Diagnosis of Food Allergy

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KEYWORDS

• Diagnosis • Food allergy • Molecular allergen analysis • Serum-specific IgE
• Skin prick test • Epitope binding • Basophil activation test
• Component-resolved diagnostic testing

KEY POINTS

- Differentiating between clinical allergy and sensitization is challenging but important to prevent overdiagnosis of food allergy.
- Double-blind placebo controlled food-challenges remain the gold standard for the diagnosis of food allergy, although their utility remains limited to research studies. In clinical settings, open oral food challenges are usually considered sufficient.
- Standard food allergy diagnosis involves the use of skin prick tests, allergen-specific immunoglobulin E, and oral food challenges. Molecular allergen analysis is a promising new technique and has increased specificity of testing for peanut and hazelnut allergies, with attention now shifting to other food allergens. Basophil activation tests and epitope binding are actively used in research and may have clinical applications for diagnosis of food allergy in the future.

INTRODUCTION

Food allergy (FA) is defined as "an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food."[1] FA prevalence increased by almost 50% over the past 2 decades in countries with a Western lifestyle.[2] FA is estimated to affect 6% to 8% of the children in the United States and approximately 3% to 4% of the adults.[3] This has led to an increased focus on all aspects of FA, from prevention to treatment.

Diagnosis of FA is challenging, with pitfalls associated with most testing methods. Despite several advances, a double-blind, placebo-controlled food challenge (DBPCFC) remains the gold standard for FA diagnosis. Correctly identifying FA is

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important, not only to prevent reactions but also to avoid unnecessary dietary restrictions that negatively affect growth.[4,5]

This article describes the diagnostic methods for immunoglobulin E (IgE)-mediated FA with a particular focus on molecular allergen analysis (MAA) and basophil activation testing (BAT). This article does not include evaluation of non–IgE-mediated food-allergies, which involve different diagnostic approaches.

CLINICAL HISTORY

As with any disease, a detailed history is important and guides further testing:

- A description of typical symptoms of IgE-mediated allergy (described in **Table 1**), timing of symptoms in relation to food ingestion (usually minutes to 1–2 hours), reproducibility of symptoms with subsequent food ingestion, form (eg, raw vs cooked), and amount of food ingested, are all relevant in FA diagnosis.
- It is important to rule out conditions that mimic FA (**Box 1**).
- Certain populations are at higher risk of FA: those with eczema, asthma, allergic rhinitis, other FA, and a family history of atopic disease (AD).[6]
- Associated cofactors, including acute febrile illness, asthma exacerbation, exercise, alcohol ingestion, drugs increasing gastric pH, and nonsteroidal antiinflammatory drugs, can worsen the severity of an allergic reaction and should be assessed.[7]
- Knowledge of cross-reactivity within food protein families should guide further tests to exclude allergy to related foods if they have not yet been ingested. This should be done cautiously because testing for all homologous proteins can result in elimination of foods that demonstrate sensitization but may not result in allergic reactions.[8] **Fig. 1** summarizes the approximate rate of cross-reactivity between different foods.[8] Decisions regarding testing should be based on likelihood of allergy and the nutritional and social importance of the food.

STANDARD TESTING

In addition to a detailed clinical history, several diagnostic tests can be considered in the evaluation of FA.

Table 1
System-based symptoms encountered in acute immunoglobulin E–mediated food reactions

System Involved	Symptoms (Usual Onset Within Minutes to 1–2 h Following Food Ingestion)
Cutaneous	Pruritus, flushing, urticaria, angioedema, flare of chronic eczematous rash
Ocular	Pruritus, conjunctival erythema, tearing, periorbital edema
Respiratory tract	Nasal congestion, pruritus, sneezing, laryngeal edema and hoarseness, cough, wheeze, chest tightness, dyspnea, cyanosis
Gastrointestinal	Nausea; emesis; crampy abdominal pain; oral pruritus; tongue, lip, palate, or pharyngeal angioedema
Cardiovascular	Tachycardia, bradycardia, hypotension, cardiac arrest, dizziness
Neurologic	Sense of impending doom, syncope, dizziness

Adapted from Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update-2014. J Allergy Clin Immunol 2014;134(5):1025.e41; with permission.