

The Role of Food Challenges in Clinical Practice



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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

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List of Design Committee Members: Andrew J. MacGinnitie, MD, PhD, and Michael C. Young, MD (authors); Michael Schatz, MD, MS (editor)

Learning objectives:

1. To identify indications for performing oral food challenges.
2. To safely perform food challenges in their allergy practice.
3. To identify patient factors that may influence the safety of food challenges in adult patients.

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Food challenges are the criterion standard for establishing the presence or absence of food allergy. However, they remain underused because of their resource-intensive nature, inadequate reimbursement, and concern for the risk of anaphylaxis. Here, we review indications for performing food challenges, including scenarios of uncertain diagnosis, quality-of-life effects following food challenges, and the impact on office practice including coding and reimbursement issues. Demand for food challenges is likely to increase and allergists should be capable of providing

this service to their patients when indicated. © 2017 American Academy of Allergy, Asthma & Immunology (*J Allergy Clin Immunol Pract* 2018;6:353-60)

Key words: Food allergy; Food challenge; Allergy testing

INTRODUCTION

The ongoing food allergy epidemic and recent research on early infant diets resulting in new infant dietary guidelines¹ have placed the allergist at the forefront for guidance on diagnosis, prevention, and treatment. The oral food challenge is uniquely performed by the allergist, and with these prominent issues, there is increased attention on this procedure. This review will examine the utility and applications of the oral food challenge in clinical practice, including impacts on quality of life and the allergist's office practice. Key points are summarized in [Table I](#).

Skin prick tests and serum specific IgE levels are imperfect predictors of true food allergy. Food challenges are therefore considered the criterion standard to establish or refute the presence of food allergies.² However, they are also time and resource intensive and carry the risk of anaphylaxis. Therefore, selecting those patients who are most likely to benefit from challenge is of great importance. Identification of appropriate patients is based not only on results of testing and risk-benefit

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Abbreviations used*EoE- Eosinophilic esophagitis**FPIES- Food protein–induced enterocolitis syndrome**HRQOL- Health-related quality of life*

analysis but also on consideration of patient and family preferences. For example, an 18-year-old individual with a single food allergy may benefit from challenge even with a low predicted chance of passing, whereas an infant with multiple nut sensitizations might forgo challenge to a single nut with a high predicted passing rate, because the family would continue avoidance of all nuts regardless of challenge outcome.

INDICATIONS FOR FOOD CHALLENGES IN CLINICAL PRACTICE

Indications for food challenge can be broadly divided into establishing the diagnosis of food allergy in equivocal cases and documenting resolution of food allergy.

Establishing the diagnosis of food allergy

With a clear reaction history supported by strongly positive testing, the diagnosis of food allergy is established without the need for food challenge. In the following common scenarios below, where the history and/or test results are equivocal, a food challenge is necessary for definitive diagnosis.

Sensitization in the absence of a clear history of clinical reaction.

It is not unusual for allergists to encounter patients referred by another provider, with positive food allergy test results in whom testing may not have been indicated, who had either never eaten the food, or who had been consuming it regularly.^{2,3} Examples would include testing performed before food introduction (eg, infants at high risk for peanut allergy), screening patients with atopic dermatitis or eosinophilic esophagitis (EoE), and testing patients with symptoms not typical of food allergy, such as chronic abdominal pain or chronic urticaria.

In general, patients who are consuming a food regularly in their diet without reactions should be encouraged to continue consumption. Exceptions are patients with severe atopic dermatitis exacerbated by specific foods, or EoE, in which case a trial of elimination may be appropriate.^{4,5} There are multiple reports indicating that in children with eczema managed with elimination diets, subsequent reexposures to the eliminated food trigger immediate-type reactions including anaphylaxis.^{6,7} There are also similar case reports of milk anaphylaxis developing after milk elimination diets prescribed for the management of EoE.^{8,9} Therefore, such patients should be challenged under observation if they have persistently positive testing.

In patients with skin wheal diameters and serum specific IgE values indicating high likelihood of reaction but no history of exposure, it is typically not necessary to challenge; rather patients are instructed to avoid that food. However, if testing is not definitive, food challenge should be offered to establish or refute the diagnosis. This determination is complicated by the fact that no studies address the predictive values of testing in this population.

Clinical history of reactions without sensitization. Conversely, allergists also see patients with history of allergic reactions to food with negative allergy testing to the food. In these cases, it is important to first establish that the observed symptoms

are consistent with an IgE-mediated mechanism. If they are, it should be recognized that testing is not 100% sensitive or specific.¹⁰ We would recommend performing both skin prick and serum specific IgE testing in these cases to minimize the risk of false-negative testing. It may also be helpful to perform prick-to-prick testing with the actual food that caused the reaction if testing with standardized extracts is negative. Examples of positive testing to the actual food but negative test result to the commercially prepared extract include pollen fruit syndrome¹¹ and parasite-contaminated fish.¹² However, even with negative blood and skin testing results, some patients can have reactions consistent with IgE-mediated allergy (eg, hives within minutes of consumption of the food) and in these cases, food challenge is indicated.

Introduction of highly allergenic foods in sensitized infants.

The landmark Learning Early about Peanut Allergy (LEAP) trial established that early introduction of peanut in high-risk infants dramatically decreased the ultimate rate of peanut allergy.^{13,14} Studies of early egg introduction have shown conflicting results,¹⁵⁻¹⁸ but the paradigm that early introduction of allergenic foods protects against allergy seems valid. Consensus guidelines on peanut introduction recommend testing for infants with moderate to severe eczema and/or a history of egg allergy, and conducting food challenges to peanut for those with skin prick test wheals of 3 to 7 mm.¹ In addition, in our experience, many parents of infants with a strong family history of peanut allergy are hesitant to introduce this food without previous testing. LEAP and consensus guidelines suggest modified challenges for those with low positive testing and, as discussed below, there may be a role for supervised feeding in these situations. Bird et al¹⁹ have recently provided guidelines for conducting peanut challenges in infants.

Other indications. Food challenges are often required before and after research interventions for food allergy such as immunotherapy to establish efficacy of the therapy. These are typically high-risk challenges because all patients are expected to have reactions and many participants are highly allergic. Currently these high-risk challenges are not performed in routine clinical practice. As new treatments for food allergy receive Food and Drug Administration approval, the use of challenges in clinical practice will likely increase. This may be particularly true for therapies such as epicutaneous immunotherapy, which do not involve regular ingestion of the allergenic food.

Finally, evidence from food immunotherapy trials and other sources indicates that many patients with food allergies do not have a reaction until they are exposed to substantial amounts of allergen.^{20,21} Thus, it has been proposed that some patients might benefit from low-dose challenges to decrease anxiety and allow ingestion of, for example, foods with precautionary labeling. However, what constitutes a low-dose challenge is not defined. There is also evidence that the typical 15- to 30-minute interval between doses during challenges may be too short and overestimate the tolerated dose.²² In addition, reaction thresholds and severity can be variable in the same individual over time, making conclusions based on a single low-dose challenge problematic.

Documenting resolution of food allergy

Up to 80% of children with egg, milk, soy, and wheat allergy will outgrow their allergy and a lower but significant proportion of peanut, tree nut, and seafood allergies are outgrown. Typically, allergists repeat some combination of skin prick and serum

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