Original Article

Impact of Allergic Reactions on Food-Specific IgE Concentrations and Skin Test Results

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What is already known about this topic? Exposure to allergens, for example, in the pollen seasons or during immunotherapy, can result in increases in specific IgE level, but it is not known whether one-time exposures to food allergen ingestion meaningfully alter IgE levels.

What does this article add to our knowledge? Accidental or food challenge exposure to milk, egg, or peanut that resulted in allergic reactions in children were not associated with significant increases in skin prick test wheal size or allergen-specific IgE levels.

How does this study impact current management guidelines? The results suggest that oral food challenges should not be deferred because of concerns that reactions could affect prognosis.

BACKGROUND: Although there is concern that food allergy reactions may negatively affect the natural history of food allergy, the impact of reactions on food-specific IgE (sIgE) levels or skin prick test (SPT) wheal size is unknown.

OBJECTIVE: To measure the effects of allergic reactions on SPT wheal size and sIgE concentrations to milk, egg, and peanut.

METHODS: Participants included 512 infants with likely milk or egg allergy enrolled in a multicenter observational study. Changes in sIgE level and SPT wheal size to milk, egg, and

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Abbreviations used
CoFAR- Consortium of Food Allergy Research
FAE- food allergy episode
OFC- oral food challenge
sIgE- food-specific IgE
SPT- skin prick test
IQR- interquartile range
NS- statistically not significant

peanut were measured before and after oral food challenge (OFC) or accidental exposure for 377 participants.
RESULTS: The median age of the cohort at the time of analysis was 8.5 years (67% males). There were no statistically significant changes in sIgE level or SPT wheal size after positive OFC to milk, egg, or peanut (n = 20-27 for each food). Change in sIgE level and SPT wheal size was measured after 446 and 453 accidental exposure reactions, respectively. The median change in sIgE level was a decrease of 0.33 kU_A/L ($P < .01$) after milk and 0.34 kU_A/L ($P < .01$) after egg reactions, but no other statistically significant changes in sIgE level or SPT wheal size were observed for milk, egg, or peanut. When we limited the analysis to only those participants who had diagnostic testing done within 6 months of an accidental exposure reaction, we found that peanut SPT wheal size increased by 1.75 mm ($P < .01$), but a significant increase was not noted when all participants with testing done within 12 months were considered.
CONCLUSIONS: The results suggest that reactions from OFCs and accidental exposure are not associated with increases in sensitization among children allergic to milk, egg, or peanut. **(J Allergy Clin Immunol Pract 2016;■:■-■)**

Key words: *Natural history; Food allergy; IgE; Skin prick test*

Food allergy is an important public health concern affecting up to 8% of children.[1] Current management strategies require strict avoidance of causal foods and prompt treatment of allergic reactions, including treatment with injectable epinephrine for severe symptoms.[2,3] Strict dietary avoidance is difficult, and accidental or purposeful exposure to causal foods may occur.[4] Accidental ingestions occur when an individual unknowingly or unintentionally ingests a food containing or contaminated with a food allergen. Purposeful (or nonaccidental) ingestions occur when an individual knowingly ingests a causal food allergen either as the result of nonadherence to dietary instructions or during a diagnostic oral food challenge (OFC).

Although the acute, potentially life-threatening risk of food allergen exposure is well described,[3] the long-term impact of accidental or purposeful food allergen exposure on the long-term prognosis of food allergy is unknown. We previously reported that the annualized allergic reaction rate due to foods was 0.81 reactions per year among the current study population, with more than 70% of the participants reporting at least 1 unsupervised community exposure resulting in a food allergy episode (FAE) to a known food allergen over a 3-year period.[4] In addition to FAEs occurring in the home or community, children with food allergies are also exposed to food allergens when diagnostic OFCs are conducted for clinical or research purposes. The potential impact of these exposures on food-specific IgE (sIgE) concentrations and skin prick test (SPT) responses has not been previously reported. The consequences of these exposures, specifically the concern that the reactions may reduce the chances of outgrowing a food allergy, is often questioned by patients, caregivers, and clinicians, and could result in deferral of OFCs.[5] In previous investigations, seasonal environmental aeroallergen exposure has been associated with a rise in both serum allergen-specific IgE concentrations[6] and increase in skin prick sensitivity.[7] It is unclear whether a similar boosting effect occurs after ingestion of a food allergen. To our knowledge, previous studies have not examined changes in sIgE concentrations or SPT wheal size before and after exposure to food allergens in a large pediatric cohort. Understanding the impact of accidental and/or purposeful food allergen exposure on these indices may inform patients, caregivers, and clinicians regarding the potential long-term impact of these exposures on the natural course of food allergy.

The aim of this investigation was to examine the change in sIgE concentration and SPT wheal size to milk, egg, and peanut before and following exposure to each respective food allergen. The study population consisted of 512 children with milk and/or egg allergy enrolled in a multicenter observational study aimed at examining immunologic, genetic, and environmental factors affecting the natural course of food allergy.[8,9] Participants had OFCs when protocol-specified criteria were met and had blood drawn for serum IgE concentrations and SPTs performed at regularly scheduled visits. Caregivers reported FAEs in "real-time" after an exposure to a food allergen.

METHODS

Subjects

Participant characteristics and study enrollment procedures were previously reported.[8,9] Briefly, this was an observational study of 512 infants in the Consortium for Food Allergy Research (CoFAR2) observational study enrolled with likely egg or milk allergy who were not yet diagnosed with a likely peanut allergy, recruited at ages 3 to 15 months, and enrolled at 5 US sites (New York, NY; Baltimore, Md; Little Rock, Ark; Denver, Colo; and Durham, NC). Infants fulfilled at least 1 of the following 2 criteria: (1) convincing allergic reaction to milk and/or egg with a positive SPT response to the trigger food(s) and/or (2) moderate to severe atopic dermatitis and a positive SPT response to milk and/or egg. Infants were not enrolled if they had a confirmed or convincing allergy to peanut. A Data Safety Monitoring Board and local institutional review boards approved study procedures, and written consents were obtained. Participants were scheduled for a clinical evaluation at 6-month intervals for 2 visits, and then yearly, with telephone contacts between each visit.

Inclusion in the current analysis required exposure to milk, egg, or peanut during a first OFC to the individual food, whether or not a reaction occurred, or a first allergic reaction, termed a food allergy episode, after enrollment if tests for sensitization were available within a year before and following the exposure or challenge. The last enrollment to CoFAR2 was in March 2008; participants are still being followed; however, the database for this report was closed on February 12, 2015.

Oral food challenges

Physician-supervised OFCs were offered at clinician discretion and family preference guided by the protocol under the following circumstances: (1) there was no recent (past 6 months) reaction to the food and (2) current test results (skin test/plasma IgE) indicated