
25–29.9 y	343 (34)	1.4 (0.0–6.0)	
30–34.9 y	312 (31)	2.5 (0.0–8.0)	
≥35 y	197 (19)	2.3 (0.0–10.0)	
Maternal basic education			<.001
Less than high school	375 (37)	1.4 (0.0–8.0)	
High school	616 (61)	2.0 (0.0–10.0)	
Missing information	27 (3)	1.6 (0.0–5.0)	
Maternal smoking in pregnancy			<.001
No	909 (89)	1.8 (0.0–10.0)	
Yes	87 (9)	0.9 (0.0–5.0)	
Missing information	23 (2)	2.1 (0.0–6.0)	
Mode of delivery			.023
Normal	889 (87)	1.8 (0.0–8.0)	
Cesarean section	120 (12)	1.0 (0.0–10.0)	
Missing information	9 (1)	0.5 (0.0–3.5)	
Ponderal index			.460
First quartile	251 (25)	1.6 (0.0–6.0)	
Second quartile	253 (25)	2.0 (0.0–10.0)	
Third quartile	253 (25)	1.8 (0.0–6.0)	
Fourth quartile	250 (24)	1.4 (0.0–8.0)	
Missing information	11 (1)	0.5 (0.0–3.5)	
Pets at home during first year			.440
No	596 (58)	1.9 (0.0–10.0)	
Yes	273 (27)	1.8 (0.0–6.0)	
Missing information	149 (15)	1.4 (0.0–8.0)	

[a] P values were calculated with the Mann-Whitney U test (for variables with 2 categories and Kruskal-Wallis test (for variables with >2 categories).

TABLE 2 Associations Between Age at Introduction of Solid Foods During First Year of Life and Sensitization to Food and Inhalant Allergens in Children 5 Years of Age

Age at Introduction of Foods[a]	All, *n* (%) (*N* = 994)	Odds Ratio (95% Confidence Interval)			
		Any Food Allergen		Any Inhalant Allergen	
		Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
Exclusive breastfeeding					
<0.92 mo	330 (33)	1.00	1.00	1.00	1.00
0.92–3.00 mo	357 (36)	1.18 (0.78–1.79)	1.29 (0.80–2.10)	0.83 (0.58–1.19)	0.84 (0.55–1.28)
>3.00 mo	307 (31)	1.33 (0.87–2.02)	1.61 (0.98–2.65)	1.29 (0.90–1.84)	1.30 (0.85–1.98)
P[c]		.415	.167	.053	.118
Total breastfeeding					
<5.00 mo	306 (31)	1.00	1.00	1.00	1.00
5.00–9.00 mo	370 (37)	1.07 (0.71–1.61)	1.40 (0.86–2.29)	1.01 (0.71–1.44)	1.19 (0.78–1.81)
>9.00 mo	318 (32)	0.96 (0.62–1.47)	1.07 (0.63–1.83)	0.86 (0.60–1.26)	0.69 (0.43–1.11)
P[c]		.854	.317	.666	.030
Cow's milk					
<0.93 mo	333 (33)	1.00	1.00	1.00	1.00
0.93–4.00 mo	337 (34)	1.09 (0.72–1.65)	1.25 (0.77–2.03)	0.91 (0.63–1.32)	0.85 (0.55–1.29)
>4.00 mo	334 (33)	1.20 (0.80–1.81)	1.51 (0.93–2.46)	1.24 (0.87–1.76)	1.40 (0.92–2.12)
P[c]		.675	.247	.223	.059
Potatoes					
<3.10 mo	346 (35)	1.00	1.00	1.00	1.00
3.10–4.00 mo	432 (43)	1.12 (0.75–1.67)	1.50 (0.93–2.42)	1.31 (0.93–1.85)	1.30 (0.86–1.95)
>4.00 mo	216 (22)	1.74 (1.12–2.70)[d]	2.56 (1.49–4.39)[e]	1.67 (1.13–2.48)[d]	1.93 (1.20–3.11)[e]
P[c]		.032	.003	.037	.025
Fruits and berries					
<3.46 mo	266 (27)	1.00	1.00	1.00	1.00
3.46–4.00 mo	405 (41)	1.08 (0.70–1.66)	1.30 (0.78–2.16)	1.01 (0.70–1.47)	1.09 (0.70–1.69)
>4.00 mo	323 (32)	1.41 (0.91–2.19)	1.70 (1.00–2.90)	1.30 (0.89–1.91)	1.54 (0.97–2.45)
P[c]		.221	.143	.257	.121
Carrots					
<3.50 mo	279 (28)	1.00	1.00	1.00	1.00
3.50–4.00 mo	417 (42)	0.98 (0.65–1.49)	1.15 (0.70–1.90)	1.09 (0.76–1.57)	1.02 (0.66–1.57)
>4.00 mo	298 (30)	1.26 (0.82–1.95)	1.66 (0.97–2.83)	1.29 (0.88–1.90)	1.37 (0.86–2.18)
P[c]		.394	.134	.394	.282
Cabbages					
<4.10 mo	346 (35)	1.00	1.00	1.00	1.00
4.10–5.20 mo	284 (29)	1.02 (0.66–1.58)	1.00 (0.61–1.65)	1.05 (0.73–1.51)	1.00 (0.66–1.52)
>5.20 mo	364 (36)	1.27 (0.85–1.88)	1.51 (0.94–2.42)	0.81 (0.57–1.15)	0.86 (0.56–1.30)
P[c]		.427	.141	.317	.704
Oats					
<5.00 mo	156 (16)	1.00	1.00	1.00	1.00
5.00–5.50 mo	566 (57)	0.76 (0.47–1.23)	0.85 (0.48–1.52)	0.75 (0.50–1.13)	0.71 (0.43–1.15)
>5.50 mo	272 (27)	1.61 (0.98–2.67)	1.82 (0.99–3.37)	1.08 (0.69–1.68)	1.20 (0.71–2.05)
P[c]		<.001	.002	.077	.021
Wheat					
<5.00 mo	339 (34)	1.00	1.00	1.00	1.00
5.00–6.00 mo	295 (30)	0.92 (0.59–1.43)	0.97 (0.58–1.61)	0.96 (0.66–1.41)	0.89 (0.57–1.38)
>6.00 mo	360 (36)	1.45 (0.98–2.14)	1.49 (0.93–2.37)	1.33 (0.94–1.88)	1.42 (0.94–2.15)
P[c]		.059	.127	.137	.066
Rye					
<5.60 mo	331 (33)	1.00	1.00	1.00	1.00
5.60–7.00 mo	353 (36)	1.19 (0.77–1.85)	1.23 (0.74–2.03)	1.03 (0.71–1.48)	1.06 (0.69–1.61)
>7.00 mo	310 (31)	2.07 (1.36–3.14)[e]	2.30 (1.40–3.75)[e]	1.48 (1.03–2.12)[d]	1.62 (1.06–2.49)[d]
P[c]		.001	.002	.057	.047
Meat					
<5.10 mo	522 (52)	1.00	1.00	1.00	1.00
5.10–5.50 mo	167 (17)	0.88 (0.54–1.46)	0.82 (0.46–1.48)	0.78 (0.50–1.22)	0.80 (0.48–1.33)
>5.50 mo	305 (31)	1.35 (0.94–1.95)	1.65 (1.07–2.55)[d]	1.38 (1.00–1.91)[d]	1.64 (1.12–2.41)[d]
P[c]		.164	.027	.031	.010
Fish					
<6.10 mo	337 (34)	1.00	1.00	1.00	1.00
6.10–8.20 mo	297 (30)	1.12 (0.71–1.77)	1.50 (0.89–2.53)	0.78 (0.53–1.16)	0.81 (0.53–1.26)
>8.20 mo	360 (36)	1.90 (1.27–2.84)[d]	2.42 (1.48–3.95)[e]	1.40 (0.99–1.97)	1.51 (1.00–2.28)[d]
P[c]		.003	.002	.007	.015
Eggs					
<8.10 mo	269 (27)	1.00	1.00	1.00	1.00
8.10–10.50 mo	329 (33)	1.16 (0.71–1.87)	1.04 (0.60–1.80)	1.09 (0.74–1.62)	1.03 (0.66–1.62)
>10.50 mo	396 (40)	2.05 (1.33–3.17)[e]	2.02 (1.23–3.32)[e]	1.47 (1.02–2.13)[d]	1.49 (0.98–2.27)
P[c]		.001	.002	.075	.093

[a] Age at introduction of solid foods categorized in thirds.

[b] Adjusted for season of birth, place of birth, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, pets at home during the first year, and ponderal index.

[c] Overall *P* values.

[d] $P < .05$.

[e] $P < .01$.

RESULTS

Baseline Characteristics of the Study Population and Introduction of Solid Foods

Allergic sensitization to any food allergen was present in 17% of the children, whereas 23% of the children were sensitized to any inhalant allergen. Sensitization to cow's milk allergen was present in 12% of the children, egg allergen in 9%, wheat allergen in 5%, and fish allergen in 1%.

The median duration of exclusive breastfeeding in the whole study population was 1.8 months (range: 0.0–10.0 months). Children born during the autumn had shorter median duration of exclusive breastfeeding, compared with those born during other seasons of the year (Table 1). Longer median durations of breastfeeding were seen among mothers ≥30 years of age, mothers with high school education, mothers who did not smoke during pregnancy, and mothers who had vaginal delivery. The median age at the introduction of cow's milk (usually in the form of infant formula) was 2 months (range: 0–23.5 months). The median age at the introduction of the first solid food was 3.5 months (range: 0.7–10.0 months). Potatoes were the earliest food introduced to the children, followed, in order, by fruits and berries, carrots, cabbages, cereals, meat, fish, and eggs (Table 2). There were no differences between the whole study population and children with parental history of asthma or allergic rhinitis regarding duration of exclusive breastfeeding or age at the introduction of any of the solid foods.

Association of Age at the Introduction of Solid Foods With Allergic Sensitization

Allergic sensitization to any food allergen was associated with late introduction of potatoes (>4 months), oats (>5.5 months), rye (>7 months),

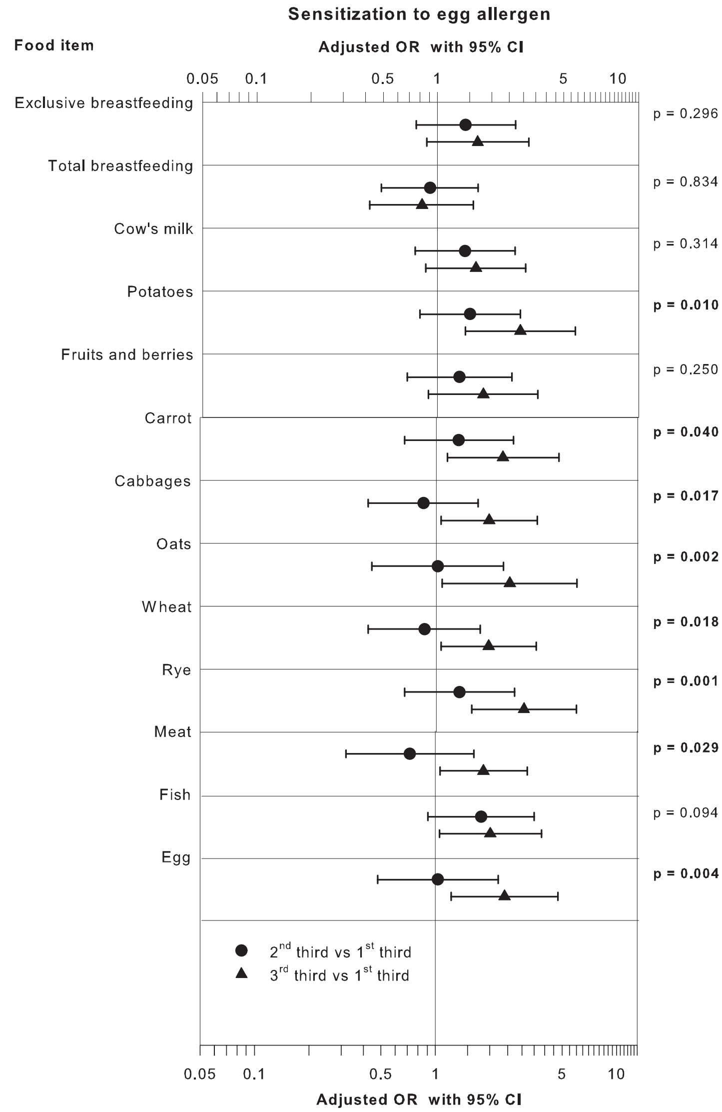

FIGURE 1

Associations between age at the introduction of solid foods and allergic sensitization to egg allergen. The odds ratios were adjusted for season of birth, delivery hospital, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, ponderal index, and pets at home during the first year. The overall *P* value for each logistic regression analysis is shown. OR indicates odds ratio; CI, confidence interval.

meat (>5.5 months), fish (>8.2 months), and eggs (>10.5 months) (Table 2). Similarly, sensitization to any inhalant allergen was associated with late introduction of potatoes, oats, rye, meat, and fish (Table 2). Allergic sensitization to egg allergen was associated with late introduction of potatoes, carrots (>4 months), cabbages (>5.2 months), oats, wheat (>6 months), rye, meat, fish, and eggs (Fig 1). Allergic sensitization to cow's milk was associated with late introduction of fish and eggs (Fig 2), whereas sensitization to wheat allergen was related to late introduction of potatoes, wheat, rye, fish, and eggs (Fig 3). No statistically significant associations with exclusive breastfeeding, total length of breastfeeding, or age at the introduction of cow's milk were found, in relation to any of the end points. There was no evidence of reverse causality in the present study; results were similar for

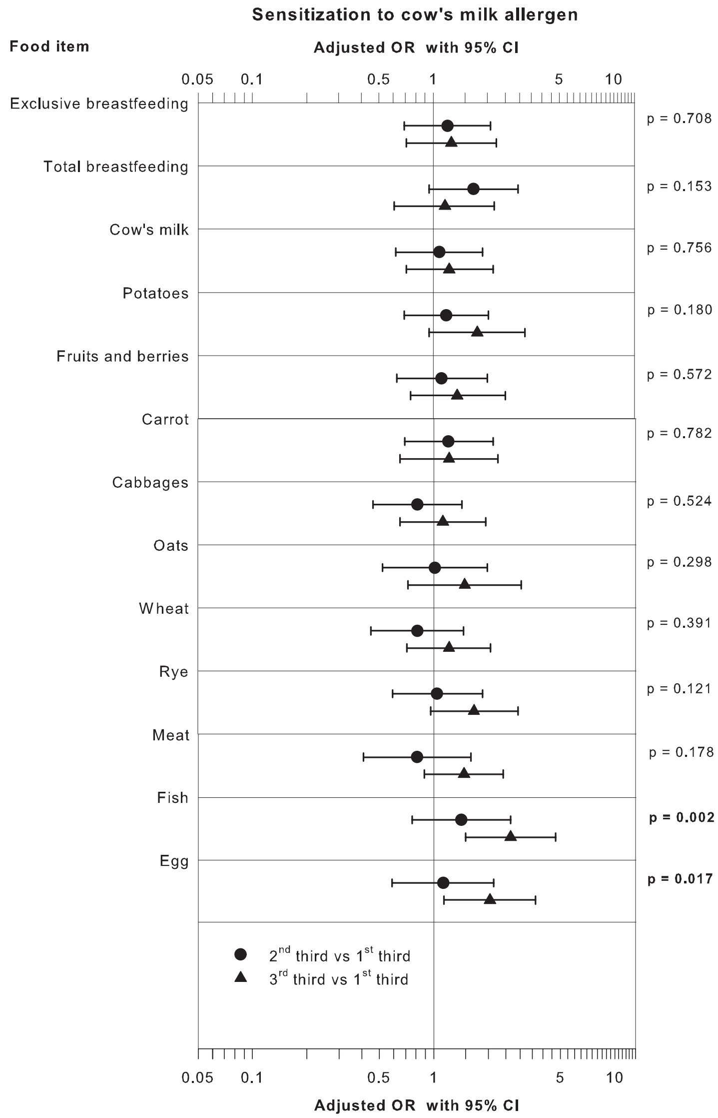

FIGURE 2
Associations between age at the introduction of solid foods and allergic sensitization to cow's milk allergen. The odds ratios were adjusted for season of birth, delivery hospital, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, ponderal index, and pets at home during the first year. The overall *P* value for each logistic regression analysis is shown. OR indicates odds ratio; CI, confidence interval.

both the whole study population and the subgroup of children with parental history of asthma and allergic rhinitis (data not shown). Adjustment for duration of exclusive breastfeeding did not change any of our results.

When the different dietary variables were studied together with respect to each end point (model II), only eggs, oats, and wheat remained significantly related to sensitization to any food allergen (Table 3), as well as sensitization to egg allergen (Table 4). Potatoes and fish were the most important foods related to sensitization to any inhalant allergen (Table 3). Only eggs remained significantly associated with allergic sensitization to cow's milk, whereas wheat was the most important food for sensitization to wheat (Table 4). These results were similar among children with parental history of asthma and allergic rhinitis (data not shown).

DISCUSSION

The results from the present, population-based, prospective, cohort study provide evidence for increased risk of allergic sensitization with delayed introduction of solid foods. Specifically, we report that late introduction of oats and eggs was associated with sensitization to food allergens when age at the introduction of all other foods was taken into account. Similarly, late introduction of potatoes and fish was significantly associated with sensitization to any inhalant allergen. These results did not change in separate analyses of data for the subgroup of children with parental history of asthma or allergic rhinitis, demonstrating no evidence of reverse causality.

One of the limitations of the present study is that our birth cohort was selected on the basis of HLA-conferred susceptibility to type 1 diabetes. This may limit the generalizability of our findings to the general population. However, our subject series included unselected children with regard to family history of allergic diseases; the prevalence of allergic sensitization in our study population was comparable to that in the general Finnish population.[10,11] The effect of the comorbidity of type 1 diabetes and IgE-mediated allergy at the population level remains controversial.[12–14] The direction and magnitude of the effects observed in our study are in accordance with findings of other studies in the general population,[1,3–5,15] which gives credence to our findings. Therefore, it is unlikely that the HLA-based selection biased our results.

The end points in the present study were sensitization against food and inhalant allergens. Consequently, our results may not indicate the effects of timing of the introduction of solid

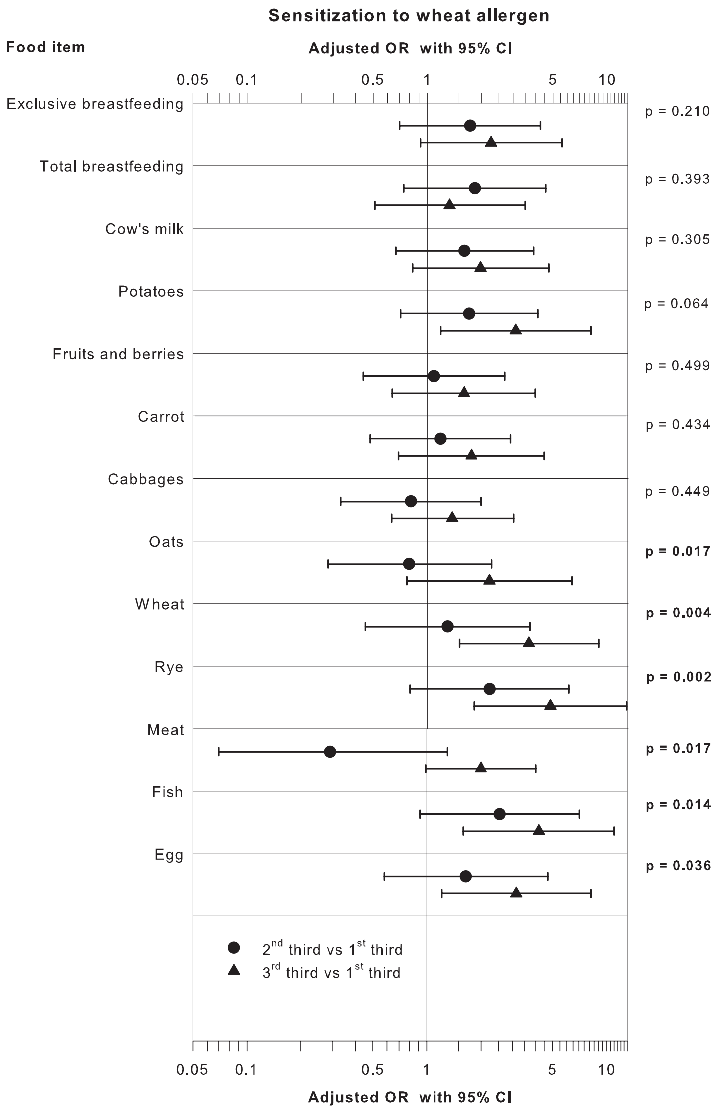

FIGURE 3
Associations between age at the introduction of solid foods and allergic sensitization to wheat allergen. The odds ratios were adjusted for season of birth, delivery hospital, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, ponderal index, and pets at home during the first year. The overall *P* value for each logistic regression analysis is shown. OR indicates odds ratio; CI, confidence interval.

foods on actual asthma, atopic eczema, or other clinical allergic outcomes. The number of these end points in the present subpopulation was small, which resulted in lack of sufficient statistical power for any meaningful analysis. However, allergen-specific IgE responses have been indicated as important precursors to the development of allergic diseases in children.[16,17] In Finland, allergic sensitization against inhalants also has been reported to predict later asthma and wheezing up to adolescence.[18] Extended follow-up monitoring of our study cohort will clarify whether our present observations can be translated into clinical allergic outcomes.

One of the strengths of the present study is its prospective nature and population-based design, which has advantages over other observational, epidemiological designs in detecting plausible causal relationships. The prospective collection of information on dietary exposures before the onset of the end points is another virtue of this study, excluding any potential bias in the selection of subjects. To avoid any posthoc or outcome-dependent choices of categorization, we used predefined third categories for the food variables. However, an important observation from our data is that, for several of the foods, there was a small time difference between the first third and the third third (for example, only 2 weeks separated the first and third thirds for oats). This narrow time window makes the analyses less sensitive for detecting any association between early exposure and atopic sensitization.

Current feeding recommendations propose exclusive breastfeeding for the first 6 months for the prevention of allergic diseases in children.[19,20] These recommendations have been based mainly on the premise that the gut mucosal barrier of the infant is immature,[21] and early introduction of solid foods may instigate sensitization against foods and inhalants. A few early studies in this area gave credence to this hypothesis,[22,23] despite some conflicting findings,[2] but emerging evidence indicates that these recommendations may lack a strong scientific basis.[1,3,5,8,15]

Our observations in the present study are in accordance with reports showing that delayed introduction of solid foods may not prevent the development of allergic diseases in children. A UK birth cohort study investigated the effect of age at the introduction of solid foods on wheezing, eczema, and atopy among 642 children 5.5 years of age.[5] Late introduction of eggs and milk was associated with increased risk of eczema. However, the retrospective collection of data on the introduction of solid foods might have introduced recall bias in that study. Similar findings were reported in a German birth cohort study, in which late introduc-

TABLE 3 Associations Between Age at Introduction of Solid Foods Included in Final Model and Allergic Sensitization to Food and Inhalant Allergens

Age at Introduction of Foods[a]	Odds Ratio (95% Confidence Interval)			
	Any Food Allergen		Inhalant Allergen	
	Model IIa[b]	Model IIb[c]	Model IIa[b]	Model IIb[c]
Eggs				
<8.10 mo	1.00	1.00	—	—
8.10–10.50 mo	1.12 (0.69–1.18)	1.01 (0.58–1.76)		
>10.50 mo	1.90 (1.22–2.96)[d]	1.87 (1.13–3.10)[e]		
P[f]	.004	.008		
Oats				
<5.00 mo	1.00	1.00	—	—
5.00–5.50 mo	0.72 (0.44–1.18)	0.81 (0.45–1.46)		
>5.50 mo	1.42 (0.86–2.38)	1.63 (0.87–3.04)		
P[f]	.002	.007		
Potatoes				
<3.10 mo	—	—	1.00	1.00
3.10–4.00 mo			1.32 (0.93–1.87)	1.30 (0.86–1.97)
>4.00 mo			1.61 (1.07–2.43)[e]	1.87 (1.15–3.05)[e]
P[f]			.071	.043
Fish				
<6.10 mo	—	—	1.00	1.00
6.10–8.20 mo			0.72 (0.49–1.07)	0.75 (0.48–1.17)
>8.20 mo			1.26 (0.88–1.79)	1.36 (0.89–2.07)
P[f]			.015	.028

[a] Age at introduction of foods categorized in thirds.
[b] All food variables that were significantly associated with each end point in Table 2 at the unadjusted level were studied together in relation to that end point by using a backward stepwise analysis. All variables that remained significant at the .05 level were included simultaneously in model IIa. Empty cells (indicated by dashes) means that the dietary variable was analyzed for that end point.
[c] Model IIb was adjusted for season of birth, place of birth, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, pets at home during the first year, and ponderal index. Empty cells (indicated by dashes) means that the dietary variable was analyzed for that end point.
[d] $P < .01$.
[e] $P < .05$.
[f] Overall P values.

tion of vegetables and meat products increased the risk of physician-diagnosed atopic dermatitis in 2-year-old children, whereas late introduction of dairy products increased the risk of symptomatic atopic dermatitis. No association with atopic sensitization was observed.[3] However, in the analysis of data for that cohort at the age of 6 years, late introduction of solid foods was associated only with increased risk of sensitization to food allergens and not with sensitization to inhalant allergens, eczema, asthma, or allergic rhinitis.[4]

In a US birth cohort, late introduction of cereals was associated with increased risk of wheat allergy in 4-year-old children with HLA-conferred susceptibility to type 1 diabetes.[8] A recent intervention study with a German birth cohort investigated the relationship of age at the introduction of several solid foods to eczema in 4-year-old children.[15] In the intervention subgroup, which included children who had family history of allergy and whose mothers received dietary recommendations for the introduction of solid foods, delayed introduction of meat beyond 6 months increased the risk of physician-diagnosed eczema. In the nonintervention group, late introduction of eggs increased the risk of physician-diagnosed eczema. Lastly, the ongoing Dutch KOALA birth cohort study[7] reported that late introduction of cow's milk and other food products increased the risk of eczema, whereas late introduction of other food products increased the risk of recurrent wheeze, any allergic sensitization, and inhalant sensitization among 2-year-old children. In contrast to our observations, no association between the introduction of solid foods and sensitization to cow's milk and hen's eggs was seen in that study.

The issue of reverse causality has been proposed as a likely explanation for the observed association between age at the introduction of solid foods and allergic outcomes.[1,5,24] With the available information on possible dietary prevention of allergic diseases in children, parents with a history of allergic diseases and those whose child manifests early signs of allergic outcomes may delay introduction of solid foods to their child. In the present study, we took reverse causality into account in 2 ways. First, we adjusted for parental asthma and parental allergic rhinitis in the statistical analyses. Second, we performed a separate analysis for the group of children with parental history of asthma or allergic rhinitis. Our results remained similar among the children in this group, in comparison with the whole study population, which indicates no evidence of reverse causality. We cannot completely exclude reverse causality as a potential explanation for our findings, given that we did not take into account early allergic symptoms. The only information available, that is, eczema by 6 months of age, was excluded from our analyses because by that age most of the children had been exposed to most of the solid foods; therefore, we think that this variable did not meet the criteria for reverse causality in the present analysis. In addition, possible residual confounding by a history of allergic diseases in siblings or other relatives of the child, which might encourage parents to introduce solid foods later, cannot be excluded completely as a possible expla-

TABLE 4 Associations Between Age at Introduction of Solid Foods Included in Final Model and Allergic Sensitization to Egg, Cow's Milk, and Wheat Allergens

Age at Introduction of Foods, mo[a]	Odds Ratio (95% Confidence Interval)					
	Egg Allergen		Cow's Milk Allergen		Wheat Allergen	
	Model IIa[b]	Model IIb[c]	Model IIa[b]	Model IIb[c]	Model IIa[b]	Model IIb[c]
Eggs						
<8.10 mo	1.00	1.00	1.00	1.00	—	—
8.10–10.50 mo	1.22 (0.63–2.35)	1.02 (0.47–2.22)	1.26 (0.72–2.19)	1.13 (0.59–2.15)		
>10.50 mo	2.26 (1.25–4.08)[d]	2.16 (1.08–4.31)[e]	1.99 (1.20–3.29)[d]	2.04 (1.14–3.64)[e]		
P[f]	.007	.017	.014	.017		
Oats						
<5.00 mo	1.00	1.00	—	—	—	—
5.00–5.50 mo	0.70 (0.37–1.33)	0.99 (0.43–2.30)				
>5.50 mo	1.56 (0.81–2.98)	2.25 (0.95–5.34)				
P[f]	.004	.067				
Wheat						
<5.00 mo	—	—	—	—	1.00	1.00
5.00–6.00 mo					1.31 (0.50–3.44)	1.29 (0.45–3.70)
>6.00 mo					3.51 (1.58–7.81)[d]	3.66 (1.50–8.94)[d]
P[f]					.002	.004

[a] Age at introduction of foods categorized in thirds.

[b] All food variables that were significantly associated with each end point in Figs 1 to 3 at the unadjusted level were studied together in relation to that end point by using a backward stepwise analysis. All variables that remained significant at the .05 level were included simultaneously in model IIa. Empty cells (indicated by dashes) means that the dietary variable was analyzed for that end point.

[c] Model IIb was adjusted for season of birth, place of birth, gender, number of siblings, parental asthma, parental allergic rhinitis, maternal age, maternal basic education, maternal smoking during pregnancy, mode of delivery, pets at home during the first year, and ponderal index. Empty cells (indicated by dashes) means that the dietary variable was analyzed for that end point.

[d] $P < .01$.

[e] $P < .05$.

[f] Overall P values.

nation for our findings. In any case, the magnitudes of the effects, which were similar for the general study population and the subgroup of children with parental history of asthma and allergic rhinitis, make reverse causality or chance finding unlikely explanations for our observations.

The median duration of exclusive breastfeeding in our study population (1.8 months) was short, in comparison with the recommended duration of 4 to 6 months.[19,20] Despite this, neither exclusive breastfeeding nor late introduction of any of the solid foods was beneficially related to allergic sensitization. Although the advantages of breast milk as the optimal form of feeding for children in the first months of life cannot be overemphasized, the role of exclusive breastfeeding in the prevention of allergic diseases is not clear.[25,26] Conflicting findings have been reported from several studies investigating the associations between breastfeeding and the development of allergic diseases.[6,7,27,28]

CONCLUSIONS

Late introduction of solid foods was associated with increased risk of allergic sensitization to food and inhalant allergens. Eggs, oats, and wheat were most strongly related to food sensitization, whereas potatoes and fish were most strongly related to inhalant sensitization. There was no evidence of reverse causality in the present study, when parental allergic rhinitis and asthma were taken into account. These findings challenge the current recommendations regarding infant feeding for the prevention of allergic diseases.

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