

Sho Hamano 

Asuka Yamamoto

Daisuke Fukuhara

Kunimasa Yan

Department of Pediatrics, Kyorin University School of Medicine,  
Mitaka, Tokyo, Japan

Email: hamano-s@ks.kyorin-u.ac.jp

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## Insights into tree nut and sesame consumption from a cohort of 80 peanut-allergic children

To the Editor

Peanut allergy is increasing in prevalence in the United States according to reports<sup>1</sup> and has become a global concern. Sensitization to tree nuts is common with reported rates of up to 86% for multi-nut sensitization with increasing age.<sup>2,3</sup> In addition, peanut allergy has been associated with an increased risk of sesame sensitization and allergy.<sup>4</sup> Patients' attitudes toward tree nut and sesame consumption can be variable following a diagnosis of peanut allergy and have not previously been examined.

Tree nut consumption can be nutritionally beneficial and is reportedly associated with better adiposity measures (lower BMI and waist circumference), and cardiovascular (lower systolic blood pressure) and metabolic syndrome health risk factors (lower insulin resistance, higher high-density lipoprotein cholesterol).<sup>5</sup> A previous European study has reported that consumption of food products by

peanut-allergic patients, including those with precautionary allergen labeling (PAL), is modulated by factors related to anxiety such as label reading and knowledge of threshold and concomitant tree nut allergy.<sup>6</sup>

We performed a prospective evaluation of a cohort of 80 peanut-allergic children, presenting in our tertiary pediatric allergy clinic for follow-up, with the aim to investigate the patients' approach to tree nut and sesame consumption (complete avoidance, selected eating or free eating) and the reasons underlying this approach. IRB approval was obtained for this study.

Eighty children with known peanut allergy (diagnosed by an allergist based on a clinical history of allergic reaction and positive specific IgE or SPT to peanut) presenting consecutively to our food allergy clinic, over a period of 6 months (February-July 2018), were asked to participate in this study. Seventy-eight agreed to participate and two declined. Skin prick testing (SPT) to tree nuts and sesame (in addition to peanut SPT) was performed to assess sensitization to these foods. Sensitization was defined as a wheal of 3 mm or higher to the food tested, compared with the negative control. Patients or caregivers (if the child was unable to provide the relevant

**Abbreviations:** IRB, Institutional Review Board; PAL, precautionary allergen labeling; SPT, skin prick tests.

IRB approval number and statement: The Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals (BCM IRB) reviewed and approved the research protocol (# H-40400).

**TABLE 1** Tree nut and sesame sensitization

| Total N = 78                             | N (%)    |          |          |          |           |            |            |
|------------------------------------------|----------|----------|----------|----------|-----------|------------|------------|
| Tree nuts and sesame                     | Almond   | Hazelnut | Walnut   | Pecan    | Cashew    | Brazil     | Sesame     |
| Consumption                              | 29 (37%) | 17 (22%) | 13 (17%) | 20 (26%) | 15 (19%)  | 8 (10%)    | 59 (76%)   |
| Avoidance                                | 49 (63%) | 61 (78%) | 65 (83%) | 58 (74%) | 63 (81%)  | 70 (90%)   | 15 (19%)   |
| Median and range of positive SPT in mm   | 4 (3-15) | 3 (3-27) | 5 (3-30) | 6 (3-22) | 18 (3-40) | 5.5 (3-20) | 5.5 (3-26) |
| Positive SPT                             | 30 (38%) | 36 (46%) | 38 (49%) | 30 (38%) | 39 (50%)  | 20 (26%)   | 22 (28%)   |
| Consuming <sup>a</sup> with positive SPT | 8 (27%)  | 7 (19%)  | 3 (8%)   | 3 (10%)  | 3 (8%)    | 0 (0%)     | 14 (64%)   |
| Negative SPT                             | 47 (60%) | 41 (53%) | 40 (51%) | 47 (60%) | 39 (50%)  | 57 (73%)   | 55 (71%)   |
| Avoiding with negative SPT               | 26 (55%) | 31 (56%) | 30 (75%) | 30 (63%) | 27 (69%)  | 49 (86%)   | 9 (18%)    |
| SPT not recorded                         | 1 (1%)   | 1 (1%)   | 0 (0%)   | 1 (1%)   | 0 (0%)    | 1 (1%)     | 1 (1%)     |

Median and N values are shown, with percentages and ranges included in brackets.

<sup>a</sup>Consumption is defined as a minimum of twice a week eating of the relevant tree nut

information) were asked about their main reason for avoiding or consuming tree nuts and/or sesame.

The mean age of our cohort was 8 years (range: 3-17 years) with a slight male predominance (60%). Our patients were highly atopic with the majority suffering from allergic rhinitis (82%) and eczema (69%). Asthma was present in 42%, and in 33%, at least one other IgE-mediated food allergy was also present.

Sensitization to at least one tree nut was present in 80% of our cohort. As shown in Table 1, sensitization to cashew and walnut was most commonly observed (50% and 49%, respectively). Hazelnut (46%), pecan (38%), and almond (38%) sensitization followed, but sensitization to Brazil nut was low (26%). The highest median SPT result was noted for cashew (18 mm) and pecan (6 mm), followed by walnut (5 mm), Brazil (5.5 mm), almond (4 mm), and hazelnut (3 mm). The most common co-sensitizations identified in our cohort were as follows: walnut/pecan ( $n = 25$ , 32%), almond/hazelnut ( $n = 19$ , 24%), and walnut/pecan/cashew ( $n = 18$ , 23%).

Among those with positive tree nut SPT, a small percentage consumed the relevant nuts at least twice a week, with almond being the most common (27%) followed by hazelnut (19%). In those with negative SPT to various tree nuts, consumption rates varied between 14% and 43%. Almond (43%) was once again the most popular tree nut, followed by pecan (36%), cashew (31%), hazelnut (24%), and walnut (15%). SPT in our center is performed with a standardized clinic panel including peanut, almond, hazelnut, walnut, pecan, cashew, Brazil nut, and sesame. The patients are unable to identify which nuts test positive on SPT, but are given the results during the clinic consultation. In this study, information on consumption/avoidance was obtained before the SPT results were discussed. Following negative testing in our clinic and reported non-consumption, families are encouraged to introduce the relevant tree nut(s) cautiously at home. For those with low sensitization on SPT, an in-hospital challenge is offered. An in-clinic challenge is also offered to patients with negative SPT who are too worried about trying tree nuts at home for the first time.

When comparing the group of children with 1-2 tree nut sensitizations vs the group with three or more tree nut sensitizations (defined as multi-sensitized), we found no significant differences in food allergy ( $P = 0.18$ ), allergic rhinitis ( $P = 1$ ), asthma ( $P = 0.42$ ), or eczema ( $P = 0.77$ ). In addition, multi-sensitized children did not appear more likely to avoid all tree nuts compared with those who were sensitized to 1-2 tree nuts only (Table S1).

Sensitization to sesame occurred in 28% of peanut-allergic children in our cohort. The majority of children with negative SPT (82%) included sesame in their diet; 64% of patients with positive SPT also ate sesame, suggesting high rates of sensitization, but not clinical allergy. In four cases, families were unsure whether sesame was ever given to the child (not tried).

As seen in Figure 1, the patient-reported reasons for avoidance of all tree nuts included a previous allergic reaction to any tree nut (17%), fear of cross-contamination with either peanut or tree nut (14%), previous positive SPTs to any tree nut (12%), and cohabitation with either a parent or sibling with diagnosed tree nut allergy (6%). Only 7 (9%) of our patients were regularly eating all tree nuts, but over 1/3 were consuming selected tree nuts regularly (regular consumption was defined as consumption of tree nuts at least twice a week). Reasons for selected consumption included (a) an allergic reaction to a different tree nut (but not the one eaten), (b) fear of cross-contamination with peanut or other tree nuts to which the patient was allergic, (c) positive SPT to other tree nuts (but negative to the nut eaten), and (d) a family or patient preference for the selected tree nut(s). Patients who feared cross-contamination in this group only ate almonds and reported buying them in shells. We found no significant difference between younger (up to 5 years old) and older children (more than 5 years of age) and tree nut consumption ( $P = 0.5$ ). There was also no significant difference between children who experienced a moderate/severe index reaction to peanut and those who experienced a mild index reaction, in terms of tree nut consumption and avoidance ( $P = 0.37$ ). For sesame, the most common

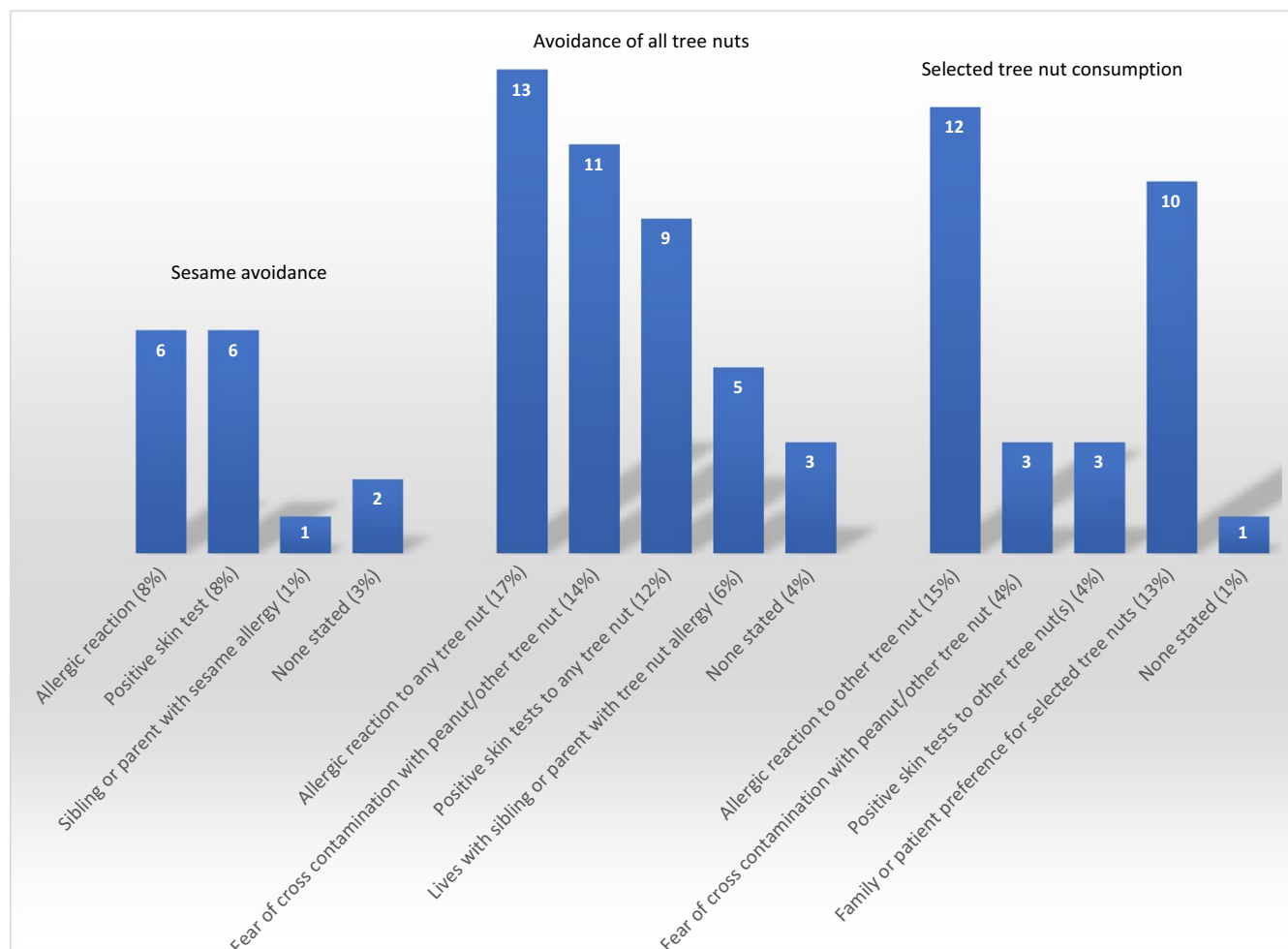


**FIGURE 1** Reported reasons for avoidance of sesame and tree nuts and for selected tree nut consumption are shown as numbers of patients per group. Percentages also shown after each reported reason [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

reasons for avoidance were a previous allergic reaction or previous positive testing to sesame. In one case, sesame was avoided due to another family member with diagnosed sesame allergy.

Limitations of our study include a small sample size and a cohort of peanut-allergic patients seen in an academic, specialist center for pediatric allergy, which may not reflect populations in community clinics.

To our knowledge, this is the first cross-sectional study to systematically examine patients' approach to tree nut and sesame consumption following a peanut allergy diagnosis and our findings reinforce observations in clinical practice. We report that sesame is generally consumed by the majority of peanut-allergic patients and avoidance is mostly the result of a previous allergic reaction to sesame. With regard to tree nuts, although 54% of peanut-allergic patients avoid all, over a third eat selected tree nuts regularly, including 15% with a previous reaction to a different tree nut. The most popular nut by far is almond. Fear of cross-contamination prevents some patients from eating tree nuts, but the most common reason for avoidance is a previous allergic reaction to any tree nut. Interestingly, the age of the child and the severity of the index reaction to peanut do not appear to influence attitudes toward tree nut consumption or avoidance in our cohort.

Among patients with negative skin testing to tree nuts, many choose to avoid these, mainly due to fear of cross-contamination with peanut or due to family preferences. Positive skin tests to tree nuts account for 18% of patients avoiding tree nuts; this suggests that less than 1/5th of patients have relevant sensitization. Considering the results of the LEAP study, which has shown the significant benefit of early introduction of peanut in preventing the development of peanut allergy,<sup>7</sup> there may be a window of opportunity for tree nut introduction also. Although no research is currently available evaluating early tree nut introduction for prevention of tree nut allergy, many centers (including ours) have incorporated a proactive approach in this area. The health benefits of tree nut consumption should also be considered. Dietetic input and patient education on how to safely consume selected tree nuts, in the context of established peanut allergy, are important for families who wish to pursue this.

#### CONFLICT OF INTEREST

None related to this work.

## ORCID

Aikaterini Anagnostou  <https://orcid.org/0000-0001-6240-7437>

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allergy, avoidance, consumption, Peanut, sesame, tree nut

Aikaterini Anagnostou<sup>1,2</sup>  

<sup>1</sup>Section of Immunology, Allergy and Rheumatology, Department of Pediatrics, Texas Children's Hospital, Houston, Texas

<sup>2</sup>Baylor College of Medicine, Houston, Texas  
Email: Aikaterini.Anagnostou@bcm.edu

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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## Using only a subset of pneumococcal serotypes is reliable for the diagnosis of specific antibody deficiency in children: A proof-of-concept study

To the Editor,

Specific or selective antibody deficiency (SAD) is one of the most commonly identified immune defects among patients with recurrent sinopulmonary infections.<sup>1</sup> SAD is defined as an impaired response to polysaccharide antigens and can be detected in approximately 15% of children older than 2 years old referred for evaluation of recurrent infections.<sup>2,3</sup> The diagnosis of SAD requires the documentation of an adequate response to polysaccharide antigens measured by immune response to the 23-polyvalent pneumococcal vaccine (Pneumovax®, 23-PPV) and exclusion of other causes of immunodeficiency.<sup>4,5</sup> Measurement of antibody responses to all serotypes in 23-PPV may not be available in all facilities, and thus, a limited set of pneumococcal serotypes are often used to diagnose SAD.<sup>6</sup> Based on previous studies that demonstrated differences in the immunogenicity among pneumococcal serotypes,<sup>7,8</sup> we hypothesized that a narrower panel of serotype-specific anti-pneumococcal antibody titers would provide comparable diagnostic utility for SAD diagnosis as the complete panel of 23 serotypes. We conducted a retrospective proof-of-concept study to test this hypothesis.

We used the Clinical Investigation Data Exploration Repository (CIDER) to identify patients 2-18 years old who had been evaluated for recurrent infections in the allergy and immunology clinic at St. Louis Children's Hospital, and who had two sets of pneumococcal titers to 23 serotypes drawn 4-12 weeks apart between January 2005 and December 2014. To define an adequate response to 23-PPV, we utilized cutoffs recommended by a task force of the American Academy of Allergy, Asthma & Immunology: a post-immunization level >1.3 mcg/mL, or at least a 4-fold rise in a titer, compared to the pre-immunization level to ≥50% of serotypes tested for 2-5 years of age, or ≥70% of serotypes tested for children 6 years and older.<sup>1</sup> In our clinics, patients with an inadequate immune response are boosted with a 23-PPV, and a second set of antibody levels were obtained 4-8 weeks following the booster. Exclusion criteria included treatment with an immunosuppressive agent in the 3 months prior to the testing, history of solid organ or bone marrow transplants, and diagnosis of another immunodeficiency. We thoroughly reviewed the patients' chart to ascertain that the SAD patients did not have clinical or laboratory features that may raise concerns for other

Table S1: Number of tree nut sensitizations in our patient cohort of 78 children.

| Number of tree nut sensitizations  | Number of patients (N) | Percentage of patients (%) |
|------------------------------------|------------------------|----------------------------|
| None                               | 16                     | 20%                        |
| Sensitization to a single tree nut | 10                     | 13%                        |
| Sensitization to two tree nuts     | 14                     | 18%                        |
| Sensitization to three tree nuts   | 15                     | 19%                        |
| Sensitization to four tree nuts    | 11                     | 14%                        |
| Sensitization to five tree nuts    | 6                      | 8%                         |
| Sensitization to six tree nuts     | 6                      | 8%                         |