Peanut Allergy: An Epidemiologic Analysis of a Large Database

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Objective To confirm new observations on peanut allergy and answer current concerns that families and healthcare providers have about peanut allergy.

Study design Children who presented with a story of peanut allergy or peanut sensitization were asked to participate in a registry, which allowed an analysis focused on questions that a food allergy support group had about children with peanut allergy or sensitization.

Results A total of 1070 children were entered into the registry over 5 years. Two-thirds had a reaction to peanut. Children with peanut allergy were predominantly male (63%), white (78%), and with private health insurance (80%). Most reactions involved the skin (55%) and anaphylaxis occurred in 35%. The median age of a reaction was 1 year old. Atopic dermatitis was noted in 60% and asthma in 41%. Additional food allergy was noted in 58%. When second exposures occurred 28% had a more severe reaction. Skin test size did not differentiate the type of a reaction and children with anaphylaxis had slightly higher specific IgE levels. Severe reactions with inadvertent exposure in children who were peanut sensitized was rare (<1%).

Conclusions The strategies for peanut allergy prevention and treatment have evolved. The data obtained in this large registry can answer many questions that families and healthcare providers have during this transition. *(J Pediatr 2018;192:223-8).*

Families faced with the diagnosis of peanut allergy or peanut sensitization encounter many challenges and have numerous questions. They seek help and guidance from the pediatrician, the allergist, the internet, and from the literature. Their search often uncovers a spectrum of information that can be contrasting and confusing. Peanut allergy and peanut sensitization are increasing in prevalence[1-3]; are often severe and potentially fatal[4-6]; are life-long[7]; will require training in proper food avoidance; will require access to injectable epinephrine; and will require training on proper treatment of an untoward event with peanut exposure.[8] Further confusion for parents is the recent focus on primary prevention[9,10] and secondary prevention via desensitization.[11]

There is a need to understand the current peanut environment as families and caregivers navigate through these newer concepts. There are few recent publications regarding real-life questions that families and caretakers may have about peanut allergy.[12] Many population studies are telephone surveys, reporting the clinical course of a child with peanut allergy or peanut sensitization; they have involved limited numbers of children or many allergy practices.[13]

The purpose of this report is to use our large single-center peanut registry to answer specific questions often encountered by healthcare providers about peanut allergy and peanut sensitization.

Methods

The Riley Peanut Registry began on April 1, 2011, and continues to enroll patients. This report is the 5-year experience with the registry and includes children who were enrolled until March 31, 2016. All families who presented with a concern about peanut allergy were asked to participate in the registry. All recruitment was performed by the attending allergist either during new patient evaluations or during follow-up visits if their diagnosis preceded the registry start date. Less than 1% of eligible families refused participation. No family opted out of the registry after they had enrolled.

Our allergy service evaluates children at 3 facilities: the Riley Outpatient Center in Indianapolis, Indiana University North in Carmel, Indiana, and Riley Children's Specialists, in Bloomington, Indiana. The study is approved by the Indiana University School of Medicine Internal Review Board. We did not employ a standardized questionnaire.

Once consents were obtained, the attending allergist asked questions about the peanut experience: the type of reaction (if any); age at initial reaction; subsequent

OFC	Oral food challenges
SPT	Skin prick testing
sIgE	Specific IgE

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reactions; presence of other food allergies, asthma, or atopic dermatitis; and a family history of food allergies (limited to siblings with peanut allergy/sensitization). Demographic data was taken from clinic registration forms and verified with each family including race (as indicated by the parent), sex, and type of healthcare insurance (private, public, or self-pay). Public insurance was used as a surrogate for poverty.

Diagnostic studies performed included skin prick tests, peanut specific IgE (sIgE), and total IgE. At return visits, families were asked about subsequent exposures and reactions. If additional diagnostic tests were performed, they were entered into the registry. This included the results of oral food challenge(s) performed in our facilities. The data was entered into the registry by the principal investigator and reviewed by the research coordinator. The third review of all data entry was again performed by the principal investigator.

Peanut allergy was defined based on a convincing history of a reaction within 2 hours after exposure to peanut (either by ingestion or by contact) and the presence of a positive allergy test.[14] Peanut sensitization was defined as having a skin prick test >3 mm bigger than the negative control; or, for those children who were seen prior to adopting caliper measurements, a wheal of 3-4+ size and/or the presence of detectable sIgE to peanut, but no clinical history of a reaction. Anaphylaxis was defined according to World Allergy Organization/American Academy of Allergy, Asthma, and Immunology criteria.[15] Reaction history data was collected by both parental report and review of the medical records. Other food allergies were listed by either parental report or through the demonstration of sIgE to other foods.

Skin prick testing (SPT) was performed with Greer (Lenoir, NC) extracts using the Greer Pick. The tests were placed on the child's back and read after 15 minutes. All measurements of wheal size were performed with a Fisher Scientific (Pittsburgh, PA) digital caliper measurement of the largest wheal diameter. Specific IgE to peanut and total IgE was performed by the ImmunoCap technique (ThermoFisher, Uppsala, Sweden). Oral food challenges (OFC) were performed at the Riley Outpatient Center and Indianapolis, Indiana University North. All peanut OFCs were open challenges, following established guidelines.[16]

Questions about peanut allergy were obtained from a Food Allergy Support Indianapolis (FASI) meeting. This local food allergy support group meets monthly. The ranked top 10 questions became the framework for this report: (1) Who are the children with peanut allergy/peanut sensitization? (2) How does peanut allergy present? (3) When does peanut allergy occur? (4) Do children with food allergy have other conditions? (5) How often are siblings also peanut allergic? (6) Have there been any deaths due to peanut allergy? (7) Will the next reaction be worse than the first reaction? (8) Do test results relate to severity? (9) Why are so many more children diagnosed with peanut allergy? (10) What are the clinical features of the children who are only sensitized to peanut?

Results include basic frequency distributions for descriptive purposes. $\chi 2$ tests were used for categorical variables, with the Fisher exact test performed when cell counts were small. Because of multiple comparisons within analyses, Bonferroni corrections used to control for type I error rate inflation, with a P value of .004 being considered significant. One-way ANOVA was used for wheal size and specific IgE comparisons. All analytic assumptions were verified to ensure the validity of model results. Statistical tests were performed with SPSS 24 (IBM Corp, Armonk, New York) and SAS v 9.4 (SAS Institute, Cary, North Carolina).

Results

Over a 5-year period, 1070 children were registered in the database; 713 (67%) with peanut allergy and 357 (33%) with peanut sensitization . The specific reactions to peanut are shown in **Table I** (available at www.jpeds.com). The skin was the organ system most frequently affected by peanut (n = 392) and accounted for 55% of the reactions. Cutaneous reactions were mixed and included generalized urticaria in 144 of 713 (20.2%); contact urticaria in 203 of 713 (28.5%); angioedema in 29 of 713 (4.1%); urticaria with angioedema in 4 of 713 (0.6%); atopic dermatitis in 8 of 713 (1.1%); and a nonspecific rash was experienced by 4 of 713 (0.6%). Anaphylaxis occurred in 34.9% (n = 248).

Table II compares demographic and other allergic features among children with peanut anaphylaxis, other peanut reactions, and peanut sensitization only. There was no difference between these 3 groups regarding sex, race, and type of healthcare insurance. However, there are significant differences in the occurrence of other allergic conditions. Children with peanut allergy have significantly less atopic dermatitis ($P < .001$), fewer siblings with peanut allergy ($P = .02$), fewer other food allergies ($P < .001$), and less chance of passing an OFC compared with those with peanut sensitization ($P = .005$). Children with peanut anaphylaxis were significantly more likely to have asthma ($P < .001$) and other food allergy ($P = .04$) than those with nonanaphylactic reactions to peanut.

There were 55 sibling pairs and 3 families with 3 children registered. Adjusting for this redundancy within the registry, 9.2% had a family history of a sibling with peanut allergy/peanut sensitization .

The mean age at the time of the first reaction was 2.06 years (SD = 2.04 years), however, the median age of the first reaction to peanut was 1.0 year, 87.6%, had their first peanut reaction <3 years of age; 35 children who reacted to peanut (4.9%) had a reaction under the age of 10 months. Common reactions in this young group included contact urticaria in 16 (45.7%), generalized urticaria in 9 (25.7%), and anaphylaxis in 6 (17.1%).

In the entire registry, 65% reported atopic dermatitis and 41% reported asthma. Having other food allergies/sensitizations was common in the registry, with 68.7% reporting additional food allergies. Egg allergy/sensitization was reported in 430 (40.2%), milk allergy/sensitization in 213 (19.9%), and milk and egg allergy/sensitization in 160 (15%). Significantly more children with peanut sensitization had milk and/or egg allergy/sensitization compared with those with peanut allergy ($P < .001$). In 335 children (31.3%), peanut was the only

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