



## Patterns of allergen sensitization and self-reported allergic disease in parents of food allergic children



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### ABSTRACT

**Background:** Sensitization in adults has not been extensively studied.

**Objective:** To investigate patterns of allergen sensitization in parents of food allergic children and to compare self-report of allergic disease with specific IgE (sIgE) measurements.

**Methods:** A total of 1,252 mothers and 1,225 fathers of food allergic children answered standardized questionnaires about demographics, home environment, history of atopic diseases, and food allergy. Skin prick testing and sIgE serum tests were performed to 9 foods and 5 aeroallergens.

**Results:** A total of 66.1% of parents were sensitized to either a food or aeroallergen. Mean sIgE levels were low for all foods tested. A total of 14.5% of mothers and 12.7% of fathers reported current food allergy. Only 28.4% had sensitization to their reported allergen. Fathers had significantly higher rates of sensitization to both foods and aeroallergens ( $P < .01$ ) than mothers. Logistic regression evaluating predictors of self-reported food allergy revealed statistically significant positive associations in fathers with self-reported asthma, environmental allergy, and eczema. For mothers, significant positive associations were found with environmental allergy and having more than 1 food allergic child.

**Conclusion:** This cohort of parents of food allergic children found higher rates of sensitization to foods and aeroallergens compared with the general population. However, food sIgE levels were low and correlated poorly with self-reported food allergy. Sex differences in sensitization to foods and aeroallergens were seen.

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### Introduction

Similar to other allergic diseases, the prevalence of food allergy has been increasing for the last several decades.<sup>1,2</sup> Although the cause for this increase in food allergy has not yet been elucidated, an interaction between genetic and environmental factors, including the timing and route of allergen exposure, has been implicated.<sup>3–7</sup> Sensitization, or the presence of allergic antibody, is a prerequisite for development of an allergic response to an allergen. Patterns of sensitization to environmental and food allergens have previously been studied in children in an effort to

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better understand allergy development. Notably, differences in sex have been observed, with a higher prevalence of sensitization in boys, although this finding is not consistent in all age ranges.<sup>8,9</sup>

Previous studies have assessed patterns of allergen sensitization in adults and differences in sex among families. In the United States, the prevalence of allergen sensitization in the adult population has previously been estimated using the National Health and Nutrition Examination Survey (NHANES). NHANES 2005–2006 measured serum specific IgE (sIgE) concentrations to multiple food and environmental allergens. Individuals were tested to 15 inhalant allergens and 4 food allergens (egg, milk, peanut, and shrimp). Nearly half (44.6%) of those surveyed had sIgE to at least 1 of the 19 allergens tested, highlighting a high prevalence of allergen sensitization in the United States.<sup>9</sup> High prevalence has been reported in other nations as well. A European multicountry survey of adults aged 20 to 54 years found a high prevalence of sIgE to foods (range, 6.6%–23.6%).<sup>10</sup> In this study, higher prevalence of sensitization was specifically noted to food allergens that are related to pollen allergens, such as apple (6.5%), peach (7.9%), and hazelnut (9.3%).<sup>10</sup>

Our family-based population study of food allergic children and their parents provided a unique opportunity to assess sensitization to foods and aeroallergens in an atopic population. This cohort was previously used to investigate familial aggregation of food allergy. Significant positive associations between parents and offspring were observed for total IgE and sIgE to all the examined food allergens and aeroallergens. Estimated heritability correlation coefficients ranged from 0.15 to 0.35 for food sIgE and 0.24 to 0.38 for aeroallergens.<sup>11</sup> Our objective was to use this population of parents of food allergic children to investigate patterns of food and aeroallergen sensitization and sex differences in sensitization.

## Methods

### Study Population and Data Collection

This study was part of a family-based food allergy study in Chicago, Illinois. Local families were recruited from both hospital clinics and the community setting from August 2005 through May 2008. Eligible families had 1 index child (aged 0–21 years) with any food allergy and 2 or more family members (biological parents and/or siblings). Clinical criteria for food allergy in the child were met if positive test results (sIgE or skin test to that food) corroborated typical symptoms of an allergic reaction to a food with onset within 2 hours of ingestion. A positive test result or sensitization to a food was defined as a positive ImmunoCAP result or a positive skin prick test result. Symptoms included any 1 of the following: skin (hives or angioedema), respiratory tract (difficulty breathing, shortness of breath, repetitive coughing, wheezing, or chest tightness), oropharyngeal (throat tightness, choking, or difficulty swallowing; tongue swelling), cardiovascular (fainting, dizziness, light-headedness, or decreased level of consciousness), or gastrointestinal (vomiting).<sup>12</sup> Parents of children with chronic health conditions other than asthma, eczema, or allergic rhinitis in the index child were excluded. Information regarding home environment, history of atopic diseases, and food allergy of each family member was collected via questionnaire-based self-report. Skin prick testing was performed. Venous blood samples were obtained from each participating family member. Allergen sensitization was defined as having an sIgE level greater than 0.35 kUA/L or a positive skin test result. The institutional review board of the former Children's Memorial Hospital (now the Ann & Robert H. Lurie Children's Hospital of Chicago) approved the study. All participating adults and children older than 12 years provided written informed consent or assent per institutional review board guidelines before entry.

### Total and sIgE Measurement

Total serum IgE, sIgE for 9 food allergens (egg white, sesame, peanut, soy, milk, shrimp, walnut, cod fish, and wheat), and sIgE for 6 perennial environmental allergens (cat dander, dog dander, cockroach, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Alternaria alternata*) were measured for each participant using Phadia ImmunoCAP. Total serum IgE was reported to range from 2.0 to 5,000 kU/L. sIgE was reported to range from 0.1 to 100 kUA/L, with a level higher than 0.35 kUA/L considered positive. All total and sIgE assays were performed by the Clinical Immunology Laboratory at Children's Memorial Hospital. Quality control and recalibration for the assays were performed as previously published.<sup>11</sup> Allergen sensitization was defined as having an sIgE level greater than 0.35 kUA/L or a positive skin test result.

### Skin Prick Testing

Skin prick tests were performed on participants using the Multitest II device (Lincoln Diagnostics, Decatur, Illinois) to 9 food allergens (cow milk, soy, egg white, wheat, fish mix [cod, flounder,

halibut, mackerel, tuna], shellfish mix [clam, crab, oyster, scallops, shrimp], peanut, sesame, and English walnut) and to 5 perennial environmental allergens (cat hair, dog epithelia, cockroach mix [American and German cockroach], house dust mite mix [equal parts mixture of *D farinae* and *D pteronyssinus*] and *A alternata*). Any skin test with a mean wheal diameter at least 3 mm greater than the saline control was considered a positive result. Histamine was used as a positive control.

### Statistical Analysis

We compared the sensitization rates in our population of adults for 4 food allergens with publically available NHANES 2005–2006 sensitization data using 1-sample binomial tests for the matching sex and age groups. Fisher exact tests or  $\chi^2$  tests with a significance level of .05 were performed to compare the sensitization rates to each allergen between mothers and fathers. A pairwise analysis was also performed. The  $\chi^2$  tests were used to compare parents who self-reported food allergy with those who did not self-report food allergy. Finally, we looked at the potential predictors of self-report of food allergy in fathers and mothers by fitting 2 separate logistic regression models. All statistical analyses were performed using SAS statistical software, version 9.3 (SAS Institute Inc, Cary, North Carolina), IBM SPSS Statistics, version 22 (SPSS Inc, Chicago, Illinois), and GraphPad Prism, version 6.03 (GraphPad Software Inc, San Diego, California).

## Results

Full data were available for 1,252 mothers and 1,225 fathers of food allergic children. Demographic information for the population is provided in Table 1. A total of 13.7% of all parents reported current food allergy, with 3.6% reporting allergy to shellfish, 2.1% to milk, 2.1% to peanut, 2.1% to tree nuts, 1.4% to fish, 1.1% to egg, 1.0% to soy, 0.9% to wheat, and 0.3% to sesame. Two-thirds of adults (66.1%) were sensitized to a food or aeroallergen. Table 2 gives the prevalence of allergen sensitization (positive skin prick test result or sIgE level >0.35 kUA/L) for mothers and fathers. A total of 14.5% of mothers and 12.7% of fathers reported current food allergy. For mothers and fathers combined, the prevalence of sensitization to peanut (15.1%) and sesame (14.4%) was substantially higher than milk (4.4%), egg (3.3%), and fish (1.2%). In their children, the most prevalent allergen was peanut (37.3%) followed by milk (29%) and egg (22.1%).

Of the parents who self-reported food allergy, only 28.4% had sensitization to the food allergen in question. The percentage of parents who reported a food allergy and who were sensitized to that food ranged from 10.7% for fish to 55.6% for peanut. We assessed the proportion of adults with sensitization (a positive skin test result or sIgE level >0.35 kUA/L) who reported food allergy to the food in question. For skin prick testing, this ranged from 11.8% for egg to 33.3% to fish and for positive sIgE result from 21.7% for egg to 72.7% for fish (eTable 1). For comparison purposes, the correlation between testing results and food allergy report in the child cohort is presented in eTable 2. Notably, the proportion of children who met stringent or probable criteria for food allergy by history with sensitization to that food was higher for milk, egg, wheat, shrimp, peanut, and walnut.

Figure 1 shows the distribution of log transformed geometric mean food sIgE concentrations. The mean sIgE levels were low. The lowest mean sensitization in mothers was to cod fish (0.65 kUA/L) and the highest mean was to peanut (1.31 kUA/L). In fathers, the lowest mean sensitization was to soy (0.73 kUA/L) and the highest mean was to shrimp (1.20 kUA/L).

Standard  $\chi^2$  tests were performed to compare the prevalence of sensitization to each specific allergen between mothers and fathers in our cohort (Table 2). Pairwise analyses were also performed for

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