Advances in Food Allergy

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KEYWORDS

• Food allergy • Biomarkers • Component-resolved testing • Oral challenge
• Peanut allergy • Oral immunotherapy • Sublingual immunotherapy
• Epicutaneous immunotherapy

KEY POINTS

- Improvements in component-resolved testing, biomarkers, and immunoglobulin G 4(IgG4)/IgE ratios may improve practitioner's ability to discriminate between patients who are food sensitive but can tolerate food, and patients who are truly food allergic.
- Studies in oral immunotherapy, sublingual immunotherapy, and epicutaneous immunotherapy show promising results as potential treatment options for food allergy.
- Changes in guidelines regarding the early introduction of foods, particularly peanuts, as well as additional investigations into adjunctive therapies, may help prevent food allergies.

INTRODUCTION

The subject of food allergy continues to gain considerable interest due, in part, to the clinical challenge it presents in diagnosis, treatment, and management. Given its potential to cause life-threatening anaphylactic reactions and its impact on quality of life and health care systems, increasing attention has been directed toward strategies to prevent food allergies, including analysis of populations, genotype, and phenotype risk factors, and timing of the introduction of foods. This article reviews some of the recent advances in the diagnosis, treatment, and prevention of food allergy.

ADVANCES IN DIAGNOSIS

Making the diagnosis of any type of allergy requires the combination of appropriate symptomatic patient history with a positive test for immunoglobulin E (IgE) to relevant antigens. When testing for food-specific IgE either by skin or by serum, the practitioner faces a similar dilemma to testing for other allergens, the dilemma that a positive test indicating sensitization does not necessarily translate to clinically relevant allergy.[1] This reality poses a diagnostic challenge to the provider and sows confusion in the patient who has difficulty reconciling a positive test result to a food he/she consumes

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without difficulty. In other situations where the test is equivocal or does not meet the threshold to comfortably recommend strict avoidance of the food in question, oral food challenges are employed to determine clinical reactivity, which carry a real risk of potential harm to the patient. When the patient under evaluation is a child, parents also seek to answer the questions of whether the food allergy will be of limited duration or lifelong, whether reactions will be mild or severe, and even whether siblings might develop the same allergy. Improvements in diagnostic testing seek to discriminate between those truly allergic and those merely sensitized without risk of clinical reaction with the goal of reducing the number of oral food challenges needed, as well as predicting duration and severity of food allergy.

Genetic biomarkers may provide 1 method of improving diagnostic accuracy. In a study by Martino and colleagues,[2] 58 food-sensitized patients ages 11 to 15 months and 13 nonallergic controls underwent skin prick testing, specific IgE testing, oral food challenges, and genome-wide DNA methylation profiling of their blood monocytes. Using 96 DNA methylation sites identified from the study group, these biomarkers were used to successfully predict the clinical reactivity and outcomes of oral food challenges with an accuracy of almost 80% (79.2%), surpassing predictive accuracy of both skin prick tests and specific IgE tests.[2] Further development of such biomarkers has the potential to provide clinically useful diagnostic assays to determine which patients are allergic versus sensitized and decrease the need for oral food challenges.

Other possibilities at improving diagnostic accuracy include component-resolved testing and the presence of IgG4 or blocking antibodies. Component-resolved testing is a diagnostic test similar to specific IgE testing, but involves measuring IgE antibodies to specific allergenic molecules that comprise the foods, rather than the crude food extract.[1] In a study of 108 peanut-allergic, 77 peanut-sensitized, and 43 nonallergic/nonsensitized children by Santos and colleagues,[3] assays of specific IgE and IgG4 to peanut and its components were performed. Although peanut-allergic patients had higher levels of specific IgE to peanut and the components Ara h 1, Ara h 2, and Ara h 8, this did not fully explain the clinical differences in reactivity.[3] However, 2 peanut component patterns emerged; all patients sensitized simultaneously to Ara h 1 and to Ara h 2 had peanut allergy, while all patients monosensitized to Ara h 1 were only peanut sensitized.[3]

Peanut IgG4 levels were 1.6-fold higher in peanut-sensitive patients without clinical allergy, but no significant differences between the levels of specific IgG4 to peanut components were seen, except for Ara h 2-specific IgG4, which was higher in peanut-allergic patients. However, the ratio of peanut-specific IgG4 to peanut-specific IgE was 8 times higher in sensitized but tolerant patients, compared with peanut-allergic patients.[3] When the ratio of IgG4 to peanut components was examined, differences between peanut-sensitive but tolerant and peanut-allergic patients became even larger, with the IgG4/IgE ratio to Ara h 1 (18.8-fold, $P = .05$), Ara h 2 (100-fold, $P = .004$), and Ara h 3 (7-fold, $P = .016$).[3] Overall, although the absolute levels of specific IgG and IgE to peanut and its components individually did not fully account for clinical differences in reactivity between peanut-allergic and peanut-sensitive/tolerant patients, the ratios between these 2 antibodies for peanuts and its components did.

Two recent studies by Santos and colleagues[4] have evaluated the usefulness of the basophil activation test (BAT) in discriminating between clinically-allergic and tolerant but sensitized patients, as well as predicting the threshold and severity of response to peanut oral food challenges. In the first study, 43 peanut-allergic, 36 peanut-sensitized but tolerant, and 25 nonallergic children underwent skin prick testing, specific IgE