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Early complementary feeding and risk of food sensitization in a birth cohort

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Abstract

Background—Exposure to solid food or cow's milk (complementary food) before age 4 months may confer immune protection (tolerance) or detriment (allergy).

Objective—We explored the relationship between introduction of complementary food <4 months and Immunoglobulin E (IgE) to egg, milk, and peanut allergen at 2 years in the WHEALS birth cohort of Detroit, Michigan, USA.

Methods—At infant age 1, 6, and 12 months, mothers were interviewed about feeding practices. Blood samples were collected at age 2 to 3 years to assess sensitization (IgE ≥ 0.35 IU/ml) to egg, milk or peanut.

Results—For the 594 maternal-infant pairs analyzed, maternal mean age was 29.7 years and 60.6% self-reported as African-American or Black. Infant exposure to complementary food < 4 months was reported by 39.7% of mothers. IgE>0.35 IU/ml for egg, milk, or peanut allergen at age 2 years was observed in 23.9% (95% Confidence Interval = 20.5–27.6%), 30.6% (26.9–34.5%), and 11.4% (8.9–14.3%) of children, respectively. The association between early feeding and sensitization was modified by parental history of asthma or allergy. In multivariable analysis, early feeding reduced the risk of peanut sensitization among children with a parental history; adjusted Odds Ratio=0.2 (0.1–0.7), p=0.007. The relationship also became significant for egg when a cut-off for IgE of > 0.70 IU/ml was used, aOR=0.5 (0.3–0.9), p=0.022.

Conclusion—In this cohort, complementary food introduced <4 months was associated with a reduced risk of peanut (and perhaps egg) sensitization by age 2–3 years, but only for children with a parental history of asthma or allergy.

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Clinical Implications—Feeding practices represent a modifiable risk factor for prevention of allergy. Avoidance of food allergy through dietary manipulation remains controversial. Identifying factors related to food sensitization could inform allergy prevention.

Capsule Summary—Among children with a parental history of asthma or allergy, exposure to early complementary food reduces the risk of peanut and egg sensitization.

Keywords

Food Allergy; food sensitization; infant feeding; birth cohort

BACKGROUND

Adverse food reactions are defined as any aberrant reaction following the ingestion of food or food additive.[1] *Food sensitization* is the production of food-specific immunologlobulin E antibodies (IgE) which initiate risk of Type 1 food hypersensitivity, or allergy.[2;3] *Food allergy* is characterized by an excessive response upon exposure to food allergens leading to the activation of mast cells and basophils by IgE, resulting in an extreme inflammatory response.[2;3]

Food sensitization is not equivalent to food allergy. Only about 40% of persons who are sensitized to food allergens will respond to an oral food challenge.[4] However, children with IgE-mediated food allergy as determined by double blind placebo controlled food challenges, almost universally have elevated food-specific IgE or a positive skin prick test for the food producing the allergic response. Investigation of factors related to food sensitization may provide clues to unanswered questions about the causal pathway to food allergy.

Studies of food sensitization drive the recent concern that the prevalence of food allergies is increasing in the US and Europe.[5–8] Reports suggest that food allergy affects approximately 2% of the US population, and about 4–8% of children.[9] According to a meta-analysis of studies conducted predominantly in European countries, prevalence estimates for IgE-mediated food allergy ranged from 0% to 3% for milk, 0% to 1.7% for egg, and 0.2–1.6% for peanuts.[6;8;10]

Food allergies are more common in infants presumably due to the immaturity of immunologic and non-immunologic mechanisms that prevent passage of foreign antigens across gastrointestinal barriers.[3] Milk, egg and peanut are three of the most common food allergies in early infancy and childhood. Peanut allergy, although less common than egg or milk allergy, is more often associated with severe allergic reactions including anaphylaxis.[11]

Feeding practices may represent a modifiable risk factor for prevention of allergy. Factors related to maternal and infant diet (e.g., placental transfer, breast milk, formula, complementary food) represent the usual routes for the infant's introduction to foreign antigens. The ability to avoid food allergy by manipulating the diet during pregnancy or early infancy remains controversial.

The objective of this analysis was to explore the relationship between the introduction of complementary foods (solid food and cow's milk) prior to age 4 months and the prevalence of IgE sensitization to egg, milk, or peanut allergen by age 2 years in a birth cohort, known as WHEALS (Wayne County Health, Environment Allergy and Asthma Longitudinal Study).

METHODS

Eligibility

All aspects of this research were approved by institutional review boards responsible for the conduct of research in human subjects at Henry Ford Hospital and the Medical College of Georgia. The WHEALS cohort comprised pregnant woman aged 21–50 years who were seen for prenatal care in one of five Henry Ford Hospital (HFH) obstetric clinics between 9/1/2003 and 11/26/2007, resided in the city of Detroit or Detroit western suburbs as defined by zip code, spoke English well enough to provide written informed consent, and had plans to stay in the Detroit area for two years after delivery.

Recruitment

Potentially eligible women were identified using a centralized automated appointment scheduling system. Each woman was sent an advance letter to introduce the study within two weeks of their mid-third trimester appointment, and was approached by a trained recruiter in the waiting room prior to her appointment. If the woman was interested, written informed consent was obtained for participation.

Home and clinic visits

Home visits were conducted at infant age 1, 6, and 12 months by research staff. When the child was 2–3 years of age, clinic visits were conducted by HFH staff allergists and nurses trained in the study protocol. During this visit a venous blood sample was collected from the child for measurement of total and specific IgE to 11 allergens, including milk, egg, and peanut allergen.

Collection of information on infant feeding

Breast feeding was defined as mother's report of breastfeeding at least once per day, including exclusive and supplemented breastfeeding. At the 6 and 12 month visits, mothers were asked about introduction of cereal or other complementary food. At the 1 year home visit and the 2–3 year clinic visit, parents were asked specifically about the age at introduction of eggs, milk, or peanuts as well as a variety of other foods. For this study, introduction of complementary foods was considered early if this occurred before infant age 4 months, which is the recommended age at which solid foods should be introduced according to the American Academy of Pediatrics.[12] In this analysis, cow's milk (not processed in a formula) is considered a “food” complementary to breastfeeding. Infants introduced to cow's milk at < 4 months of age are included in the category of early introduction of complementary food.

Concentration of Total and Allergen-specific IgE

Total and allergen specific IgE measurements in samples collected at 2–3 years of age were performed using the Phadia UniCAP system (Phadia USA, Portage, MI). Total serum IgE concentrations were measured using the UniCAP low range assay. Samples were tested for IgE antibodies to milk, egg, and peanut allergen. Sensitization was defined as specific IgE ≥ 0.35 IU/ml.

Statistical analysis

The study population for these analyses includes cohort children with 6 or 12 month interview data, data from the clinic visit at 2–3 years, and specific IgE measures at 2–3 years. Chi-square tests were used to make subgroup comparisons of participant characteristics for binary and categorical variables, and Student's t tests were used for comparison of continuous variables. Odds ratios and corresponding 95% confidence

intervals were calculated to describe the relationship of early complementary feeding and sensitization to food allergens (egg, milk, peanut).

To minimize bias resulting from changes in infant feeding behavior due to allergic manifestations (e.g., atopic dermatitis), or parental history of asthma or allergy, we first examined associations between food sensitization at 2 years and the following variables selected a priori: parental history of asthma and allergy, food avoidance due to allergic manifestations reported at 1 year (i.e., “Do you currently avoid feeding your child any foods because they have caused health problems?”), and physician diagnosis of atopic dermatitis (AD) reported by age 1 year. We then stratified our analyses by these variables. To assess the difference in the effect of early complementary feeding on the risk of sensitization by parental history, we conducted a test for interaction, using a p value < 0.15 as criteria for the presence of an interaction.[13;14]

Logistic regression was used to calculate odds ratios (OR) and corresponding 95% confidence intervals to describe the association between the selected variables and sensitization. Independent variables included maternal age, maternal race (African-American/Black vs. Non-African-American/Black), infant sex (male/female), yearly household income < $40,000 (yes/no), mother's education (≤ than high school vs. > high school), father's education (≤high school vs. > high school), marital status (married vs. not married), firstborn (yes/no), breastfeeding < 6 months (yes/no), environmental tobacco smoke (ETS) reported at pre-delivery interview (yes/no), ETS reported at 1 month interview (yes/no), and current smoker in household, i.e., any adult smoker in household reported at 2–3 year clinic visit (yes/no). Independent variables were retained in the final model if their inclusion changed the estimate of effect between early complementary food and sensitization by more than 15%.[15] All models were stratified by parental history of asthma/allergy.[1–3]

RESULTS

A total of 1258 women were enrolled in the WHEALS study. Based on maternal report, 44.9% of infants had a parental history of asthma or allergy. Infants with missing information for IgE were excluded (Figure 1). More participants with a history of asthma or allergy completed the 2 year visit compared to those without a history (59% vs. 52%), p=0.032 (data not shown). A total of 800 participants had completed a clinic visit at infant age 2–3 years, of which 594 (74.2%) had data for this analysis (See Figure 1 and Tables E1 and E2 in the online supplement). We compared maternal characteristics for women included in our analysis to that of women excluded (Table 1). No significant differences in outcomes were observed, although there were slightly more African-American/Black participants included in the analysis sample (p=0.091). Mean age for mothers in the analysis sample was 29.7 years (±5.2 years) and 60.6% were African-American/Black. Table 2 is a comparison of maternal characteristics by infant age at introduction of complementary food. A higher percentage of mothers introducing complementary food at < 4 months also breastfed for less than 6 months (includes exclusive and supplemented breastfeeding), when compared to mothers who delayed introduction of complementary foods, (p<0.001).

Prevalence of sensitization by food allergen is shown in Figure 2. Overall, 40.4% of infants were sensitized (IgE≥0.35 IU/ml) to egg, milk or peanut. A higher percentage of African-American/Black infants were sensitized to these food allergens compared to Non-African-American infants, (44.1% vs. 34.7%, p=0.024). The p values for comparisons of sensitization by race for egg, milk, and peanut IgE were 0.047, 0.046, and 0.009, respectively.

Table 3 shows the results of bivariate analysis for the association of early introduction of complementary foods to IgE sensitization for each food allergen. Overall, early complementary food was not significantly related to food sensitization. The OR for early complementary food and peanut sensitization was less than 1.0, suggesting a protective relationship (Table 3). When stratified by race, results were very similar. ORs for early complementary food and sensitization to egg or milk ranged from 0.9–1.1 (Data not shown). Early feeding trended toward an inverse association with peanut sensitization for both race groups with ORs for complementary food < 4 months and peanut IgE≥0.35 = 0.6 (0.3–1.3), p=0.166 and 0.6 (0.2–1.8), p=0.324 for African-American/Black and Non-African-American/Black, respectively (Data not shown).

Table 4 shows the association between early complementary food and food sensitization, stratified by parental history of asthma or allergy, physician diagnosis of eczema by age 1 year, and food avoidance by age 1 year. The reason for the latter being that parents may have changed behavior early in infancy if symptoms were observed. Among infants with a parental history, the OR for early feeding and peanut IgE ≥ 0.35 IU/ml = 0.3 (0.1–0.8), p=0.017. Among infants with AD, none of the 7 infants fed complementary foods < 4 months had peanut IgE≥ 0.35 IU/ml, while 6 of 13 infants (53.9%) not exposed to complementary foods before 4 months had elevated IgE to peanut (p=0.051). Similarly, an inverse association was observed for infants with no report of food avoidance at 1 year, OR=0.4 (0.2–0.9), p=0.024.

We also examined the association of parental history, food avoidance by age 1 year, and AD by infant age 1 year to sensitization (Data not shown). A positive parental history was significantly related to egg sensitization, OR=1.5 (1.0, 2.3), p=0.033. Food avoidance by age 1 year was significantly related to egg sensitization, OR=3.5 (2.0–5.9), p<0.001 and to peanut sensitization, OR=4.3 (2.3–8.0), p<0.001. The relationship between atopic dermatitis by age 1 year and egg sensitization was marginally significant, OR=2.3 (0.96–5.5), p=0.055, and was significantly related to peanut sensitization, OR=3.5 (1.3–9.5), p=0.020 (Data not shown).

We felt the bivariate analyses above provided sufficient evidence that food avoidance and AD represent potential allergic manifestations along the causal pathway of food sensitization and therefore should not be included in multivariable models for which sensitization would be the dependent variable. Also based on these analyses, we analyzed egg and milk separately from peanut, using sensitization to egg or milk as the dependent variable in one logistic regression model. The p value corresponding to a test for an interaction between parental history and early feeding for egg/milk sensitization was 0.113, and was 0.146 for an interaction between parental history and early feeding for peanut sensitization.

Logistic regression models were stratified by parental report of a history of asthma or allergy. Among infants with a parental history, early introduction of complementary food was inversely related to IgE ≥ 0.35 IU/ml in both models (Table 5). This relationship was statistically significant for peanut, aOR=0.2 (0.1–0.7), p=0.007. Among infants with no parental history of asthma or allergy, early feeding was not associated with sensitization to egg/milk or peanut (Table 5). Point estimates from Table 5 were similar when models were re-run using a more stringent cutoff for food allergen specific IgE (0.70 IU/ml instead of 0.35 IU/ml). Doubling the criteria for sensitization caused the relationship with early complementary food to become significant for egg, aOR=0.5 (0.3–0.9), p=0.022. Models using IgE ≥ 0.10 IU/ as the outcome resulted in an aOR=0.8 for egg/milk, but peanut remained significant at this level, aOR= 0.4 (0.2–0.9), p=0.031.

In other analyses, 2×2 tables examining the prevalence of food sensitization among children with reported early exposure to that particular food follow a pattern similar to that of the logistic regression (See Table E3 in the online supplement). ORs for exposure to egg and milk prior to 4 months of age and sensitization to egg and milk were 0.6 and 1.0 respectively; p values > 0.05. For infants exposed to peanut before 4 months of age, 0/2 (0%) with early exposure were sensitized to peanut, while 57/474 (12%) without this early exposure were sensitized to peanut. Cell sizes were too small to examine these associations by parental history of asthma or allergy. Previous studies have shown a relationship between food sensitization and atopic manifestations such as AD and wheeze.[3] In our study sample, we also found that food sensitization was significantly related to AD by age 2 years for milk (p=0.015), egg (p<0.001), and peanut (p<0.001). Early complementary food, however, was not related to AD by age 2 years (OR=1.1, p=0.758). The OR for early feeding and wheeze by age 2 years suggested a reduced risk, but was not statistically significant (OR=0.6, p= 0.136).

DISCUSSION

We explored the relationship between age at introduction of complementary foods and IgE sensitization to egg, milk, or peanut in a diverse birth cohort. Although trends in the direction of risk were similar for all three allergens, only risk estimates for peanut sensitization reached statistical significance.

The relationship between early complementary feeding and risk of food sensitization was modified by parental history. Parental history of asthma or allergy may be a marker for the infant's reduced ability to induce tolerance upon exposure to large quantities of food proteins at a time when the gut and immune system are yet immature.[3] It has been suggested that healthy development of gut immunity or tolerance requires exposure to food proteins before age 4–6 months which would ideally coincide with development of the infant gut microbiota. This may be particularly important for infants with a parental history of allergy.[16;17]

Much controversy surrounds the issue of dietary intervention and the development of atopic disease in infants.[12;18–25] Three review papers published in 2008 serve to illustrate this controversy. A report from the Committee on Nutrition and Section on Allergy and Immunology of the American Academy of Pediatrics states that there is little support for the delay of complementary foods as a measure to prevent development of atopy during infancy.[19] Host et al[23] in the same year published an amendment to previously published articles by the Section on Pediatrics, European Academy of Allergology and Clinical Immunology,[21] supporting conclusions on the effectiveness of dietary regimens, including breast feeding or hypoallergenic formula for high risk infants, and delay of complementary foods for the first 4 months. Prescott et al, also in 2008,[18] challenged recommendations from the World Health Organization[26] and expressed concern about the under-recognition of evidence of an increased risk of atopy with delay of complementary foods beyond 6 months, which is in keeping with our findings. Since the above publications, Kwinta et al.[27] studied the effect of early feeding of extensively hydrolyzed milk formula on incidence of atopic disease by age 5–7 years in 136 children who were very low birth weight in infancy. A comparison group received cow's milk-based formula. Prevalence of atopic disease (total and specific IgE, lymphocyte CD4+CCR4+/CD4+CXCR3+ ratio and skin prick tests) did not differ between the two groups.[27] More recently, using data from the GINI cohort (German Infant Nutrition Intervention), Berg et al. reported that hydrolyzed formula seemed to mitigate the effect of parental history of allergy on risk of eczema by age 6 years. This was a large cohort study of 5991 children of which 2252 with a family history of allergy were invited to participate in a randomized trial. Children were randomized to partially or

extensively hydrolyzed whey, extensively hydrolyzed casein, or standard cow's milk formula. Interpretation is complex since the comparison group included GINI cohort children with a family history of allergy who declined to participate in the trial, as well as children with no family history.[28]

Are we observing reverse causation (altered behavior due to observed symptoms) in our study? We do not believe this to be the case for at least three reasons: (1) Using information on food avoidance, AD by age 1 year, and report of parental history, we stratified our analyses. Although we are limited in the conclusions that can be drawn with regard to a specific type of allergic disease (e.g., food allergy), by definition, the stratum-specific measures are largely unaffected by the confounding variable. (2) Table 4 illustrates the complement to this association, in that among mothers who report food avoidance, the odds of peanut sensitization is elevated, while the reverse is seen for children of families who report no food avoidance. (3) Exploratory analyses suggest an inverse relationship between early exposure to a particular food and later sensitization to that food. A similar method for assessing reverse causation was used by Zutavern et al. in analysis of the LISA cohort (Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood)[29]

Limitations to our analysis include that maternal report of infant feeding and other variables are subject to recall bias. Our maternal recall periods for infant feeding, however, are relatively short, with initial participant contacts at 1 and 6 months after birth and continuing over the course of 24 months for this analysis. The relationship between early exposure to complementary food and food sensitization was not significantly modified by race, with the exception of peanut, for which race remained in the final model. Our analysis was limited to a comparison of African-American/Black to Non-African-American/Black, and did not include a comprehensive examination of potential racial or ethnic differences in the relationship between early exposure to complementary food and food sensitization. This remains an area in need of exploration, given reports using NHANES data suggesting that non-Hispanic Black race is a risk factor for food allergy.[30;31]

The prevalence of food sensitization in our cohort is higher than that reported in other US studies. Wang et al. using data from the National Cooperative Inner City Asthma study reported prevalence estimates for milk, egg, and peanut sensitization as 23%, 15%, and 17% respectively, but these children were 4–9 years of age at enrollment and had asthma.[32] Barnum et al, reported an overall prevalence of detectable serum IgE of 3.9% of US children using a series of national surveys collected from 1993–2007 from the National Center for Health Statistics.[30] Antibodies to egg, milk, and peanut were 6.7, 12.2%, and 9.3%, respectively for children 1–17 years of age.[30] Liu used the National Health and Nutrition Examination survey of 2005–2006 and reported that 28.1% of children aged 1–5 years were sensitized (serum IgE>0.35 kU/L) to at least one food allergen. This estimate is closer, but still lower than what was observed in our cohort. The higher prevalence of food sensitization in our cohort could be a reflection of the number of African-Americans in our cohort,[30–35] as well as a tendency for families with a history of allergy to enroll and remain in the study. Selection bias in both recruitment and retention could have influenced our results. To minimize the impact of selection bias in our cohort, all analyses are stratified by parental history and all models were adjusted for confounders.

There is also the potential for misclassification in our analysis. We were not able to determine the exact age at introduction of formula. Therefore, cow's milk-based formula could be included in the unexposed group. This type of non-differential misclassification typically results in a bias toward the null, i.e., our estimates of the association between our exposure and outcome are likely conservative. Finally, we created more stringent criteria for

sensitization, but a larger sample size would have allowed application of the serum specific IgE decision points (95–100% positive predictive value for a positive reaction to double blind placebo controlled food challenge) published by Sampson: >7 IU_A/L, 15 IU_A/L, and 14 IU_A/L for egg, milk and peanut, respectively 36;37 Such an analysis would benefit from large groups of infants sensitized to peanut.

In summary, among children with parental history of asthma or allergy, and exposed to complementary food before age 4 months, we observed a reduction in the risk of peanut (and perhaps egg) sensitization by age 2–3 years. We observed this association in our cohort of women and their babies recruited from a geographically-defined area in metropolitan Detroit. We acknowledge that caution must be used in generalizing these results to other populations or study samples (including cohort members who did not complete the clinic visit), and that further study is needed before drawing conclusions about a cause and effect relationship.

Controversy over the benefits or risks of different feeding patterns dates back over 60 years. More research on modifiable factors related to food sensitization and food allergy are needed to address knowledge gaps. These gaps include a lack of published research focusing on food allergy as an outcome, the results of which could lead to a better understanding of how the environment and behavior interact to confer risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

95% CI	95% Confidence interval
AD	Atopic Dermatitis
HFH	Henry Ford Hospital
IgE	Immunoglobulin E
IU	International units
ml	Milliliter
NHANES	National Health and Nutrition Examination Survey
WHEALS	Wayne County Health, Environment, Allergy and. Asthma Longitudinal Study

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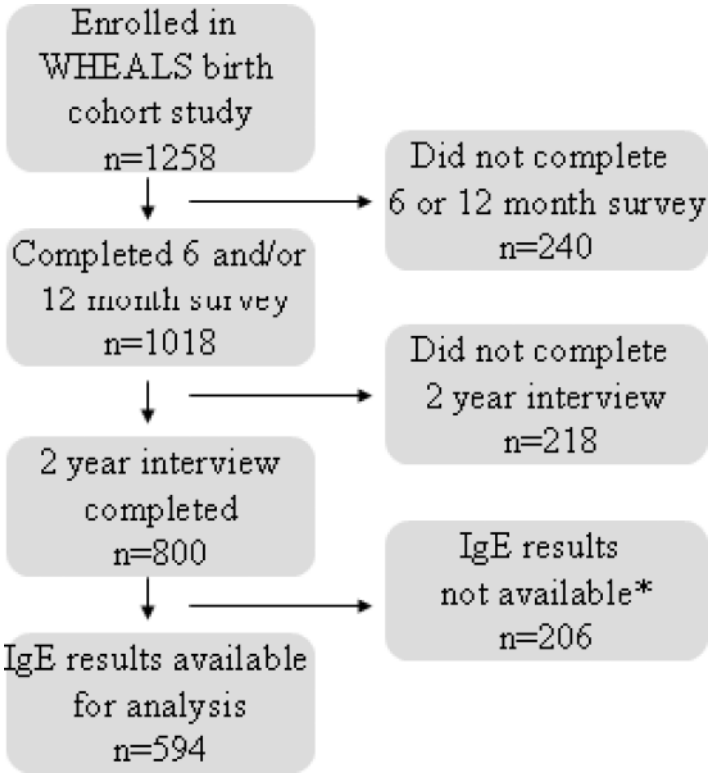

Figure 1.
Flowchart showing available data for children enrolled in the WHEALS birth cohort study and included in the analysis of the introduction of complementary food before the infant is 4 months of age and sensitization to egg, milk, or peanut by age 2–3 years.
*Declined blood draw at 2 years (n=177); insufficient blood sample for measurement of IgE (n=29).

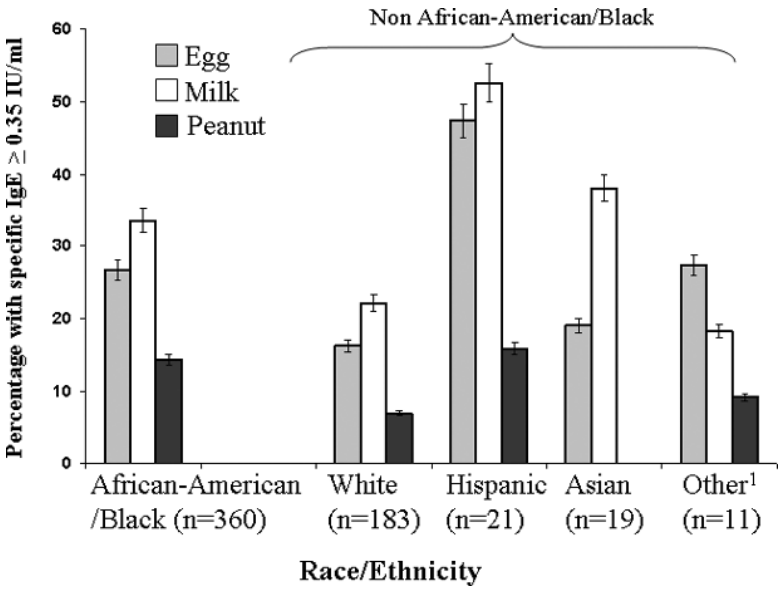

Figure 2.

Proportion of children enrolled in the WHEALS birth cohort study with serum IgE ≥ 0.35 IU/ml to egg, milk, or peanut at age 2 to 3 years.

[1]Other n=11 (includes American Indian/Alaska Native n=3, Multiracial n=4, and Unable to determine n=4)

Table 1

Comparison of selected maternal and infant characteristics for the WHEALS birth cohort study, by whether or not included in the analysis of age at introduction of complementary food and food sensitization

	Included		Not included		
Characteristic	**n=594**		**n=206**		***P***
African-American/Black race, n (%)	360	(60.6)	111	(53.9)	0.091
Maternal age at study enrollment, mean (s.d.)	29.7	(5.2)	30.1	(5.2)	0.279
Married at study enrollment, n (%)	388	(65.3)	141	(68.4)	0.414
≥ high school education (maternal), n (%)	121	(20.4)	38	(18.4)	0.551
≥ high school education (paternal) [1] **, n (%)**	199	(37.6)	71	(37.2)	0.927
< $40,000 household income [2] **,n (%)**	189	(36.5)	73	(41.0)	0.284
Parent history of asthma/allergy [3] **, n (%)**	245	(44.9)	86	(46.5)	0.703
Firstborn	217	(36.5)	80	(38.8)	0.555
Ever breastfed, n (%)	460	(77.4)	162	(78.6)	0.721
Breastfed < 6 months [4] **, n (%)**	431	(73.4)	144	(69.9)	0.330
ETS [5] **reported at pre-delivery interview, n (%)**	147	(24.7)	48	(23.3)	0.677
ETS reported at 1 month interview [6] **, n (%)**	96	(17.1)	31	(16.3)	0.800
Current smoker in household [7] **, n (%)**	117	(19.7)	40	(19.4)	0.931
Atopic dermatitis at or before age 2 years, n (%)	162	(27.3)	52	(25.2)	0.571
Complementary food < 4 months, n (%)	236	(39.7)	82	(39.8)	0.985

[1] 79 with missing information for education

[2] 104 subjects with missing income information

[3] 69 subjects with missing information on parental history of asthma or allergy

[4] 7 subjects with missing information on length of breastfeeding

[5] Environmental tobacco smoke

[6] 49 missing information on ETS at 1 month

[7] Reported at 2–3 year clinic visit

Table 2

Comparison of maternal characteristics by infant age at the introduction of complementary food for members of the WHEALS birth cohort study

	Infant age at introduction of complementary food				
	< 4 months		≥ 4 months		
Characteristic	**n=236**		**n=358**		***P***
African-American/Black race, n (%)	151	(64.0)	209	(58.4)	0.171
Maternal age at study enrollment, mean (s.d.)	29.3	(5.1)	29.9	(5.3)	0.143
Married at study enrollment, n (%)	150	(63.6)	238	(66.5)	0.464
≤ high school education (maternal), n (%)	49	(20.8)	72	(20.1)	0.847
≤ high school education (paternal) [1], n (%)	90	(41.9)	109	(34.6)	0.090
< $40,000 household income [2], n (%)	76	(36.7)	113	(36.3)	0.930
Parent history of asthma/allergy [3], n (%)	95	(43.2)	150	(46.0)	0.514
Firstborn	86	(36.4)	131	(36.6)	0.970
Ever breastfed, n (%)	179	(75.9)	281	(78.5)	0.451
Breastfed < 6 months [4], n (%)	194	(82.5)	237	(67.3)	<0.001
ETS [5] reported at pre-delivery interview, n (%)	60	(25.4)	87	(24.3)	0.757
ETS reported at 1 month interview [6], n (%)	38	(17.6)	58	(16.8)	0.811
Current smoker in household [7], n (%)	49	(20.8)	68	(19.0)	0.596
Atopic dermatitis at or before age 2 years, n (%)	66	(28.0)	96	(26.8)	0.758

[1] 64 with missing information for education

[2] 76 subjects with missing income information

[3] 48 subjects with missing information on parental history of asthma or allergy

[4] 7 subjects with missing information on length of breastfeeding

[5] Environmental tobacco smoke

[6] 33 missing information on ETS at 1 month

[7] Reported at 2–3 year clinic visit

Table 3

Introduction of any complementary foods at < 4 months of age and IgE > 0.35 IU/ml to egg, milk or peanut by age 2–3 years among children in the WHEALS birth cohort study

Any complementary food < 4 months						
Sensitization to food	**Yes**		**No**			
	n	**(%)**	**n**	**(%)**	**Crude OR (95% CI)**[1]	***P***
IgE to egg						
Yes	57	(24.4)	84	(23.7)	1.0(0.7–1.5)	0.846
No	177	(75.6)	271	(76.3)		
IgE to milk						
Yes	73	(31.2)	107	(30.1)	1.1 (0.7–1.5)	0.786
No	161	(68.8)	248	(69.9)		
IgE to peanut						
Yes	20	(8.9)	45	(13.1)	0.6(0.4–1.1)	0.121
No	205	(91.1)	298	(86.9)		

[1]Crude odds ratio and 95% Confidence Interval

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Table 4

Association between complementary food introduced < 4 months and IgE ≥0.35 IU/ml to egg, milk, and peanut, by factors potentially related to food avoidance before infant age 1 year among children in the WHEALS birth cohort study

Parental history of asthma or allergy								**No parental history of asthma or allergy**					
Complementary food < age 4 months								**Complementary food < age 4 months**					
		Yes		**No**		**Crude**		**Yes**		**No**		**Crude**	
IgE to:		**n**	**(%)**	**n**	**(%)**	**OR(95%CI)**	***P***	**n**	**(%)**	**n**	**(%)**	**OR (95%CI)**	***P***
Egg	Yes	22	(23.4)	45	(30.2)	0.7 (0.4–1.3)	0.248	29	(23.4)	30	(17.2)	1.5 (0.8–2.6)	0.189
	No	72	(76.6)	104	(69.8)			95	(76.6)	144	(82.8)		
Milk	Yes	28	(30.1)	49	(33.1)	0.9 (0.5–1.5)	0.627	39	(31.2)	49	(28.0)	1.2 (0.7–1.9)	0.548
	No	65	(69.9)	99	(66.9)			86	(68.8)	126	(72.0)		
Peanut	Yes	5	(5.6)	23	(16.1)	0.3 (0.1–0.8)	0.017	14	(11.7)	18	(10.6)	1.1 (0.5–2.3)	0.773
	No	84	(94.4)	120	(83.9)			106	(88.3)	152	(89.4)		

Food avoidance by infant age 1 year								**No reported food avoidance by infant age 1 year**					
Complementary food < age 4 months								**Complementary food < age 4 months**					
		Yes		**No**		**Crude**		**Yes**		**No**		**Crude**	
IgE to:		**n**	**(%)**	**n**	**(%)**	**OR(95%CI)**	***P***	**n**	**(%)**	**n**	**(%)**	**OR (95%CI)**	***P***
Egg	Yes	12	(60.0)	19	(41.3)	2.1 (0.7–6.2)	0.162	41	(21.8)	52	(19.4)	1.2 (0.7–1.8)	0.530
	No	8	(40.0)	27	(58.7)			147	(78.2)	216	(80.6)		
Milk	Yes	8	(40.0)	17	(37.0)	1.1 (0.4–3.3)	0.815	60	(31.9)	77	(28.7)	1.2 (0.8–1.7)	0.465
	No	12	(60.0)	29	(63.0)			128	(68.1)	191	(71.3)		
Peanut	Yes	7	(35.0)	12	(26.1)	1.5 (0.5–4.7)	0.462	9	(5.0)	29	(11.2)	0.4 (0.2–0.9)	0.024
	No	13	(65.0)	34	(73.9)			170	(95.0)	230	(88.8)		

AD[1] reported by infant age 1 year								**No AD reported by infant age 1 year**					
Complementary food < age 4 months								**Complementary food < age 4 months**					
		Yes		**No**		**Crude**		**Yes**		**No**		**Crude**	
IgE to:		**n**	**(%)**	**n**	**(%)**	**OR(95%CI)**	***P***	**n**	**(%)**	**n**	**(%)**	**OR (95%CI)**	***P***
Egg	Yes	3	(33.3)	6	(46.1)	0.6 (0.1–3.4)	0.674	50	(25.0)	66	(21.8)	1.2 (0.8–1.8)	0.413
	No	6	(66.7)	7	(53.9)			150	(75.0)	236	(78.2)		

AD[1] reported by infant age 1 year								No AD reported by infant age 1 year					
Complementary food < age 4 months								Complementary food < age 4 months					
		Yes		No		Crude		Yes		No		Crude	
IgE to:		n	(%)	n	(%)	OR(95%CI)	*P*	n	(%)	n	(%)	OR (95%CI)	*P*
Milk	Yes	5	(62.5)	4	(30.8)	3.7 (0.6–23.9)	0.203	63	(31.3)	90	(29.8)	1.1 (0.7–1.6)	0.713
	No	3	(37.5)	9	(69.2)			138	(69.7)	212	(70.2)		
Peanut	Yes	0	(0.0)	6	(46.1)	n/a	0.051	17	(8.8)	36	(12.3)	0.7 (0.4–1.3)	0.229
	No	7	(100)	7	(53.9)			176	(91.2)	257	(87.7)		

[1]Atopic dermatitis

Table 5

Results of logistic regression for the association of complementary foods introduced < 4 months and sensitization to milk. egg, or peanut, by parental history of asthma or allergy[1] among children in the WHEALS birth cohort study

		Risk estimates for complementary food < 4 months					
		IgE ≥ 0.35IU/ml			IgE≥0.70 IU/ml		
Stratum	**Dependent Variable**	**aOR**	**(95%CI)[2]**	***P***	**aOR**	**(95%CI)**	***P***
Parental history of asthma or allergy	IgE to egg/milk[3]	0.8	(0.5–1.3)	0.375	0.5	(0.3–0.9)	0.023
	IgE to peanut[4]	0.2	(0.1–0.7)	0.007	0.4	(0.1–12)	0.086
No parental history of asthma or allergy	IgE to egg/milk[5]	1.5	(0.9–2.6)	0.147	1.0	(0.6–2.0)	0.894
	IgE to peanut[6]	1.3	(0.6–2.7)	0.544	1.5	(0.6–3.9)	0.410

[1]Variables available for logistic regression analysis were maternal age, maternal race (African-American/Black vs. Non- African-American/Black), infant sex (male/female), yearly household income < $40,000 (yes/no), mother's education (≤ than high school vs. > high school), father's education (≤high school vs. > high school), marital status (married vs. not married), firstborn (yes/no), breastfeeding at least once per day < 6 months (yes/no),environmental tobacco smoke(ETS) reported at pre-delivery interview (yes/no), ETS reported at 1 month interview (yes/no),and current smoking in household reported at 2–3 year clinic visit (yes/no). Variables were retained in the final model if their inclusion changed the estimate of effect between early complementary food and sensitization by more than 15%[15])

[2]Adjusted odds ratio and 95% confidence interval

[3]Variables retained in model included male gender

[4]Variables retained in model included male gender and African-American/Black race

[5]Variables retained in model included maternal age and household income < $40,000

[6]Variables retained in model included male sender and marital status.