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Maternal Consumption of Peanut during Pregnancy is Associated with Peanut Sensitization in Atopic Infants

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Abstract

Background—Peanut allergy is typically severe, life-long and prevalent.

Objective—To identify factors associated with peanut sensitization.

Methods—We evaluated 503 infants 3–15 months of age (mean, 9.4 months) with likely milk or egg allergy but no previous diagnosis of peanut allergy. A total of 308 had experienced an immediate allergic reaction to cow's milk and/or egg and 204 had moderate to severe atopic dermatitis and a positive allergy test to milk and/or egg. A peanut IgE level of ≥ 5 kU_A/L was considered likely indicative of peanut allergy.

Results—A total of 140 (27.8%) infants had PN-IgE levels ≥5 kU_A/L. Multivariate analysis including clinical, laboratory and demographic variables showed frequent peanut consumption during pregnancy (OR 2.9, 95% CI 1.7–4.9, $p < 0.001$), IgE levels to milk ($p = 0.001$) and egg ($p < 0.001$), male sex ($p = 0.02$) and non-white race ($p = 0.02$) to be the primary factors associated with peanut IgE ≥5 kUA/L. Frequency of peanut consumption during pregnancy and breast feeding showed a dose-response association with peanut IgE ≥ 5 kU_A/L, but only consumption during pregnancy was a significant predictor. Among 71 infants never breastfed, frequent consumption of peanut during pregnancy was strongly associated with peanut IgE ≥ 5 kU_A/L (OR-4.99, 95% CI-1.69–14.74, $p < 0.004$).

Conclusions—In this cohort of infants with likely milk or egg allergy, maternal ingestion of peanut during pregnancy was strongly associated with a high level of peanut sensitization.

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Clinical Implication: In this observational study, maternal ingestion of peanut during pregnancy was associated with peanut IgE ≥ 5 kU_A/L in infants, implying that maternal avoidance as a strategy to reduce allergy risk is an area worthy of additional study.

Keywords

food allergy; sensitization; atopy; peanut allergy

INTRODUCTION

Peanut allergy is often severe, typically life-long, affects approximately 1% of children, (1–6) and may have increased in prevalence among children over the last decade.(1–4;6) With the goal of preventing peanut allergy, the Committee on Toxicology in the UK and the American Academy of Pediatrics (AAP) in 1998–2000 recommended that mothers at risk for atopy avoid peanut during pregnancy and lactation.(7) However, this advice was based upon extremely limited evidence and has been recently called into question.(8) In 2008, the AAP rescinded their recommendation and replaced it with a statement that the efficacy of this practice remains unproven.(9) As a result of limited studies, a European expert panel also recommended no maternal dietary restrictions during pregnancy or lactation.(10;11)

The Consortium of Food Allergy Research (CoFAR) has enrolled infants with likely egg or milk allergy but without previously known peanut allergy in an observational study to address the immunologic, genetic and environmental factors that impact the course of food allergy.(12) A surprisingly high rate of peanut sensitization (> 0.35 kU_A/L), 69%, was observed at the time of enrollment. Here we report clinical, demographic and immunologic factors influencing an elevated (≥ 5 kU_A/L) peanut-specific IgE level observed at the time of enrollment, with emphasis on the role of maternal ingestion of peanut, a potentially modifiable risk factor.

METHODS

Subjects

The cohort includes 512 infants enrolled at 3–15 months of age (mean age, 9.4 months, median age 9 months) at 5 sites, Mount Sinai School of Medicine, New York; Duke University Medical Center, Durham, NC; Johns Hopkins University School of Medicine, Baltimore, MD; National Jewish Health, Denver, CO, and the Arkansas Children's Hospital, Little Rock, AR. Enrollment criteria included atopic children at risk to develop peanut allergy as previously described.(12) Briefly, enrollment required either 1) a history of a convincing immediate allergic reaction to cow's milk (and/or egg) and a positive prick skin test (3 mm larger than the negative control) to cow's milk (and/or egg, if the clinical reaction was to egg), and/or 2) moderate to severe atopic dermatitis, and a positive prick skin test to milk and/or egg. The study aimed to observe the development of peanut allergy longitudinally, so children were not enrolled if they had a known allergy to peanut or had a peanut-specific IgE antibody level ≥ 5 kU_A/L performed prior to study enrollment. In total, 308 children had experienced an immediate clinical reaction to cow's milk and/or egg consisting of urticaria and/or angioedema, respiratory distress, wheezing, and/or vomiting, and had a positive prick skin test to the trigger food. The remaining 204 had moderate to severe atopic dermatitis(13) and a positive prick skin test to milk and/or egg. The study was approved by the participating site's Institutional Review Boards and written informed consent was obtained.

Atopic disease history in parents of the enrolled infants was based upon previously published definitions and was recorded by parental report.(14) Dietary, social and environmental histories were obtained using questionnaires completed during enrollment interviews. Maternal ingestion of peanut was queried for each pregnancy trimester and during breastfeeding, and recorded as either avoided, ingested <2 times/week, ≥ 2 times/

week but < daily, daily or unknown. Categorical analysis of maternal ingestion defines "frequent" as twice or more per week. Peanut consumption in the 3rd trimester was selected as an independent variable for analyses, being the period least susceptible to recall bias.

Tests for IgE Sensitization

Prick skin tests (PST) were performed on the infant's back using the GreerPick® and standard skin test reagents (egg, milk, peanut, dust mites, mold, and cockroach; Greer Labs, Lenoir, NC). The size of the longest wheal diameter (mm) and its longest perpendicular were averaged. A positive PST is defined by a mean wheal diameter of 3 mm or greater, after subtraction of the saline control. The concentration of specific IgE antibody to egg, milk and peanut were measured from plasma at a single central laboratory using the Phadia ImmunoCAP® system (Uppsala, Sweden) reported in kU_A/L. A level ≥ 0.35 kU_A/L was considered positive. The concentration of IgG and IgG4 antibodies to peanut were also measured from plasma samples using the Phadia ImmunoCAP® system. The detection limit for IgG and IgG4 is 0.02 and 0.07 mg/L respectively.

Statistics

We sought to estimate a peanut-specific IgE level signifying a high likelihood of peanut allergy. Oral food challenges are not typically performed to peanut in this age group and therefore diagnostic properties of the test have not been determined in infants.(15;16) There are, therefore, no studies correlating peanut specific IgE levels with clinical outcomes in a cohort of infants such as those described in this study. We selected a peanut IgE ≥ 5 kU_A/L as an endpoint of interest because several studies of older children evaluated for a variety of reasons indicated an increased likelihood (>70%) of peanut allergy above this value.(15–17) We examined clinical and laboratory variables with potential influence on this outcome using the chi-square test. To identify the factors with the greatest association with peanut specific IgE ≥ 5 kU_A/L, logistic regression was used with a step-wise selection procedure retaining variables that were significant ($p < 0.05$) in the resulting multivariate model. Variables that had the greatest predictive influence on peanut IgE outcomes were examined simultaneously using receiver operator characteristics(18) (ROC) (e.g., comparing the sensitivity versus 1-specificity) to evaluate the predictive quality of the model combining these factors. Trend tests used to evaluate the association of maternal ingestion with the primary outcome employed logistic regression with a single slope parameter and equally spaced ingestion categories.

Additional analyses of peanut specific IgE sensitization (≥ 0.35 kU_A/L) and linear regression modeling was performed. Food specific IgE and IgG values were log base10 transformed and zero values were scored below the lowest detected value (i.e. as 0.001 kU_A/L for IgE, 0.005 mg/L for IgG, and IgG4). The IgE to IgG ratio is presented as the antilog of the log ratio. Standard descriptive statistics were employed including Spearman's rank correlation coefficient. Immunoglobulin levels were compared with theWilcoxon or Kruskal-Wallis test depending on the number of grouping levels.

RESULTS

Relationship of peanut sensitization to clinical, demographic and dietary characteristics

Of the 512 subjects enrolled, blood samples were obtained in 503 and analyzed further. Overall, 270 of 503 children (53.7%) had a positive PST to peanut, 305 (60.6%) had detectable (≥ 0.35 kU_A/L) IgE to peanut and 346 (68.8%) had sensitization detected by at least one of the test methods at enrollment. There were 140 (27.8%) children with PN-IgE levels ≥5 kU_A/L. The association of key categorical clinical and demographic factors with elevated peanut IgE levels ≥5 kU_A/L are shown in Table 1, without adjustment for multiple

analyses. Several variables that reflect stronger atopic phenotypes, such as AD severity, having more than one food allergy, or being enrolled with both AD and a food reaction were expected significant variables influencing peanut IgE in the univariate analysis. In addition to variables shown in Table 1, no significant associations were found between peanut IgE levels ≥ 5 kU_A/L and age (months) at enrollment (OR-1.03; 95% CI, 0.96–1.09, p = 0.45), age when introducing formula (OR-1.05; 95% CI, 0.97–1.14, p = 0.22) or solid foods (OR-1.03; 95% CI, 0.89–1.18, p = 0.71), household income, parental educational level, parental atopic disease, use of soy formula, whether a child was breastfed, mode of delivery at birth, or lifetime antibiotic courses. Univariate analyses were also performed for detectable peanut IgE (≥ 0.35 kU_A/L) and results showed similar trends and conclusions as those for PN IgE ≥ 5 kU_A/L. Univariate analysis of peanut IgE ≥ 5 kU_A/L according to sensitization to allergens is shown in Table 2. Peanut IgE levels were highly correlated with egg (r=0.68, p<0.001) and milk (r=0.52, p<0.001) IgE levels.

A multivariate model including all of the clinical variables and results of egg and milk sensitization showed peanut consumption during pregnancy, race and sex to be the primary clinical and demographic factors associated with peanut IgE ≥5 kU_A/L (Table 3). Multivariate analyses were also performed examining sensitized subjects (peanut specific IgE ≥ 0.35 kU_A/L). In the model including clinical, laboratory (milk and egg IgE) and milk and egg PST, for both IgE categories (≥ 5 and ≥ 0.35 kU_A/L), the top three significant variables were frequent peanut consumption during pregnancy, egg-specific IgE and milk-specific IgE levels. The variables in Table 3 were evaluated for their ability to predict peanut sensitization when tested in a model that combines all 5 variables. The ROC analysis showed a very good predictive ability, with the area under the ROC of 0.86 and 0.85 for peanut IgE ≥ 5 and ≥ 0.35 kUA/L, respectively.

Additional analysis of maternal diet

The frequency of peanut consumption during the 3rd trimester and during breast feeding (Figure 1) revealed a dose-dependent association of maternal peanut ingestion with the outcome of peanut IgE ≥ 5 kU_A/L, which was significant only for pregnancy consumption (trend p=0.001). There were a total of 188 infants who consumed formula only or who were breast fed while their mothers avoided peanut; among these 27% had peanut IgE ≥ 5 kU_A/L. The histogram in Figure 1 shows these two groups (maternal avoidance while breast feeding or formula fed) separately. Maternal ingestion of peanut was essentially constant from the first through third trimesters of pregnancy with concordance on the 4 levels of ingestion (e.g., avoid, ingested < twice/week, >= twice/week but < daily, or daily) of at least 92% for each of the pair-wise relationships. Analyses of data relating peanut consumption during each trimester separately to outcome of peanut IgE > 5 kU_A/L also showed a similar association, with trimester-specific elevated peanut IgE rates ranging from 35.4% to 36.4% for the frequent consumption group. Compared to 3rd trimester peanut consumption, breastfeeding mothers reported the same (67.9%), decreased (23.3%) or increased (7.8%) consumption of peanut during breastfeeding.

To explore the association of peanut exposure during pregnancy without any influence of maternal peanut ingestion during breastfeeding, on peanut IgE, we analyzed 71 children who were never breast fed. Frequent consumption of peanut during pregnancy (versus infrequent) was strongly associated with peanut IgE ≥ 5 kU_A/L (OR-4.99, 95%CI 1.69 to14.74, p < 0.004) in this subgroup.

Additional analyses were performed to test the result of the multivariate model with respect to maternal ingestion of peanut. To further address the relative association of maternal consumption of peanut during pregnancy compared to breastfeeding on dichotomized peanut IgE outcomes, frequent versus infrequent consumption was analyzed simultaneously with

only these 2 variables as predictors of peanut IgE > 5 kU_A/L in a logistic regression model. This analysis revealed consumption of peanut during pregnancy to be significant ($p = 0.002$), and peanut consumption during breastfeeding to have no discernable association with peanut IgE ($p > 0.8$) in the joint model. Additionally, the data were analyzed with peanut IgE levels as a continuous variable. In a linear regression analysis of log peanut IgE levels, after adjusting for egg IgE, milk IgE, atopic dermatitis severity, gender, study site and race, only peanut ingestion during pregnancy significantly predicted peanut IgE levels ($p < 0.001$). This analysis was consistent with the importance of peanut consumption during pregnancy, relative to breastfeeding consumption, as the latter variable was not significant when added to the model ($p>0.40$) while the pregnancy consumption variable maintained its significance. Thus, these additional analyses support the results of the multivariate model identifying maternal pregnancy consumption as a significant predictor of peanut IgE outcomes.

To further explore the impact of maternal diet during pregnancy, we analyzed egg consumption. There were 143 mothers with infrequent egg ingestion and 356 with frequent egg ingestion in the 3rd trimester. Frequent ingestion of egg in the 3rd trimester was associated with an increased risk for egg IgE ≥ 2 kU_A/L (OR 1.53; 95% CI, 1.03–2.25, $p = 0.03$), which was a level associated with immediate type allergic reactions in one study of children under age 2 years suspected of egg allergy.(19) In multivariate analysis, consumption of egg, after adjusting for milk and peanut specific IgE levels, still remained a significant predictor of egg IgE ≥ 2 kU_A/L (OR=1.75 p=0.026). We could not analyze milk consumption because too few mothers had infrequent milk consumption (n=37).

The ratio of food specific IgE to IgG is noted to decrease in persons achieving natural tolerance to a food and in those undergoing oral immunotherapy.(20) Conversely, a higher IgE to IgG ratio may reflect a higher risk of clinical allergy. Therefore, we explored the relationship of the infant's peanut-specific IgE, IgG and IgG4 to maternal ingestion of peanut. Although we found substantial correlation of PN-IgE with peanut specific IgG (Rs 0.61, $p < 0.001$) and IgG4 (Rs 0.58, $P < 0.001$), the relative concentrations were affected by peanut consumption. Infants of mothers with frequent, compared to infrequent, ingestion of peanut during pregnancy and during breastfeeding had significantly higher levels of all 3 immunoglobulin subtypes, but had a stronger relative increase in IgE compared to IgG and IgG4 (Table 4). The relationship was also noted in those who were never breastfed (data not shown).

Household exposure to peanut was not a significant predictor of peanut IgE outcomes as indicated in Table 1, and this variable did not survive the multivariate model. Since there is interest in the influence of environmental exposure to peanut on sensitization, we also reviewed the relationship of exposure to peanut-specific IgE/IgG ratios. In a linear regression analysis of $\log_{10}$ IgE/IgG ratios, considering the key variables of maternal ingestion during pregnancy, breastfeeding and exclusion of peanut from the home during breastfeeding, only pregnancy consumption remained in the model as a significant predictor, with an effect size of −0.45.

DISCUSSION

We found that maternal ingestion of peanut during pregnancy had a dose-dependent association with peanut sensitization and likely peanut allergy in infants with likely egg or milk allergy. Our result is in accordance with a previous small study.(21) In that study, 25 children with IgE to peanut were compared to 18 who had positive tests to milk or egg but not peanut. Ingestion of peanut more than once per week during pregnancy trended toward being a risk for peanut sensitization (O.R. 3.97, $p = 0.063$). This small study was potentially

biased by dietary recall because children were up to age 3 years and their peanut allergies were already known. One additional study implicated maternal ingestion of peanut as a risk factor for peanut allergy. Hourihane et al(22) used a questionnaire to evaluate 622 individuals with peanut allergy and noted that probands under 6 years of age were more likely to have mothers who consumed peanut during pregnancy or while breastfeeding compared to older probands. The onset of peanut allergy was earlier in the younger probands and had increased in prevalence over generations, leading the authors to conclude that maternal ingestion may be a risk factor. However, the study could not control for recall bias and may have been influenced by a general increase in atopic disease over the past 3 decades. In contrast to these 2 studies, our study includes evidence of a dose-response and is not affected by comparing participants from different generations, or by a significant potential for dietary recall bias.

In contrast to our data, 2 population based studies concluded that peanut consumption during pregnancy/lactation was not a risk factor for peanut allergy. Lack et al(23) used a part retrospective (several years delay for recall for diet) approach and evaluated a cohort of 13,971 preschool children; data regarding risk factors were limited to analysis of 48 affected children, 23 with confirmed peanut allergy. In a birth cohort of 1218 children followed to age 4 years, Tariq et al(24) also did not identify a relationship between maternal peanut or nut ingestion with sensitization, but only 15 cases were evaluated. It is possible that the low numbers of affected children reduced the power to determine maternal dietary influences in these studies.

The paucity of studies, conflicting results and their limitations has lead to controversies regarding advice to mothers. In 1998 – 2000, the Committee on Toxicology [UK], and the American Academy of Pediatrics [US](7) recommended that women with infants at risk for atopy should avoid peanuts during pregnancy and lactation. The outcome of this advice is unclear. Hourihane et al(4) evaluated parent-child pairs in a UK school cohort born after the avoidance advice (n=1072). In evaluating children with peanut allergy (n=20), 8 mothers had reduced and one stopped peanut ingestion during pregnancy. Dean et al(25) followed a birth cohort on the Isle of Wight, UK born between Sept 2001 and August 2002, and noted that 65% of 838 children available for follow-up had avoided peanut. A total of 658 were skin tested to peanut and 13 were positive; mothers had avoided peanut in 10/13 cases (85% of these had a family history of atopy). The authors of both of these studies interpreted their findings to suggest that avoidance of peanut had no discernable effect. Indeed, the number of affected children in both of these studies was low, reducing the ability to draw firm conclusions.

We identified several additional factors associated with strong sensitization to peanut that are not amenable to risk reduction, including male sex, non-white race and elevated milk/egg IgE levels. Studies of food allergies and atopy in children typically disclose a male preponderance although the pathophysiological reason for this relationship remains unknown.(2;26) Our observation that non-whites, especially Asians, were at higher risk is novel and deserves further study. Lastly, it is not unexpected that sensitization to milk or egg was a risk factor because strong sensitization to these multiple foods has been noted in previous studies, and likely indicates a strong atopic disposition that includes a risk for peanut allergy.(2;26;27)

Atopic disease is influenced by heredity, and previous studies have noted parental atopic disease to be an influence on outcomes of peanut allergy. (23;28) However, we did not identify atopic disease as a risk factor, possibly because our cohort was preselected for having atopic disease; 67% of mothers and 60% of the fathers were atopic. We also did not find an association with soy ingestion and peanut allergy, a factor identified as an

independent risk in a previous population-based study,(23) but not confirmed in two subsequent studies.(29;30) Lastly, it has been suggested that the use of acid suppression medications, by reducing protein digestion, may increase the risk of sensitization and reactions to food proteins,(31) but we did not observe this relationship.

Environmental, non-ingestion exposure to peanut, such as contact from skin creams containing peanut, from residual protein on the hands of caregivers or siblings, or in the home has also been cited as a risk factor for peanut allergy because the skin may be a sensitizing route of exposure.(23;32;33) We did not query about skin products containing peanut because these are not typically available in the US. We did not find having peanuts in the home to be a risk factor for sensitization to peanut, however, we had very few homes that excluded peanut, perhaps limiting power to evaluate this variable.

Our results concerning maternal peanut consumption must be interpreted with caution. This is an observational study and as such we do not know if additional subtle influences affected our findings, especially regarding reporting of dietary habits. To minimize recall bias, we enrolled children between 3 – 15 months of age and families were not informed of peanut IgE test results at the time of the dietary history; however, we cannot exclude the possibility of subtle reporting biases. Our observational study design excluded enrollment of children with known peanut allergy and/or peanut IgE ≥ 5 kU_A/L prior to screening for enrollment; the impact of this exclusion on the current analysis is unknown. Nonetheless, maternal peanut consumption during pregnancy was identified as a significant predictive factor for peanut sensitization in our cohort through a variety of analyses including: univariate, multivariate, models focusing on household ingestion, models isolated to maternal consumption, different trimesters, and considering formula fed infants separately; and was in agreement with our additional novel observation that maternal ingestion of egg during pregnancy was associated with elevated levels of egg specific IgE in the infants.

One might postulate that maternal ingestion is protective, perhaps stimulating an IgG response and transferring IgG to the infant. We interpret our results of the peanut specific IgG and IgG4 data as supporting the notion that maternal ingestion of peanut during pregnancy did not result in favorable IgE/IgG ratios compared to infants whose mothers ingested less peanut. Although we await determination of the final clinical outcomes for these infants, we do not anticipate that the elevated IgE levels are modulated by “protective” levels of IgG. Additionally, we did not observe higher peanut-specific IgG levels in the younger infants, which might have indicated passive transfer (data not shown).

We emphasize that this work focused upon sensitization to peanut, not clinical allergy. Oral food challenges are not typically performed to peanut in this age group and, therefore, diagnostic properties of the test have not been determined in infants. We chose a peanut IgE ≥ 5 kUA/L as an endpoint of interest because several studies(15–17) indicate that this level is associated with a high likelihood of peanut allergy (70–85%) in older children evaluated for a variety of reasons. In a large study by Komata et al(34) that addressed milk and egg allergy, younger infants were more likely to react to the tested food compared to older infants with the same IgE level (e.g., an egg-specific IgE concentration of 3 kUA/L represented an 80% risk for infants under age 1 year and a 40% risk for children over age 2 years). The study by Komata may indicate that the peanut IgE level we selected indicates a higher risk than noted in studies of older children. However, studies in infants with the characteristics of our cohort would be needed to specifically address this possibility.

Longitudinal evaluation of the children in our cohort children will be needed to determine final expression rates of symptomatic peanut allergy. Following standard care, we have suggested not feeding peanut to these young atopic children according to prior guidelines.(7)

The influence of this advice on outcomes of peanut allergy remains unknown because early oral exposure may induce tolerance, as suggested by observations that peanut allergy is less common in Israeli Jews whose infants ingest peanut early, compared to a similar population in the UK who delay ingestion.(32;35) A study is currently underway to determine the effects of early feeding of peanut to infants at risk for peanut allergy (www.leapstudy.co.uk). The interaction of maternal ingestion of peanut and timing of infant introduction may be complex.

Recent studies in children have estimated the prevalence of peanut allergy to be over 1% and approaching 2%(4;36;37) indicating an epidemic.(3) Peanut allergy is usually lifelong(38;39) and can be fatal.(40;41) These observations indicate a need for prevention measures. Our study has identified maternal consumption of peanut during pregnancy as a primary modifiable risk factor. Our observation of a dose-dependent response of peanut ingestion during pregnancy on outcomes of peanut IgE > 5 kU_A/L, as well as a parallel association of maternal egg ingestion on outcomes of egg specific IgE, are striking observations worthy of further exploration in controlled interventional studies.

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Abbreviations

AD	atopic dermatitis
CoFAR	Consortium of Food Allergy Research
PST	prick skin test

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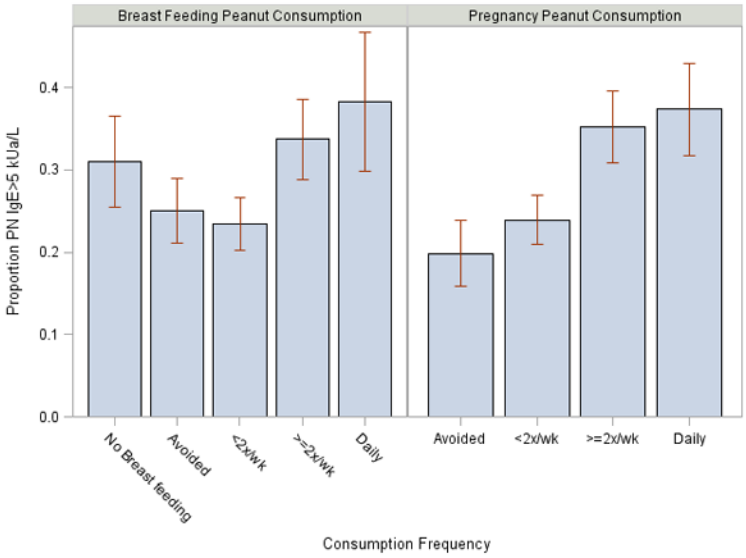

Figure 1.

Proportion of children with elevated peanut specific IgE ≥5 kU_A/L by maternal peanut ingestion status. There was a significant dose-response relationship of peanut consumption during pregnancy with outcomes of elevated peanut IgE (p trend= 0.001), which was not the case for peanut consumption during breastfeeding, p trend = 0.10 (see text).

Table 1

Results of univariate analysis of key clinical and demographic factors in relation to Peanut IgE ≥ 5 kU_A/L (additional factors described in text).

Variable	Total (N) number of subjects	N with Peanut IgE≥5 kU_A/L (%)	Odds Ratio	95% CI	P-value
Site					0.002
Denver	96	22 (22.9%)	0.92	0.47, 1.79	
Duke	101	22(21.8%)	0.86	0.44, 1.67	
Johns Hopkins	108	47(43.5%)	2.38	1.30, 4.36	
Mount Sinai	104	26(25.0%)	1.03	0.54, 1.96	
Arkansas	94	23(24.5%)	reference		
Sex					0.007
Male	342	108 (31.6%)	1.86	1.19, 2.92	
Female	161	32 (19.9%)	reference		
Race					0.003
Black	79	29 (36.7%)	1.87	1.11, 3.13	
Asian	39	19 (48.7%)	3.05	1.56, 5.98	
Other	14	4 (28.6%)	1.29	0.39, 4.20	
White	371	88 (23.7%)	reference		
Parental Allergy/Asthma					0.339
No Known	83	28 (33.7%)	reference		
Maternal	120	36 (30.0%)	0.84	0.46, 1.53	
Paternal	83	24 (28.9%)	0.80	0.41, 1.54	
Both	217	52 (24.00%)	0.62	0.36, 1.08	
AD severity					0.005
None	40	2 (5.0%)	reference		
Mild	50	10 (20.0%)	5.00	1.03, 24.3	
Moderate	253	72 (28.5%)	7.76	1.83, 32.95	
Severe	160	56 (35.0%)	10.50	2.44, 45.1	
Milk, egg or both allergy (clinical reaction)					<0.0001

Variable	Total (N) number of subjects	N with Peanut IgE≥5 kU_A/L (%)	Odds Ratio	95% CI	P-value
Egg	162	32 (19.8%)	0.37	0.23, 0.59	
Milk	99	11 (11.1%)	0.19	0.10, 0.37	
Both	242	97 (40.1%)	reference		
Enrolled with AD or clinical reaction					0.003
AD	196	56 (28.6%)	0.81	0.53, 1.23	
Clinical reaction	90	12 (13.3%)	0.31	0.16, 0.61	
Both	217	72 (33.2%)	reference		
Stomach Acid Control Agents					0.036
Yes	74	13 (17.6%)	0.51	0.2700, 0.96	
No	429	127 (29.6%)	reference		
Breastfed					0.811
Yes	174	48 (27.6%)	0.85	0.46, 1.55	
Prior to enrollment	258	70 (27.1%)	0.83	0.47, 1.47	
Never	71	22 (31.00%)	reference		
Peanut present in house during breast feeding					0.270
Yes	373	107 (28.7%)	1.72	0.86, 3.44	
No	58	11 (19.00%)	reference		
Soy formula					0.143
Yes	243	75 (30.9%)	1.34	0.91, 1.98	
No	260	65 (25.0%)	reference		
Peanut consumption- pregnancy					0.002
Frequent (>=2x/wk)	211	74 (35.1%)	1.85	1.25, 2.74	
Infrequent (<2x/wk)	292	66 (22.6%)	reference		
Peanut consumption during breast feeding					0.039
Frequent (>=2x/wk)	129	45 (34.9%)	1.57	1.02, 2.42	
Infrequent (<2x/wk)	374	95 (25.4%)	reference		

Table 2

Univariate association of immune factors with peanut IgE ≥ 5 kU_A/L. Additional allergens tested by prick skin tests (PST) that did not reach significance include: mold, dust mites and cockroach.

Variable	Total	Odds Ratio	CI	P-value
Log_{10} (milk IgE)	503	2.46	1.97, 3.06	<0.0001
Log_{10} (egg IgE)	503	4.98	3.51, 7.06	<0.0001
Milk PST	502	1.11	1.07, 1.16	<0.0001
Egg PST	502	1.15	1.10, 1.21	<0.0001
Peanut PST	503	1.37	1.30, 1.46	<0.0001
Cat PST	495	1.11	1.03, 1.20	0.007
Dog PST	494	1.13	1.02, 1.25	0.016

Table 3

Multivariate analysis of predictors of peanut specific IgE≥5 kU_A/L. Stepwise, multivariate logistic regression was performed using variables from Tables 1 and 2. Model intercept is −1.44. A significance level of < 0.05 was required to stay in the model.

Effect	Odds Ratio	P-Value	95% Confidence Limits	
SEX (male vs female)	1.92	0.024	1.09	3.37
RACE vs White		0.019		
Black	2.32		1.20	4.51
Asian	2.85		1.18	6.87
Other	1.18		0.29	4.87
Pregnancy Peanut Consumption Frequent vs Infrequent	2.93	<0.001	1.76	4.88
Log_{10} (Milk IgE)	1.55	0.001	1.19	2.01
Log_{10} (Egg IgE)	3.87	<0.001	2.59	5.78

Table 4

Peanut specific IgE (kU_A/L), IgG and IgG4 (mg/L) and IgE/IgG ratio in relation to maternal ingestion. Frequent consumers have median levels 1.5 to 4 times higher. Each variable differs within the consumption groups (all p<.001 except E/G during breastfeeding p=.006).

Peanut consumption		Peanut IgE (median)	Peanut IgG (median)	Peanut IgG4 (median)	Peanut IgE/IgG ratio
Consumption during 3rd trimester of pregnancy	Frequent	2.06	6.69	0.08	0.22
	Infrequent	0.50	3.90	0.04	0.12
Consumption during breastfeeding	Frequent	1.74	6.68	0.08	0.22
	Infrequent	0.54	3.74	0.03	0.14
	Not breastfed	0.88	7.04	0.10	0.19