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Clinical Characteristics of Peanut-Allergic Children: Recent Changes

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**ABSTRACT**

**OBJECTIVE.** The goal was to determine whether patients seen in a referral clinic are experiencing initial allergic reactions to peanuts earlier, compared with a similar population profiled at a different medical center 10 years ago, and to investigate other changes in clinical characteristics of the patients between the 2 groups.

**METHODS.** We reviewed the medical charts of peanut-allergic patients seen in the Duke University pediatric allergy and immunology clinic between July 2000 and April 2006.

**RESULTS.** The median ages of first peanut exposure and reaction were 14 and 18 months, respectively; the respective ages in a similar population profiled between 1995 and 1997 were 22 and 24 months. Within our patient group, those born before 2000 were first exposed to peanuts at a median age of 19 months and reacted at a median age of 21 months, compared with first exposure at 12 months and first reaction at 14 months for those born in or after 2000. Most patients (68%) demonstrated sensitization or clinical allergy to other foods (53% to eggs, 26% to cow’s milk, 20% to tree nuts, 11% to fish, 9% to shellfish, 7% to soy, 6% to wheat, and 6% to sesame seeds).

**CONCLUSIONS.** In the past decade, the ages of first peanut exposure and reaction have declined among peanut-allergic children seen in a referral clinic. Egg allergy is very common in peanut-allergic patients, and sesame seeds should perhaps be considered one of the major food allergens. The decline in the age of first peanut reaction seems to be attributable to earlier exposure.
PUBLIC AWARENESS OF food allergies (in particular, peanut allergy) has increased recently, and at least 2 studies have documented an increase in the prevalence of peanut allergy among children. In a cohort study from the Isle of Wight (United Kingdom), Grundy et al reported that the prevalence of peanut allergy among 3- and 4-year-old children increased from 0.5% among those born in 1989 to 1% among those born between 1994 and 1996. In the United States, a follow-up, random-digit dial, telephone survey found that prevalence rates among children increased from 0.4% to 0.8% between 1997 and 2002. There has been a perception among clinicians that the average age of presentation of peanut allergy has decreased recently, and the literature offers some support for this. A questionnaire survey of 102 peanut-allergic patients evaluated in the Johns Hopkins University pediatric allergy clinic between 1995 and 1997 determined that the median ages for first peanut exposures and reactions were 22 and 24 months, respectively, whereas 4685 peanut-allergic individuals entered into a voluntary registry established through the Food Allergy and Anaphylaxis Network (FAAN) between 1997 and 2000 experienced first exposures and reactions at median ages of 12 and 14 months, respectively.

A voluntary registry such as the one established by FAAN may reflect a slightly different patient population, compared with that seen routinely in a referral clinic. We were interested in evaluating the clinical characteristics of peanut-allergic patients seen in our referral center in the past 5 years. We hypothesized that these patients would have had their first peanut exposures and experienced their initial allergic reactions at younger ages, in comparison with the group of referred patients profiled 10 years ago. We were interested in determining whether there were changes in other important clinical characteristics as well.

METHODS
Medical charts of children evaluated and diagnosed as having peanut allergy in the Duke University pediatric allergy and immunology clinic were reviewed. Patients who were evaluated in the clinic between July 2000 and April 2006 were included. Attempts were made to telephone patients or their families to obtain information that was not readily discernible from the medical charts. Diagnosis of peanut allergy was made with a combination of the following criteria: convincing clinical history and evidence of food-specific IgE, that is, positive skin-prick test results with glycerinated peanut extract (1:20, w/v; Greer Laboratories, Lenoir, NC) or detection in serum with a Pharmacia CAP System fluorescein-enzyme immunoassay (Phadia AB, Uppsala, Sweden). The lower limit of the latter assay is <0.35 kU/L, and the upper limit is >100 kU/L; for calculation purposes, values of 0.34 and 100.1 kU/L were used if concentration results were beyond these limits. Previously established positive predictive values for food-specific IgE concentrations, when available, were used to support diagnoses of allergies to other major foods. When such values were not available, diagnoses of allergies were made by the evaluating physician on the basis of a combination of history, serum food-specific IgE concentrations, skin-prick test results, and oral food challenge results. Challenges were performed in an open manner, using peanut butter as the challenge food. Challenges began with initial placement of 1/32 teaspoon on the patient’s tongue, with gradually increasing ingestions approximately every 10 minutes until either a total of 2 tablespoons was consumed or a reaction occurred and the challenge was deemed a failure.

Descriptive statistics, including means, medians, and ranges, were calculated for all included parameters. Means and medians were based on the observed data. For each calculation, the number of observations used is presented. No imputation was applied for missing data. Two-sample, unpaired t tests were performed for comparisons of interest, with P < .05 defined as statistically significant; χ2 tests with 3 degrees of freedom were performed for birth-month groupings, comparing observed and expected frequencies. Approval for this study was granted by the Duke University institutional review board, under protocol 7490-05-7R0ER.

RESULTS
One hundred forty patients (70 born between 1988 and 1999 and 70 born between 2000 and 2005) were included in the study. Despite review of clinic records and attempts to contact families by telephone, complete information was not available for every patient. Summary patient demographic data are displayed in Table 1. Most patients were male (66%) and highly atopic; 82% had a past or current history of atopic dermatitis, 62% had asthma, and 57% had allergic rhinitis. A family history of atopy was common, with 82% of patients having a first-degree relative with allergic rhinitis, atopic dermatitis, asthma, or food allergy. The median age at the first visit to our clinic was 28 months (mean: 43.2 months; range: 3–204 months); the median age was 31 months (mean: 41.4 months; range: 8–193 months) for girls and 25 months (mean: 44.1 months; range: 3–204 months).

<table>
<thead>
<tr>
<th>Demographic Characteristics of Peanut-Allergic Patients</th>
<th>Proportion</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td><strong>Male, %</strong></td>
<td>66.4</td>
<td>140</td>
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<tr>
<td><strong>Allergic rhinitis, %</strong></td>
<td>57.1</td>
<td>140</td>
</tr>
<tr>
<td><strong>Asthma, %</strong></td>
<td>62.1</td>
<td>140</td>
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<td><strong>Atopic dermatitis, %</strong></td>
<td>81.9</td>
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<tr>
<td><strong>Other food allergy, %</strong></td>
<td>67.9</td>
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<tr>
<td><strong>First-degree relative with atopy, %</strong></td>
<td>82.3</td>
<td>124</td>
</tr>
<tr>
<td><strong>Median age at first visit, mo</strong></td>
<td>28</td>
<td>140</td>
</tr>
</tbody>
</table>

TABLE 1

![Image of Demographic Characteristics of Peanut-Allergic Patients](pediatrics.aappublications.org)
for boys. As illustrated in Fig 1, 31% of patients were born in the months of October through December and 18% were born in April through June.

Ninety-five patients (68%) had evidence of IgE-mediated sensitivity to foods other than peanuts, and proportions did not vary between boys and girls. The most common additional foods are presented in Fig 2. Egg allergy was present for 53% of all patients. The vast majority of patients were avoiding tree nuts as well as peanuts, as is the general recommendation at our institution and from many other allergists, particularly in younger patients and when tolerance to a particular tree nut is unknown.1,4,8 Twenty percent of patients had evidence of allergies to H11350 type of tree nut, with pecans, walnuts, cashews, and almonds being most frequently implicated; macadamia and pine nuts were also involved. Forty-four percent of patients had been prescribed self-injectable epinephrine before their first visit to our clinic, and 90% of those patients reported that epinephrine was always accessible.

Sixty-five percent of patients had knowingly ingested peanuts before being diagnosed as having peanut allergy; all except 1 of those patients reported a reaction in association with ingestion. Eight individuals (5.7%) among the group of 140 patients underwent office-supervised challenges to peanuts, as described above. Those without a known history of ever eating peanut protein were initially diagnosed through a combination of skin prick and serum testing, as described above. No cases were diagnosed on the basis of skin prick alone, without supporting evidence of peanut-specific IgE. The median initial CAP System fluorescein-enzyme immunoassay concentration was 34 kU/L (mean: 47.3 kU/L; range: <0.35 to >100 kU/L); the median initial concentration for girls was 59.15 kU/L, and that for boys was 30.7 kU/L. Reactions to first ingestions of peanuts were common. Among the patients who had documented information about the number of times they had previously eaten peanuts, 83% reacted to the first ingestion. The median age of first peanut exposure was 14 months (mean: 20.5 months; range: 1–84 months). The median age of first reaction was 18 months (mean: 21.9 months; range: 1–84 months); the median age for girls was 17 months, and that for boys was 18 months.

We looked for a correlation between birth-month group (Fig 1) and time period during which patients experienced their first reactions. These results are shown in Table 2. A majority (55%) of children born during the months of January through March experienced their first reactions to peanuts during those same months.
Similarly, 57% of children born in October through December experienced their first reactions during that 3-month period. A similar trend was seen for patients born between April and June. The P value for the overall test of association for this comparison was 0.023.

First reactions occurred at home in 54% of cases. Day care (22%) and grandparents’ homes (8%) were leading locations for reactions occurring outside the home; school was the site of the initial reaction in 3% of cases. Clinical signs of first reactions generally developed fairly rapidly. Eighty-six percent of reactions developed within 10 minutes after ingestion, whereas 93% began within 30 minutes and 95% within 1 hour. The vast majority (92%) of first reactions, although not all, featured skin changes (urticaria, erythema, angioedema, or pruritus); 58% involved skin symptoms alone. The gastrointestinal system was the next most frequently involved, with symptoms (emesis or diarrhea) in 27% of cases and gastrointestinal symptoms as the only manifestation in 8% of cases. Respiratory symptoms (repetitive cough, trouble breathing, or wheeze) occurred with 17% of first reactions and did not occur in isolation in any cases. One patient reported hypotension (documented by paramedics), and no patients experienced loss of consciousness.

Most patients (80%) were treated for their initial reactions. Of the patients who were treated during their first reactions, 94% received an antihistamine as part of treatment and 64% were treated with an antihistamine alone. Eleven percent were treated with an inhaled β-receptor agonist, 19% with epinephrine, and 15% with steroids. Approximately one third (35%) received care outside a medical setting, primarily in the home, whereas the rest were treated in a physician’s office or emergency department.

Thirty-nine percent of patients reported accidental ingestion after the diagnosis of peanut allergy, with a mean number of 1.8 accidental ingestions per patient (range: 1-10 ingestions). The median time to first accidental ingestion was 12.5 months after diagnosis. One fourth (25%) of patients reported a subsequent reaction that was more severe than the first. Four patients in the group (3%) developed tolerance to peanuts, at a median age of 55.5 months (mean: 69.5 months; range: 53-114 months). Tolerance was proven by physician-supervised challenge for 2 of those patients (50%), whereas the others reported discovering tolerance through home ingestion.

As mentioned, the total number of patients was equally divided between those born before 2000 (range: 1988-1999) and those born in or after 2000 (range: 2000-2005). As seen in Fig 3, the group born in or after 2000 experienced first exposures and reactions at younger ages, compared with the older group. Patients born before 2000 experienced first peanut exposures at a median age of 19 months (mean: 28.6 months; range: 5-84 months), compared with a median age of 12 months (mean: 14.7 months; range: 1-45 months) for those born between 2000 and 2005 (P = .005 between means). The group born before 2000 experienced first reactions at a median age of 21 months (mean: 28.8 months; range: 5-84 months), compared with 14 months (mean: 14.9 months; range: 1-45 months) for those born between 2000 and 2005 (P = .005 between means). Patients born in or after 2000 were also more likely to have an allergy to another food (77% vs 59%; P = .029). There was no significant difference in the times from first exposure to first reaction or in the proportions of patients with a first-degree atopic relative between the 2 groups.

**DISCUSSION**

The prevalence of peanut allergy in children has reportedly doubled in approximately the past decade, on the basis of work from at least 2 different groups on 2 different continents.2,3 However, the question of whether this increase can be at least partially attributed to greater public awareness has remained. A cohort study of 6-year-old children...
on the Isle of Wight (United Kingdom) found that reported rates of food allergies far exceeded those determined by food challenges,7 and other studies portrayed similar gaps between rates of perceived and proven food allergies.10–13 Data from the recently established FAAN registry suggest that pediatric peanut-allergic patients are experiencing reactions with a younger age of onset, compared with patients profiled in an academic allergy clinic 10 years ago.4,5 Clinical impressions of many support this observation. We examined our referral population to determine whether this perception of a younger onset of peanut allergy could be confirmed.

Findings from this study indicated that patients seen in an academic allergy clinic were both being exposed and reacting to peanuts at younger ages in the past 5 years, compared with the previous 5 years. Patients seen at the Johns Hopkins University pediatric allergy clinic between 1995 and 1997 experienced first exposures and reactions at median ages of 22 and 24 months, respectively. The respective ages for our population of referred patients were 14 and 18 months. The fact that these ages for the FAAN registry patients were even younger (12 and 14 months, respectively) may be a reflection of the self-selecting nature of such a registry.

We considered whether the earlier age of presentation of these patients might be attributable primarily to heightened awareness of peanut allergy on the part of patients’ families and providers. However, when patients were subdivided into those born before versus after 2000, those born between 1988 and 1999 experienced first exposures and reactions at median ages of 19 and 21 months, respectively, compared with 12 and 14 months for those born later. It is possible to speculate that increased public awareness may lead to children being diagnosed at younger ages and in greater numbers on the basis of skin test or serum test results alone, rather than on histories of reactions to ingestions. Although a significant percentage (35%) of the patients in the study group received diagnoses without a history of peanut ingestion, it is worth emphasizing that the differences seen here between patients born before versus after 2000 were limited to those with actual histories of ingestions and reactions.

The proportion of our patients who were male (66%) was remarkably similar to the proportions in both the FAAN (67%) and Johns Hopkins University (63%) groups.4,5 Other studies found similar trends.14,15 The reason for this is unclear, but the finding is consistent with the predominance of male patients at younger ages and female patients at older ages seen for other food allergies, as well as asthma.8,16,17 The large proportion of our patients with other atopic diseases is also consistent with other characterizations of peanut-allergic patients.2,4,5,8,18

Thirty-one percent of patients were born in October through December, compared with 18% in April through June. The χ² tests did not show a significant difference for this comparison, but these trends are in agreement with earlier findings that led to the grouping in this study,1 and the lack of statistical significance here is likely related to sample size. A study from the Netherlands also detected an increased relative risk of cow’s milk and egg allergies among patients born in November through January, with a decrease in May.19 Much has been written about the relationship of birth month to risk of allergic diseases, with no clear consensus on the subject.20–22 Previous authors speculated that the increase in perennial allergies seen among those born during winter months might be attributable to viral adjuvant effects.5 Why springtime (April through June) birth dates may lead to protection from the development of peanut allergy remains a matter of speculation and future investigation, although this seems to point to an interaction between genetic and environmental factors. Using the same 3-month periods, we found a reasonable correlation between the period of birth and the period during which the first peanut reaction was experienced. The primary limitation of this analysis is the high degree of missing data, because of the retrospective nature of this study, but the correlation raises interesting questions and may be related to dietary changes that parents implement on or near a child’s birthday.

Similar to other profiles of peanut-allergic patients, reactions tended to develop fairly rapidly (95% within 1 hour after ingestion).4,5,23 Most (92%) but not all first reactions involved skin symptoms. Although 19% of reactions were severe enough to result in treatment with epinephrine, no patients were admitted for first reactions. Most (83%) of our patients reacted to their first known ingestion of peanuts. This phenomenon was noted previously4,5,18,23,24 and has raised questions about where and how these patients are sensitized. The fact that fewer than one half of our patients had been prescribed self-injectable epinephrine before their first clinic visit also may reflect known problems with epinephrine underprescription.25–27

Most (68%) of our patients were allergic to other foods, as determined from a combination of history, serum food-specific IgE levels, skin prick testing, and oral food challenges. The proportion of patients with sesame allergy (6%) in this study was similar to the proportions of patients with wheat (6%), soy (7%), and shellfish (9%) allergies. The US Food Allergy Labeling and Consumer Protection Act, which took effect January 1, 2006, mandates clear labeling of products that contain the 8 foods deemed responsible for 90% of food allergens (milk, egg, fish, crustacean shellfish, tree nuts, peanuts, wheat, and soy). Studies from countries where sesame is a dietary staple have demonstrated its prevalence in allergic reactions to foods in those countries.28–30 In Israel, for example, a cross-sectional study found that sesame was second only to cow’s milk in causing anaphylaxis.28 Increasing internationalization of eating habi-
its has caused awareness of this allergy even in areas such as the United Kingdom, where sesame is not a dietary staple. A recent review highlights the fact that, although the US Food and Drug Administration has focused attention on the 8 common allergenic foods noted above, similar agencies in Canada and Europe now include sesame on their lists of common allergens. Our study seems to lend support to the inclusion of sesame on this list in the United States. At a minimum, health care providers should be aware of the growing importance of this food as they assess their food-allergic patients.

The major limitations of this study concern its retrospective nature. As with any retrospective chart review, there were missing data points because all providers did not include all of the same information in their clinic notes. Not all patients were seen in follow-up visits, and not all follow-up visit notes included the same information; therefore, data were incomplete regarding factors such as subsequent development of tolerance, accidental ingestion reactions, and characteristics of subsequent reactions. The proportion of patients in this study who experienced accidental ingestions was smaller than in other studies, but it is possible that a retrospective chart review would underestimate this frequency. Similarly, only 3% of the patients in this study developed tolerance, which is much lower than the rate of ~22% that was reported previously, and it may be that other patients simply did not return to our clinic once they had established tolerance. Attempts were made to fill in missing data through telephone calls and letters, but this necessarily led to recall bias, as well as potential confounding issues related to whether patients and families were able to be contacted. Future attempts to characterize food-allergic patients and the natural history of their allergies will be prospective, so that the same information can be collected from each patient at the time of encounter.

CONCLUSIONS

This study confirms clinical impressions that the ages of first exposures and reactions for peanut-allergic patients are declining. The American Academy of Pediatrics has endorsed the delayed introduction of peanuts until 3 years of age for infants with a strong (both parents or parent and sibling) family history of allergies, as well as maternal avoidance of peanuts during breastfeeding and possibly during pregnancy for the mothers of such infants. A review from the European Academy of Allergology and Clinical Immunology. Section on Pediatrics, recommended exclusive breastfeeding and delayed introduction of solids for 4 to 6 months for all children, supplementing with extensively hydrolyzed formula until 4 months of age for infants with a single allergic, first-degree relative; these summarize the current general recommendations in Europe and the United Kingdom. In addition, in 1998 the United Kingdom Committee on Toxicity of Chemicals in Food, Consumer Products, and the Environment issued a statement recommending that atopic mothers, or mothers of children with a first-degree atopic relative, “may wish to avoid eating peanuts and peanut products during pregnancy and lactation,” a recommendation that seems to have been adopted by many not in the target population.

Although there is limited evidence to support the effectiveness of delayed introduction in the primary prevention of peanut allergy, the large proportion of our patients with atopic family members, combined with the declining age of peanut introduction, suggests that these guidelines have not been widely followed in the United States. Our patients born in or after 2000 first reacted at younger ages, compared with patients born earlier, but there was no difference in the time from first exposure to first reaction between the 2 groups. This may suggest that the decrease in age of first reaction may be attributable only to earlier exposure. It is interesting that this change has occurred at the same time that public awareness of peanut allergy has grown. Whether the declining age of first peanut exposure is related to the recent increase in peanut allergy prevalence is not known. Conversely, investigators are currently examining whether early introduction of peanuts actually promotes tolerance and prevents peanut allergy. Whether early or delayed introduction makes a difference in the development of peanut allergy remains open for debate; it is likely a multifactorial issue, involving genetics and the complex immunologic features of the gastrointestinal system. As we learn more about the factors involved, we should continue to progress toward prevention and treatment of peanut and other food allergies.

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