

Food Challenge and Community-Reported Reaction Profiles in Food-Allergic Children Aged 1 and 4 Years: A Population-Based Study



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What is already known about this topic? Little is known about clinical reaction profiles in infants and young children undergoing food challenges irrespective of skin prick test wheal size and community-based history of reaction.

What does this article add to our knowledge? Urticaria is the most common presenting symptom following food challenges in 1- and 4-year-old children, although there is a shift to more angioedema at age 4 years. Anaphylaxis during food challenges in this age group is rare, as are parent-reported breathing problems on accidental exposures.

How does this study impact current management guidelines? Food challenges in this age group rarely result in severe reactions and anaphylaxis. High serum food-specific IgE levels are associated with moderate to severe reactions during food challenges.

BACKGROUND: Oral food challenge is the main tool for diagnosing food allergy, but there is little data on the reaction profiles of young children undergoing challenges, nor how these reactions compare to reactions on accidental ingestion in the community.

OBJECTIVES: To compare reaction profiles from food challenges and parent-reported reactions on accidental ingestion, and assess predictors of severe reactions.

METHODS: HealthNuts is a longitudinal population-based cohort study of 5276 1-year-old infants. Infants underwent skin

prick tests and those with identifiable wheals were offered food challenges. Food challenges were repeated at age 4 years in those with previous food allergy or reporting new food allergies. Community-reported reactions were ascertained from parent questionnaires.

RESULTS: Food challenges were undertaken in 916 children at age 1 year and 357 children at age 4 years (a total of 2047 peanut, egg, or sesame challenges). Urticaria was the most common sign in positive challenges at both ages (age 1 year, 88.7%, and age 4 years, 71.2%) although angioedema was

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Abbreviations used

DBPCFC- double-blind placebo-controlled food challenge
sIgE- serum food-specific IgE
SPT- skin prick test

significantly more common at age 4 years (40.1%) than at age 1 year (12.9%). Anaphylaxis was equally uncommon at both ages (2.1% and 2.8% of positive challenges at ages 1 and 4 years, respectively) but more common for peanut than for egg (4.5% and 1.2% of positive challenges at ages 1 and 4 years, respectively). The patterns of presenting signs reported during community reactions were similar to those observed in formal food challenges. Serum food-specific IgE levels of 15 kU/L or more were associated with moderate to severe reactions but skin prick test was not.

CONCLUSIONS: There was a shift from the most common presenting reaction of urticaria during food challenges toward more angioedema in older children. Serum food-specific IgE levels were associated with reaction severity. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:398-409)

Key words: Food allergy; Egg allergy; Peanut allergy; Sesame allergy; Oral food challenge; Reaction profiles; Anaphylaxis; Community reactions; Urticaria; Angioedema; Skin prick test; Specific IgE

The prevalence of food allergy is reported to have increased over the past 20 years.¹⁻³ Formal food challenges are currently the main tool for diagnosing food allergy, with double-blind placebo-controlled food challenges (DBPCFCs) being the criterion standard.⁴ Nonetheless, the use of food challenges in both clinical practice and research settings has been limited by restraints in available resources and concerns of placing children under unnecessary risk of severe or even fatal allergic reactions. Most children with a large skin prick test (SPT) wheal size do not undergo a food challenge, because perceived benefits are not sufficient to offset potential risks. Because of these limitations, data on patterns of food challenge outcomes, irrespective of SPTs, which require a large number of tests to be performed and systematically examined across time, are limited.

The objective clinical end points of food challenges include noncontact urticaria, angioedema, vomiting, and anaphylaxis. However, differences in food challenge stopping criteria across different centers have hindered the ability to compare results between studies, particularly where studies include subjective symptoms.^{5,6} Previously there was no standard definition for a positive food challenge although a consensus on a standardized criteria for stopping food challenges has recently been developed as part of the PRACTALL guidelines, which reduces these limitations.⁷ However, there is little data on the actual reaction profiles of children undergoing food challenges irrespective of SPT wheal size and reaction history and as such, it is not known whether the signs and symptoms of infants undergoing food challenges differ from those of older children and whether their outcomes should be interpreted in the same manner. In addition, previous research shows that SPT and serum food-specific IgE (sIgE) level cannot predict the type or severity of reaction elicited during a food challenge,⁸⁻¹¹ although a limited number

of studies have suggested that increasing sIgE levels may be associated with more severe reactions.¹²⁻¹⁴ This question has not been comprehensively assessed in a population-representative cohort of children undergoing food challenges at specific ages irrespective of SPT, sIgE, and reaction history. Finally, it is not clear whether reactions observed in controlled food challenges reflect those that may occur in a community setting on accidental allergen ingestion. These will be important to clinicians in deciding the management plans for children presenting with food allergy at different ages and risks of exposure.

The HealthNuts study, a longitudinal population-based cohort study of infants in Melbourne, Australia, is uniquely placed to examine these questions because food challenges were undertaken in all sensitized participants irrespective of SPT wheal size, with challenge staff blinded to SPT result. The aim of this study was to compare clinical reaction profiles from food challenges to peanut, egg, and sesame in infants and young children at age 1 and 4 years and assess whether SPT wheal size or sIgE level could predict the type of reaction. In addition, parental-reported reaction patterns following allergen ingestion in the community setting were examined.

METHODS

Study design

Recruitment. The HealthNuts study is a longitudinal population-based cohort study of childhood food allergy in Melbourne, Australia. The recruitment methods have been described in previous publications.^{15,16} A total of 5276 (out of 7134 approached, 74% participation rate) 12-month-old infants were recruited at council-run immunization sessions, and had SPTs performed to 4 common food allergens, including peanut, egg, and sesame. All children with a detectable wheal size of greater than 1 mm were invited to undergo supervised food challenges at a specialist clinic at Melbourne's Royal Children's Hospital. SPT was repeated on the day of the food challenge, and blood was also taken to measure sIgE level.

Questionnaires. During recruitment, parents completed a questionnaire that collected information on demographic characteristics, family history of allergy, and environmental and dietary exposures, including whether the child had ever had a reaction and type of reaction to a food. Reactions occurring within 4 hours of ingestions were categorized into urticaria, facial swelling/angioedema, vomiting, and breathing problems, corresponding to the 4 signs in our food challenge stopping criteria (see below).

SPTs and serum samples. SPTs were administered with a single-tine lancet (Stallergenes, Antony, France) on the child's back using allergen extracts (ALK-Abello, Madrid, Spain), along with a positive control (10 mg/mL histamine) and a negative control (saline). Wheal size was measured after 15 minutes and calculated as the average of the longest diameter and the diameter perpendicular to that, after subtracting the negative control. Blood samples were collected, and plasma was isolated for specific IgE assays to individual food items using the ImmunoCAP System FEIA (Phadia AB, Uppsala, Sweden).

Oral food challenges. The protocol and predetermined cessation criteria of food challenge have been described previously.¹⁷ All challenges were performed with staff blinded to both SPT results

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