Food allergy: Symptoms and diagnosis

Elissa M. Abrams, M.D., M.P.H.

ABSTRACT

Food allergy is common and has increased in prevalence over time. Although there are many types of reactions to foods, immunoglobulin E (IgE) mediated food allergy is acute in onset and resolves quickly, and is reproducible in nature. Anaphylaxis is the most severe form of IgE-mediated food allergy and has a range of clinical manifestations. First-line food allergy diagnostic testing is sensitive but not specific and should only be done in the context of a convincing history of a reaction. Oral food challenge is the criterion standard in diagnosis but carries the risk of a reaction. The only therapy for anaphylaxis is immediate intramuscular epinephrine. Traditional management of food allergy consists of avoidance management, with strict avoidance, reading labels, and carrying an epinephrine autoinjector at all times. Although effective, accidental reactions do occur, and this management strategy has a profound impact on quality of life.

(J Food Allergy 4:19–21, 2022; doi: 10.2500/jfa.2022.4.220012)

Food allergy is estimated to directly affect ~8%–11% of the U.S. population, with an apparent increase in prevalence over time.[1] Food allergy disproportionately impacts children and is more prevalent in high-income countries.[2] It has an all-encompassing impact on the lives of those directly and indirectly impacted, and poses a burden to quality of life (QoL), interpersonal relationships, and health-care expenses.[1] The goal of this article is to provide a brief overview on the following topics: classification of food allergy, overview of anaphylaxis, diagnosis of food allergy, and avoidance management.

TYPES OF FOOD ALLERGY

Food allergy is defined, overall, as "an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food."[2] Food allergies are subclassified based on the type of immune response and generally can be categorized as immunoglobulin E (IgE) mediated, non-IgE mediated, or mixed IgE and non-IgE mediated (Table 1).[3] IgE-mediated food reactions have a fairly classic presentation, which tends to be acute (within 2 hours), short-lasting (resolving within 24 hours), and reproducible. Symptoms may include one or more of cutaneous, respiratory, gastrointestinal, or cardiovascular symptoms.[4] Cutaneous symptoms are, by far, the most common and are present in > 80% of acute food allergic reactions in children.[4] Immune-mediated food allergy must be differentiated from nonimmune-mediated reactions, which are otherwise termed food intolerances.[2] Food intolerances can be further divided into metabolic, pharmacologic, toxic, or undefined mechanisms,[2] and include lactose intolerance, food poisoning, and the pharmacologic effects of caffeine.[4]

OVERVIEW OF ANAPHYLAXIS

Anaphylaxis is defined as an acute, potentially life-threatening allergic reaction that is usually rapid in onset and has a range of clinical manifestations.[1] It is the most severe clinical presentation of an allergic reaction to a food or other allergen.[5] The lifetime prevalence of anaphylaxis in the United States has been estimated to be between 1.6% and 5.1%, with the largest burden among children and adolescents.[1] Fatal anaphylaxis is relatively rare, with an overall prevalence in the United States and the United Kingdom between 0.47 and 0.69 per million persons.[1] Most episodes of anaphylaxis are IgE mediated.[1,6] Food allergy is one of the leading causes of anaphylaxis, with ~30,000 patients presenting to the emergency department in the United States per year.[1] Different clinical definitions of anaphylaxis exist. In general, anaphylaxis diagnostic criteria rely on clinical involvement of two body organ systems, although more recent guidance by the World Allergy Organization notes that isolated

From the Section of Allergy and Clinical Immunology, Department of Pediatrics, University of Manitoba, Winnipeg, Manitoba, Canada

E.M. Abrams is an employee of Public Health Agency of Canada. The views expressed in this article are her own and not those of Public Health Agency of Canada

The author has no additional conflicts to disclose pertaining to this article

No external funding sources reported

Address correspondence to Elissa M. Abrams, M.D., Division of Allergy and Immunology, Department of Pediatrics, University of Manitoba, FE125-685 William Avenue, Winnipeg, Manitoba, Canada R2A 5L9

E-mail address: Elissa.abrams@gmail.com

*This manuscript is part of the **Journal of Food Allergy** collection of published works referred to as the "Oral Immunotherapy Manual." The contents of this work reflects the opinion(s) of the author(s) and is not intended to replace published guidelines or the clinician's medical advice in the doctor-patient relationship*

This article is distributed under the terms of the Creative Commons Attribution License-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) license (https://creativecommons.org/licenses/by-nc-nd/4.0/), which permits reproduction and redistribution in any medium or format according to the license terms, provided the work is not used for commercial purposes and provided the original authors and source are properly credited and a link is provided to the Creative Commons license. For commercial permissions, visit https://oceansidepubl.com/permission-to-use-content/

Copyright © 2022, The Author(s). Published by OceanSide Publications, Inc., U.S.A.

Table 1 **Categorization of immune-mediated food allergy***

Category of Food Allergy	Name	Clinical Presentation
IgE mediated	Anaphylaxis	Cutaneous (urticaria, angioedema, erythema), respiratory (sneezing, nasal congestion, nasal pruritus, shortness of breath, wheeze, cough), gastrointestinal (severe vomiting, diarrhea, abdominal pain, nausea), cardiovascular (syncope, hypotension)
Non–IgE mediated	FPIES	Delayed profuse emesis, diarrhea, pallor, lethargy
	FPIP	Isolated bloody stools in an otherwise healthy infant
Mixed IgE and non–IgE mediated	Eosinophilic esophagitis	Feeding aversion, abdominal pain, dysphagia, food impaction, choking

IgE = Immunoglobulin E; FPIES = food protein–induced enterocolitis syndrome; FPIP = food protein–induced proctocolitis.
**Reproduced from refs. 2 and 4.*

laryngeal involvement, bronchospasm, or hypotension in the context of a known or highly probable allergenic exposure meets criteria for anaphylaxis.[5]

Anaphylaxis is a medical emergency, and the only first-line therapy is administration of epinephrine (0.01 mg/kg to a maximum of 0.5 mg).[5] The beneficial mechanisms of epinephrine include vasoconstriction (alleviating hypotension and laryngeal angioedema), bronchodilation, and inotropic and/or chronotropic effects.[5] When used *via* the intramuscular route, it is safe and there is no contraindication to epinephrine use during anaphylaxis.[5] Adjunct therapies may include H_1-antihistamines, bronchodilators, and corticosteroids, although none are life-saving and none should be used in place of epinephrine.[1] Delay in epinephrine administration is a consistent factor associated with anaphylaxis fatality.[5]

THE IMPORTANCE OF A CORRECT DIAGNOSIS

The diagnosis of a food allergy relies heavily on a clinical history that is consistent with an allergic reaction.[7] First-line allergy testing involves either skin-prick testing (SPT) or allergen specific IgE testing (sIgE).[4] Both SPT and sIgE are highly sensitive in the diagnosis of IgE-mediated food allergy, with a sensitivity of >90% for SPT and 70%–90% for sIgE, and both wheal size and sIgE level are correlated with the likelihood of "true" allergy.[4] Testing should only be done in the context of a convincing clinical history because the specificity of first-line testing is < 50%.[4] Sensitization on allergy testing does not necessarily reliably predict clinical reactivity, and, if done in the absence of a clinical history, can lead to unnecessary food avoidances and restrictions. In some studies, up to 80%–100% of children with positive testing results to foods could reintroduce those foods into their diets.[8] In general, preemptive screening is not recommended and panel testing is uniformly discouraged.[4,9]

Emerging tests include component-resolved diagnostics (CRD) tests and basophil activation tests. CRD measures binding to specific proteins in an allergen instead of a mixture of allergens. For example, for peanut, CRD can measure six commercially available proteins (Ara h1, 2, 3, 6, 8, 9), instead of SPT and sIgE testing, which measure a combination of these proteins.[7] CRD is increasingly available.[10] In some studies, CRD (such as Ara h 2 to peanut) has a higher likelihood of predicting clinical reactivity and allergy severity than traditional first-line allergy testing.[10] The basophil activation test is also an emerging test but is still used predominantly in research settings.[10]

ORAL FOOD CHALLENGES

Oral food challenges (OFC) are the criterion standard in the diagnosis of food allergy and involve incremental ingestion of a food in a medically supervised environment.[4] OFCs can be open, single-blind, or double-blind placebo controlled. They can be used both diagnostically and to help determine if an allergy has been outgrown.[4] They can also be used to establish an eliciting dose in the case of oral immunotherapy (OIT) and may inform the choice of the OIT starting dose.[11] In addition, OFCs may be necessary if a diagnosis is uncertain before starting OIT (such as in the absence of very clear and attributable IgE-mediated symptoms).[12] Although the double-blind challenge is the most specific, it is the most time-consuming and is rarely used outside a research setting.[4] Open challenge (both the patient and the clinician are aware of the allergen being ingested) or single-blind challenge (the patient is unaware but the clinician is aware) are used most commonly in the clinical setting. Although OFCs are the

diagnostic criterion standard, there are ongoing implementation barriers, including a risk of anaphylaxis, high resource utility, poor acceptability for some families, and, in some cases, poor feasibility due to long wait lists in some centers.[7,13]

THE AVOIDANCE MANAGEMENT STRATEGY

Traditional management of food allergy, often termed the avoidance management strategy, consists of avoidance of the target allergen, strict label reading, and carry an epinephrine autoinjector at all times.[7,14] Accidental reactions are common and can be life-threatening.[14] For example, accidental reactions to peanut in patients with peanut allergy have been shown to occur in > 50% of patients with peanut allergy, with up to 17% of these reactions being severe.[14] The risk of accidental exposure, and avoidance management, has a significant and ongoing impact on day-to-day QoL in individuals with food allergy. In children, avoidance management impacts social activities, including play dates, camps and after-school activities, and social activities at school.[14] Studies of children with food allergy indicate a significant impact on several aspects of QoL, including overall QoL, emotional QoL, and health-related QoL.[7] Children with food allergy are more likely to report bullying at school and to have separation anxiety.[7] In some studies, children with food allergy have a more significant impact on their QoL than the impact of other chronic conditions of childhood.[7]

CONCLUSION

Food allergy is common and disproportionately impacts children as one of the most common chronic diseases of childhood. Although there are many types of reactions to foods, IgE-mediated food allergy is acute in onset, quickly resolves, and is reproducible. Anaphylaxis, the most severe form of IgE-mediated food allergy, is potentially life-threatening and has a range of clinical manifestations. A diagnosis usually relies on first-line SPT and sIgE results, which, although sensitive, are not specific and should only be done in the context of a convincing history of a reaction. The OFC is the criterion standard in diagnosis but carries the risk of a reaction and can be poorly feasible, and acceptable to caregivers. The only therapy for anaphylaxis is expedient use of intramuscular epinephrine. Traditional management of food allergy consists of avoidance management, with strict avoidance, label reading, and carrying an epinephrine autoinjector at all times. Although avoidance is effective do occur and this management strategy has a profound impact on QoL.

CLINICAL PEARLS

- IgE-mediated food allergy is immediate, short lasting, and reproducible.
- Anaphylaxis is a medical emergency, and the only first-line therapy is administration of epinephrine.
- The diagnosis of a food allergy relies heavily on a clinical history that is consistent with an allergic reaction.
- The traditional avoidance management strategy for food allergy has a significant and ongoing impact on day-to-day QoL in individuals with food allergy.

REFERENCES

1. Shaker MS, Wallace DV, Golden DBK, et al. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol. 2020; 145:1082–1123.
2. NIAID-Sponsored Expert Panel; Boyce JA, Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010; 126(suppl):S1–S58.
3. Sicherer SH, Sampson HA. Food allergy. J Allergy Clin Immunol. 2010; 125(suppl):S116–S125.
4. Abrams EM, Sicherer SH. Diagnosis and management of food allergy. CMAJ. 2016; 188:1087–1093.
5. Cardona V, Ansotegui IJ, Ebisawa M, et al. World Allergy Organization anaphylaxis guidance 2020. World Allergy Organ J. 2020; 13:100472.
6. Fischer D, Vander Leek TK, Ellis AK, et al. Anaphylaxis. Allergy Asthma Clin Immunol. 2018; 14(suppl):54.
7. Abrams EM, Chan ES, Sicherer S. Peanut allergy: new advances and ongoing controversies. Pediatrics. 2020; 145:e20192102.
8. Fleischer DM, Bock SA, Spears GC, et al. Oral food challenges in children with a diagnosis of food allergy. J Pediatr. 2011; 158:578–583.e1.
9. Fleischer DM, Chan ES, Venter C, et al. A consensus approach to the primary prevention of food allergy through nutrition: guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical. J Allergy Clin Immunol Pract. 2021; 9:22-43.e4.
10. Sicherer SH, Sampson HA. Food allergy: a review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. J Allergy Clin Immunol. 2018; 141:41–58.
11. Burks AW, Sampson HA, Plaut M, et al. Treatment for food allergy. J Allergy Clin Immunol. 2018; 141:1–9.
12. Wasserman RL, Factor J, Windom HH, et al. An approach to the office-based practice of food oral immunotherapy. J Allergy Clin Immunol Pract. 2021; 9:1826–1838.e8.
13. Greiwe J, Oppenheimer J, Fleischer DM, et al. Trends in oral food challenge practices among allergists in the United States—a workgroup report. J Allergy Clin Immunol. 2019; 143:AB163.
14. Lieberman JA, Gupta RS, Knibb RC, et al. The global burden of illness of peanut allergy: a comprehensive literature review. Allergy. 2021; 76:1367–1384. □