Complete Summary

GUIDELINE TITLE

Food allergy: a practice parameter.

BIBLIOGRAPHIC SOURCE(S)

American College of Allergy, Asthma, & Immunology. Food allergy: a practice parameter. Ann Allergy Asthma Immunol 2006 Mar;96(3 Suppl 2):S1-68. [682 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Food allergy, defined as a condition caused by an immunoglobulin E (IgE)-mediated reaction to a food substance

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Emergency Medicine
Family Practice
Internal Medicine
Pediatrics
Preventive Medicine

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

To improve the care of patients by providing the practicing physician with an evidence-based approach to the diagnosis and management of immunoglobulin E (IgE)-mediated (allergic) food reactions

TARGET POPULATION

Patients with food allergy or suspected of having food allergy

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Patient history (including diet records)
2. Physical examination
3. Skin prick or puncture tests
4. Serum tests for food specific immunoglobulin E (IgE) antibody
5. Oral challenge testing
6. Trial elimination diet
7. Periodic reassessment of food allergy
8. Tests for differential diagnosis of non-IgE mediated adverse reactions to food

Management/Treatment

1. Food avoidance
2. Education of patients and caregivers in dietary management
3. Injectable epinephrine
4. Policies at schools and childcare centers for facilitating allergy avoidance and ensuring prompt treatment of food anaphylaxis
5. Counseling of patients to inform restaurant workers about food allergies
6. Counseling of patients with food-dependent exercise-induced anaphylaxis to avoid exercise in proximity to food consumption, carry self-injectable epinephrine, exercise with a "buddy," and wear medic-alert jewelry

Risk Assessment

1. Family history screening for atopy, or food allergy in particular

Prevention

1. Breast feeding
2. Maternal dietary restrictions
3. Delayed introduction of solid or particular allergenic foods
4. Use of supplemental hypoallergenic or reduced allergenicity infant formulae
5. Avoidance of tobacco smoke

MAJOR OUTCOMES CONSIDERED

- Rate of food allergy in various populations
- Sensitivity and specificity of diagnostic tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Preparation of this draft included a review of the medical literature using a variety of search engines such as PubMed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Ia Evidence from meta-analysis of randomized controlled trials

Ib Evidence from at least one randomized controlled trial

IIa Evidence from at least one controlled study without randomization

IIb Evidence from at least one other type of quasi-experimental study

III Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV Evidence from expert committee reports, opinions or clinical experiences of respected authorities, or both

LB Evidence from laboratory-based studies

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Published clinical studies were rated by category of evidence and used to establish the strength of a clinical recommendation.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This guideline was developed by the Joint Task Force on Practice Parameters, which has published 20 practice parameters for the field of allergy-immunology (see list of publications in the "Acknowledgments" section of the original Guideline document). The three national allergy and immunology societies (the American College of Allergy, Asthma and Immunology [ACAA], the American Academy of Allergy, Asthma, and Immunology [AAAAI], and the Joint Council of Allergy, Asthma and Immunology [JCAAI]) have given the Joint Task Force the responsibility for both creating new parameters and updating existing parameters. Although several previous parameters have addressed the diagnosis and management of anaphylaxis, this document is the first parameter that focuses on such reactions with respect to foods. It was written and reviewed by specialists in the field of allergy and immunology and was supported by the three allergy and immunology organizations noted above.

This document represents an evidence-based, broadly accepted consensus opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

A. Directly based on category I evidence
B. Directly based on category II evidence or extrapolated recommendation from category I evidence
C. Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D. Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
E. Directly based on category LB evidence
F. Based on consensus of the Joint Task Force on Practice Parameters

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The working draft of the Parameter was reviewed by a number of experts on food allergy selected by the supporting organizations.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

This practice parameter includes an algorithm on the diagnosis and management of food allergy accompanied by annotations (numbered to correspond with the algorithm). Guideline recommendations are presented in the form of summary statements. After each statement is a letter in parentheses that indicates the strength of the recommendation. Categories of evidence (Ia, Ib, IIa, IIb, III, IV, LB) and strength of recommendations (A-F) are defined at the end of the "Major Recommendations" field.

Annotations

1. Adverse reactions to food are common in the population. In contrast, food allergy represents a small percentage of all adverse reactions to food. The proper diagnosis and subsequent management of food allergy rely heavily on historical features of the adverse reaction. The following historical information should be obtained: (1) identification of the suspect food or foods, (2) the amount of time between ingestion of the food and development of symptoms, (3) symptoms attributed to the food, (4) amount of food required for a reaction, (5) reproducibility of symptoms on prior or subsequent ingestion, (6) requirement for other cofactors (e.g., exercise), and (7) length of time from last reaction. After a detailed history has been obtained, a determination of whether the adverse reaction to food is likely to be immunoglobulin E (IgE) mediated or IgE associated is essential.
2. There are several historical features that are suggestive of an IgE-mediated food reaction. Manifestations of an IgE-mediated reaction may include pruritus, urticaria or angioedema, gastrointestinal symptoms, rhinoconjunctivitis, bronchospasm, and anaphylaxis. Symptoms of oral allergy syndrome are usually restricted to the oropharynx and include pruritus, tingling, and angioedema of the lips, tongue, palate, and throat. Rhinoconjunctivitis or asthma as a sole manifestation of food allergy is rare; however, these symptoms occur commonly in association with other manifestations in food allergy. The time from ingestion to symptom onset in food allergy is typically rapid, usually within minutes, but may be delayed up to an hour and rarely up to a few hours. In addition, small quantities of food may elicit even severe reactions. Re-exposure also provokes a reaction.

   IgE-associated food reactions such as those triggering atopic dermatitis are more difficult to discern by history alone. The symptoms seen with IgE-associated reactions in atopic dermatitis are primarily pruritus and

papulovesicular eruptions. These symptoms may develop minutes to hours after ingestion of the food.

3. Only a minority of adverse reactions to food are IgE mediated or IgE associated. Some adverse reactions to foods may be immune mediated but not involve IgE in their pathogenesis. Examples include gastrointestinal reactions (e.g., food-induced enterocolitis, celiac disease, Crohn disease), cutaneous reactions (e.g., dermatitis herpetiformis), and pulmonary reactions (Heiner syndrome). Nonimmunologic food reactions include diverse entities such as lactose intolerance, food poisoning, and scombroid poisoning. The evaluation for these non-IgE-mediated reactions may include diagnostic procedures such as food challenge, skin biopsy, stool cultures, and gastrointestinal biopsy. Specific evaluation for each of these non-IgE-mediated reactions is discussed in further detail in the "Differential Diagnosis of Adverse Reactions to Food" section of the original guideline document.
4. If the history is consistent with an IgE-mediated or IgE-associated food reaction, specific IgE testing is the next step. Methods of testing for food-specific IgE include percutaneous skin testing (PSTs) (prick or puncture) and serum tests for specific IgE. Both methods offer high sensitivity and are therefore useful in helping exclude a diagnosis of food allergy. The PSTs and serum tests for specific IgE are only moderately specific, and therefore other diagnostic evaluation is typically required. Intracutaneous (intradermal) skin tests for foods are potentially dangerous, overly sensitive (increasing the rate of a false-positive test result), and not recommended. Commercial food extracts (except for some raw fruits and vegetables) typically are adequate to detect specific IgE in most cases of food allergy. In the case of pollen food-related reactions, testing with the fresh food may provide greater sensitivity. For example, for food reactions that involve raw fruits or vegetables, the PST can be performed using liquid foods, by creating an in-house extract, or using a prick-prick technique (pricking the fruit and then the patient, thereby transferring the soluble fruit proteins). These techniques may offer greater sensitivity and hence a higher negative predictive value to exclude food allergy.
5. Even in a patient whose history is suggestive of an IgE-mediated reaction, if testing for food-specific IgE is negative, the patient will likely tolerate the food. In some cases of atopic dermatitis, particularly in infants, reactions to foods may occur in the absence of detectable IgE. In cases where the reaction to the food was more severe, an open challenge to the negatively tested food may be considered to definitively exclude food allergy. Oral challenges can elicit severe, anaphylactic reactions, so the physician should be prepared with appropriate emergency medications and equipment to promptly treat such a reaction.
6. In patients whose food reaction was that of anaphylaxis and test results for food specific IgE are positive, no further evaluation is typically required. The risk of a potentially severe reaction on food challenge in such a patient warrants a more prudent approach of eliminating the food.

   For a few foods, increasingly higher concentrations of food specific IgE antibody, reflected by larger PST responses or high serum IgE antibody concentrations, are correlated with increasing risks for clinical reactions. However, for most foods, types of reactions, and age groups, diagnostic thresholds for clinical correlations have not been established.

7. Once the diagnosis of food allergy has been established, the only proven therapy is strict avoidance of the specific food. Patients and families need to be educated to avoid unintentional ingestion of food allergens. Reading food labels and recognition of the unfamiliar terms used in labeling constituents that may indicate the presence of a given food allergen is essential. Vague or inaccurate labeling of foods and cross-contamination at the time of packaging or during food preparation (especially in restaurant settings) are other potential hazards in food avoidance. Strict food avoidance is usually a complex task and additional educational resources may be required, such as those available through the Food Allergy and Anaphylaxis Network (Fairfax, VA, 1-800-929-4040 or http://www.foodallergy.org). For patients with a history of anaphylaxis (or reactions with anaphylactic potential), self-injectable epinephrine should be prescribed and patients should be instructed on its proper use. Additionally, identification of risks by cards or jewelry, such as MedicAlert, should be considered.
8. In patients with a history of anaphylaxis after ingesting a specific food who have specific IgE to that food, food avoidance is recommended. If these patients continue to have anaphylactic reactions despite avoiding the culprit food, further evaluation is required. Detailed food diaries, including specific ingredient lists of prepared meals resulting in anaphylaxis, should be obtained by the patient and reviewed by the physician. Details of other cofactors, such as relationship to exercise, should also be obtained. In many cases, given the complexity of food avoidance, the patient may still be inadvertently ingesting the allergenic food. Inadvertent ingestion of "hidden foods" due to improper or imprecise labeling or cross-contamination is a well-known pitfall in food avoidance. In some cases, patients may be reacting to cross-reacting foods. Proper identification of potential cross-reacting foods and additional avoidance of these foods would also be required. In other cases, the specific IgE detected to the culprit food may have detected sensitization or the presence of IgE that is not clinically relevant. Another unidentified food allergen or even idiopathic anaphylaxis may be the true cause of recurrent anaphylaxis.

   In patients with persistent symptoms despite strict avoidance of the food, an oral food challenge could be considered to prove or disprove that the culprit food is indeed the causative allergen in the patient's recurrent symptoms. For patients with presumed food-induced anaphylaxis, either an open or blinded food challenge could be performed cautiously.

   In other IgE-mediated reactions to certain foods, the level of specific IgE or size of the wheal-and-flare reaction on PST in certain instances may add enough diagnostic and prognostic information to warrant food avoidance even in the absence of a history of anaphylaxis. Further evaluation is required in these patients without a history of food anaphylaxis who have been avoiding a food based on a diagnostic test yet continue to have symptoms. Given the complexity of food avoidance, the patient may still be inadvertently ingesting the allergenic food or cross-reacting food(s). In other patients without a history of food anaphylaxis, the diagnostic test, although highly predictive, may not be completely predictive and might give a false-positive result (e.g., sensitization without clinical relevance). For example, in a limited number of foods and age groups, a given level of food-specific IgE may yield a 95% likelihood of a positive challenge to that food. However, 5% of patients with

this same level of specific IgE may be able to tolerate the food without symptoms.

In patients without a history of food anaphylaxis who have been avoiding a food based on a diagnostic test, oral challenge to that food can also be performed. In these circumstances a blinded food challenge would typically be preferred. In these patients with food specific IgE who remain symptomatic despite avoidance, if the oral challenge result is positive, true food allergy is indicated and usually suggests that food avoidance has not been complete. Rarely, another food may be the causative factor and a food diary may help identify another culprit food allergen. In contrast, if the food challenge result is negative, despite the presence of food specific IgE, other causes of the symptoms should be sought and the negatively challenged food may be added back to the diet.

9. For most patients being evaluated for food allergy, there is neither a history of anaphylaxis nor a highly predictive, diagnostic test result. For these patients, further evaluation is typically required before diagnosing a food allergy simply based on a positive food specific IgE test result. Oral food challenges provide the most definitive means to diagnose an adverse reaction to food and are particularly useful in patients with episodic symptoms suggestive of food allergy. Although oral food challenges offer a more precise method for diagnosing food allergy, the complexities involved with oral food challenges may not be suitable for all clinical situations. In the evaluation of disorders with chronic symptoms where foods may be causal (atopic dermatitis, gastrointestinal symptoms), elimination of suspected causal foods may be undertaken to prove the concept that symptoms are diet responsive.
10. Oral food challenges provide the most definitive means to diagnose food allergy. These include open challenges or placebo-controlled blinded challenges in which the food or a placebo is masked in a carrier food or opaque capsules. Blinded challenges can be performed in a single-blind fashion, where the patient is unaware of the content of the test substances, or a double-blind fashion, where neither patient nor physician is aware of the content of the tested substances. Food challenges in patients with specific IgE have the potential to elicit serious reactions, including anaphylaxis. Therefore, these challenges should be performed in a controlled setting where emergency supplies for the treatment of anaphylaxis are readily available. The supplies in this setting are similar to those required for safe administration of allergen immunotherapy (see Practice Parameters for Practice Allergen Immunotherapy).

    Open challenges may be preferred in certain situations. Since they are the simplest to perform, in cases where multiple foods are in question, foods tolerated in an open challenge can be excluded. Since the open challenge is most prone to bias, positive results must be viewed with caution. Foods that result in physiologically relevant symptoms can be further investigated in a blinded controlled challenge.

    Single-blind challenges offer another method for food challenges. There are several advantages of single-blind food challenges. As opposed to an open challenge, the single-blind challenge helps eliminate patient bias. Single-blind challenges are technically easier to perform, since they do not involve an

additional unblinded participant to prepare the placebo and active doses. Single-blind challenges have more flexibility in design, such as the addition of multiple initial placebo doses. This can be particularly helpful in patients in whom food reactions are not causally related to foods.

The double-blind placebo-controlled food challenge remains the gold standard for the diagnosis of food allergy. Although the single-blind challenge helps eliminate patient bias, the individual(s) performing the food challenge have the potential to be biased in the interpretation of the results. Nevertheless, double-blind placebo-controlled food challenges are usually not necessary in most clinical situations but remain an essential tool in food allergy research.

If a double-blind placebo-controlled food challenge result is positive, in most cases this indicates food allergy and food elimination is recommended. In contrast, a positive single-blind or open challenge does not necessarily indicate a true food allergy. In cases of a positive single-blind or open food challenge where doubt exists, a double-blind placebo-controlled challenge could be performed. Especially in cases where the positive challenge result is based on subjective symptoms (e.g., pruritus, dyspnea), blinded challenges may need to be performed to help prove causality. In blinded challenges, technical limitations exist, such as quantity of food required for reaction, ability to mask food, and if the test food has been eliminated for 2 weeks before the challenge (see "Diagnosis of Food Allergy" section in the original guideline document).

A negative food challenge result indicates that the food-specific IgE is not clinically relevant and the tested food is not responsible for the patient's symptoms. In cases of negative results after blinded food challenges, particularly if foods are encapsulated, an open challenge with the food in its "natural" state may be required to ensure tolerability of the food.

11. Same as Annotation 7.
12. If a patient has no reaction on oral challenge to the incriminated food, the tested food is likely to be well tolerated. Nevertheless, to help exclude false-negative results, it has long been suggested to include an open feeding under supervision of a meal-size portion of the tested food prepared in its usual manner as a follow-up to any negative double-blind, placebo-controlled food challenge. It is also important to appreciate that certain preparation methods (canning, dehydration) may alter the allergens; hence, an open challenge with a meal-size portion of the food prepared in its natural state for consumption following a negative double-blind, placebo-controlled food challenge may be helpful.
13. Because of the poor positive predictive value of food-specific IgE tests, a positive test result does not always equate with clinical food allergy. Trial elimination diets are diagnostic and therapeutic procedures that may be used in patients with presumed food allergy. Elimination diets are particularly helpful in cases where several culprit allergens have been identified based on positive food specific IgE tests, since food challenges would need to be done individually to the multiple foods and can be time-consuming.
14. In patients who have symptoms suggestive of food allergy and specific IgE to a food or foods, improvement or resolution of symptoms following food elimination provides supporting evidence for causality. Nevertheless, a

placebo effect should be considered. In cases where diagnostic uncertainty exists, a blinded food challenge may be performed to confirm a true food allergy.

15. Most children allergic to egg, milk, wheat, and/or soy lose their sensitivity within the first 3 to 5 years of life. Although food-specific IgE generally declines with the onset of clinical tolerance, many children who become clinically tolerant of a food may still have specific IgE. Food challenges may also be required to determine if tolerance has developed. Approximately 20% of children with peanut allergy may lose their sensitivity over time. Since peanut is a food frequently associated with anaphylaxis, care must be taken to select patients for peanut challenge.

Summary Statements

Mucosal Immune Responses Induced by Foods

1. Mucosal adaptive immunity has dual functions of protection against enteric pathogens and maintenance of autotolerance against dietary proteins and commensal bacteria. (E)
2. Factors that regulate gastrointestinal immune balance include the nature and dose of the antigen, immaturity of the host, genetic susceptibility, the rate of absorption of a dietary protein, and the conditions of antigen processing. (E)
3. Food allergens are generally glycoproteins with molecular weights ranging from 10 kDa to 70 kDa. (E)
4. The more common food allergens in infants and young children are cow's milk, hen's egg, peanut, tree nuts, soybeans, and wheat, whereas the adult counterparts are peanuts, tree nuts, fish, crustaceans, mollusks, fruits, and vegetables. (B)
5. Major allergenic epitopes have been identified and genes for some of the major allergens have been cloned and sequenced. (E)
6. Innate allergenicity of foods may be determined by a combination of factors such as solubility, resistance to pH, heat, and proteolysis by digestive enzymes. (E)
7. Structural amino acid sequences, either sequential or conformational, account for cross-reactivity between foods. Sequential epitopes may be particularly important for persistence of allergenicity beyond childhood (e.g., casein hypersensitivity). (B)
8. The specific factor(s) that confer allergenicity rather than tolerogenicity are unknown. (E)
9. Characteristic IgE- and mast cell-mediated mechanisms occur in food-induced anaphylaxis, the oral allergy syndrome, and atopic dermatitis. (B)
10. IgE-mediated reactions to foods may occur in neonates on first postnatal exposure, presumably due to in utero sensitization. Since sensitization to dietary allergens in breast milk may occur in the late postnatal period, breastfeeding mothers should avoid highly allergenic foods if familial allergic susceptibility is present. (B)
11. Both serum and secretory specific immunoglobulin A (IgA) to dietary proteins may be produced in healthy subjects and allergic patients. (B)
12. The significance of immunoglobulin M (IgM), immunoglobulin G (IgG), and IgG subclass antibodies (e.g., the role of IgG4) in food allergy is less well understood and highly controversial. (B)

13. The role of cellular in vitro correlates as diagnostic or prognostic indicators of food allergy is not established. (B)
14. The role of specific cytokine profiles in serum or peripheral mononuclear cells of food allergic patients has not been established in the mechanism of food allergy. (B)
15. Certain bacterial products, viruses, parasites, and T-cell-independent antigens stimulate systemic immune responses rather than tolerance to the oral protein when coadministered with oral proteins. (B)
16. Sensitization to foods is much more likely to occur in the early neonatal period. (B)
17. Intestinal malabsorption and/or stasis may predispose patients to food allergy. (B)
18. Genetic susceptibility, as defined by single nucleotide polymorphisms or specific haplotypes, has been implicated in several common food allergy phenotypes. (B)

The Clinical Spectrum of Food Allergy

19. Allergic food reactions to foods (IgE-mediated reactions) are characterized by a temporal relationship between the reaction and prior exposure to food. Such reactions can be generalized or localized to a specific organ system and can be sudden, unexpected, severe, and life-threatening. (D)
20. Food allergens are a frequent cause of severe anaphylaxis, particularly in patients with concomitant asthma and allergy to peanut, nut, or seafood. Such reactions may be biphasic or protracted. Food allergy should be considered in the differential diagnosis of patients who have idiopathic anaphylaxis. (C)
21. The pollen-food allergy syndrome (oral allergy syndrome) is characterized by the acute onset of oropharyngeal pruritus, sometimes including lip angioedema, usually beginning within a few minutes after oral mucosal contact with particular raw fruits and vegetables during eating. (B)
22. IgE-mediated gastrointestinal reactions can present with only gastrointestinal symptoms or with other nongastrointestinal manifestations. (D)
23. Allergic eosinophilic gastroenteritis (eosinophilic gastroenteropathy) is characterized by postprandial gastrointestinal symptoms associated with weight loss in adults and failure to thrive in infants. (C)
24. Upper and lower respiratory tract manifestations of IgE-mediated reactions to foods, such as rhinoconjunctivitis, laryngeal edema, and asthma, can occur with or without other IgE-mediated symptoms. Isolated respiratory manifestations from exposure to foods are rare and have been reported most frequently in an occupational setting. (C)
25. Many inhaled food proteins in occupational settings may affect workers regularly exposed to such foods as flour (bakers' asthma), egg white, and crustaceans. (A)
26. IgE-mediated cutaneous reactions, such as acute urticaria or angioedema and acute contact urticaria, are among the most common manifestations of food allergy. Food allergy is commonly suspected though rarely incriminated in chronic urticaria and angioedema but is implicated in at least one third of children with atopic dermatitis. (B)

Prevalence and Epidemiology

27. The prevalence of food allergy as reported in double-blind studies is not as great as that perceived by the public. It varies between 2% and 5% in most studies, with definite ethnic differences. (B)
28. The prevalence of food allergy is higher in certain subgroups such as individuals with atopic dermatitis, certain pollen sensitivities, or latex sensitivity. (B)

Natural History of Food Allergy

29. Although sensitivity to most food allergens such as milk, wheat, and eggs tends to remit in late childhood, persistence of certain food allergies such as peanut, tree nut, and seafood most commonly continues throughout one's lifetime. (B)
30. The natural history of specific foods varies considerably. (C)

Risk Factors and Prevention of Food Allergy

31. The rate of observed food allergy in children born to families with parental asthma was approximately 4-fold higher than expected when compared with an unselected population. (B)
32. Food allergy prevention strategies include breastfeeding, maternal dietary restrictions during breastfeeding, delayed introduction of solid foods, delayed introduction of particular allergenic foods, and the use of supplemental infant formulae that are hypoallergenic or of reduced allergenicity. However, the effectiveness of these strategies for safeguarding against the development of food allergies has not been established. (B)

Cross-Reactivity of Food Allergens

33. Recent studies with molecular biological techniques have characterized a variety of cross-reacting allergens among foods. (C)
34. In vitro cross-reactivity to multiple shared food allergens is common, but clinical correlation of the cross-reactivity is variable. (C)
35. Cow's milk allergy is a common disease of infancy and childhood. Goat's milk cross-reacts with cow's milk. Ninety percent of cow's milk allergic patients will react to goat and/or sheep's milk. (A)
36. Hen's egg allergens cross-react with certain avian egg allergens, but the clinical implications of such cross-reactivity are unclear. (B)
37. In vitro cross-reactivity between soybean and other legume foods is extensive, but oral food challenges demonstrate that clinical cross-reactivity to other legumes in soy bean sensitive children is uncommon and generally transitory. (B)
38. Patients with peanut allergy generally tolerate other beans (95%), even soy. Evaluation of legume allergy in a patient with peanut allergy should be individualized but avoidance of all legumes is generally unwarranted. (B)
39. There is significant cross-reaction between different species of fish. Although there is limited investigation of the clinical relevance of such cross-reactivity, patients who are clinically allergic to any species of fish should be cautious about eating fish of another species until the clinical relevance of such cross-reactions to that species can be demonstrated by an accepted food challenge. (B)

40. Crustaceans, such as shrimp, crab, crawfish, and lobster, are a frequent cause of adverse food reactions, including life-threatening anaphylaxis. There is considerable risk of cross-reactivity between crustaceans. Less well defined is cross-reactivity between mollusks and crustaceans. (C)
41. Crustaceans do not cross-react with vertebrate fish. (B)
42. Seafood allergy is not associated with increased risk of anaphylactoid reaction from radiocontrast media. (F)
43. Patients with wheat allergy alone show extensive in vitro cross-reactivity to other grains that is not reflected clinically. Therefore, elimination of all grains from the diet (i.e., wheat, rye, barley, oats, rice, corn) of a patient with grain allergy is clinically unwarranted and may be nutritionally detrimental. (B)
44. Evaluation of cross-reactivity among tree nuts (walnut, hazelnut, Brazil nut, pecan) is characterized by shared allergens among tree nuts and between tree nuts and other plant-derived foods and pollen. Clinical reactions to tree nuts can be severe and potentially fatal and can occur from the first exposure to a tree nut in patients allergic to other tree nuts. In most cases, elimination of all tree nuts from the diet is appropriate. (C)
45. Since the proteins of cacao nut undergo extensive modification into relatively nonallergenic complexes during the processing of commercial chocolate, clinical sensitivity to chocolate is vanishingly rare. (D)
46. Although IgE-mediated reactions to fruits and vegetables are commonly reported, clinically relevant cross-reactivity resulting in severe reactions is uncommon. (C)
47. The latex-fruit syndrome is the result of cross-reactivity between natural rubber latex proteins and fruit proteins. Class 1 chitinases (Hev b 6, hevein-like proteins), profilins (Hev b 8), beta-1, 3-gluconases (Hev b 2), and other cross-reactive polypeptides have been implicated. The most commonly reported cross-reactive foods include banana, avocado, kiwi, and chestnut, but many other fruits and some nuts have been identified in cross-reactivity studies. (D)
48. Seed storage proteins appear to be the main allergens in the edible seeds; in particular, 2S albumin family proteins (part of the cereal prolamin superfamily) have been demonstrated as allergens in sesame, mustard, sunflower, and cottonseed. Cross-reactivity has not been well-studied. (E)

Adverse Reactions to Food Additives

49. The number of additives used by the food industry is extensive. Only a small number of additives have been implicated in IgE-mediated or other (immunologic or nonimmunologic) adverse reactions. Adverse reactions to food additives, therefore, are rare. (C)
50. Food additives may cause anaphylaxis, urticaria or angioedema, or asthma. These reactions can be severe or even life-threatening; fatalities have been described. (C).
51. Tartrazine (Federal Food, Drug, and Cosmetic Act [FD&C] yellow No. 5) sensitivity is extremely rare. There is no convincing evidence to support the contention that tartrazine "cross-reacts" with cyclooxygenase-inhibiting drugs. (B)
52. Monosodium glutamate (MSG) sensitivity is a rare cause of urticaria or angioedema. (C) It is also a rare cause of bronchospasm in patients with asthma. (B)

53. Sulfites produce bronchospasm in 5% of the asthmatic population, in most cases due to generation of sulfur dioxide in the oropharynx. (A) Sulfite-induced anaphylaxis has also been described. (B)
54. "Natural" food additives, including annatto, carmine, and saffron, as well as erythritol (ERT; 1,2,3,4-butanetetrol), a sweetener, may be rare causes of anaphylaxis. (C)
55. Adverse reactions (anaphylaxis, urticaria or angioedema, or bronchospasm) from food additives should be suspected when symptoms after food or beverage consumption occur some but not all the time, suggesting that the reaction occurs only when an additive is present. (C)
56. Management entails avoiding foods or beverages that contain the implicated additive and using self-injectable epinephrine for life-threatening reactions, especially for individuals who are sulfite sensitive. (B)

Genetically Modified Foods

57. Many of the major food groups have undergone modification by gene manipulation or replacement, and several of these food products are currently on grocery store shelves. (C)
58. The possibility exists that transgenic plant proteins in novel genetically modified foods could cause severe food allergy, including anaphylactic shock, if allergenic determinants (amino acid sequences) in the transgenic proteins share a high degree of homology to those of known food allergens. (E)
59. As illustrated by recent introduction of corn engineered to contain a pesticide, gamma endotoxin (derived from Bacillus thuringiensis), into the human food chain, food allergy to such engineered foods could occur in workers previously exposed and sensitized to this endotoxin or in other highly susceptible atopic patients. (A)
60. The potential allergenicity of newly developed genetically modified foods should be investigated on a case-by-case basis by individual commercial developers and appropriate regulatory agencies. (D)

Diagnosis of Food Allergy

61. The primary tools available to diagnose adverse reactions to foods include history (including diet records), physical examination, skin prick or puncture tests, serum tests for food specific IgE antibodies, trial elimination diets, and oral food challenges. (B)
62. A detailed dietary history, at times augmented with written diet records, is necessary to determine the likelihood that food is causing the disorder, identify the potential triggers, and determine the potential immunopathophysiology. (D)
63. A physical examination may reveal the presence of atopic disorders, such as asthma, atopic dermatitis, and allergic rhinitis, that indicate an increased risk for food allergy or reveal alternative diagnoses that may reduce the likelihood of food allergy. (C)
64. Tests for food specific IgE antibody include PSTs (prick or puncture) and serum assays. These tests are highly sensitive (generally >90%) but only modestly specific (approximately 50%) and therefore are well suited for use when suspicion of a particular food or foods is high but are poor for the purpose of screening (e.g., using panels of tests without consideration of likely causes). (B)

65. Intracutaneous (intradermal) skin tests for foods are potentially dangerous, overly sensitive (increasing the rate of a false-positive test result), and not recommended. (D)
66. Results of PSTs and serum tests for food specific IgE antibody may be influenced by patient characteristics (e.g., age), the quality and characteristics of reagents (e.g., variations in commercial extracts, cross-reacting proteins among food extracts), and techniques (e.g., assay types, skin test devices, location of test placement, mode of measurement). (B)
67. Increasingly higher concentrations of food specific IgE antibodies (reflected by increasingly larger PST response size and/or higher concentrations of food-specific serum IgE antibody) correlate with an increasing risk for a clinical reaction. (C)
68. A trial elimination diet may be helpful to determine if a disorder with frequent or chronic symptoms is responsive to dietary manipulation. (D)
69. Graded oral food challenge is a useful means to diagnose an adverse reaction to food. (B)
70. A number of additional diagnostic tests are under investigation, including atopy patch tests, basophil activation assays, and tests for IgE binding to specific epitopes. (E)
71. Some tests, including provocation neutralization, cytotoxic tests, IgG antibodies directed to foods, and hair analysis, are either disproved or unproven; therefore, they are not recommended for the diagnosis of food allergy. (C)
72. Ancillary tests may be needed to confirm the diagnosis of food intolerance or immune reactions to foods, such as breath hydrogen tests for lactose intolerance or gastrointestinal biopsy to determine eosinophilic inflammation or atrophic villi. (D)
73. The rational selection, application, and interpretation of tests for food-specific IgE antibodies require consideration of the epidemiology and underlying immunopathophysiology of the disorder under investigation, the importance of making a definitive diagnosis, estimation of prior probability that a disorder or reaction is attributable to particular foods, and an understanding of the test utility. (D)

Food-Dependent Exercise-Induced Anaphylaxis (EIA)

74. Individuals with food-dependent EIA develop neither anaphylaxis with ingestion of food without subsequent exercise nor anaphylaxis after exercise without temporally related ingestion of food. (A)
75. Two subsets of patients with food-dependent EIA have been described (Bock 1987): one subset may develop anaphylaxis when exercising in temporal proximity to ingestion of any type of food (Young et al., 1994); another subset may experience anaphylaxis with exercise in conjunction with ingestion of a specific food. (A)
76. Management of food-dependent EIA entails avoiding exercising in proximity to food consumption, carrying self-injectable epinephrine, exercising with a "buddy," and wearing medic-alert jewelry. (C)

Differential Diagnosis of Adverse Reactions to Foods

77. Non-IgE-mediated immunologic reactions to foods have been implicated in such entities as (1) food-induced enterocolitis and colitis, (2) malabsorption

syndromes (e.g., celiac disease), (3) cow's milk-induced syndromes, and (4) dermatitis herpetiformis. (C)

78. Food-induced enterocolitis and colitis are most commonly seen in infants several hours after ingestion of food proteins, most notably those in cow's milk or soy formulas. Infants with food-induced enterocolitis develop severe protracted vomiting and diarrhea compared with infants with food-induced colitis who usually appear healthy. Both groups of patients present with blood and eosinophils in the stool, although colitis more often presents with gross blood. (C)
79. Immune-mediated malabsorption syndromes that result in diarrhea and weight loss (or lack of weight gain) may occur secondary to intolerance to a variety of food proteins, including those in cow's milk, soy, wheat, other cereal grains, and eggs. (C)
80. Celiac disease is a severe form of malabsorption characterized by total villous atrophy and extensive cellular infiltrates due to an immunologic reaction to gliadin, a component of gluten found in wheat, oat, rye, and barley. The diagnosis of the disease is crucial, since the removal of gluten from the diet can lead to reversal of histopathologic changes and recovery of gastrointestinal function. (C)
81. In a subset of infants, colic and gastroesophageal reflux disease have been attributed to adverse reactions to cow's milk. However, an immunologic basis for these conditions has not been clearly established. (A)
82. Dermatitis herpetiformis is characterized by a chronic, intensely pruritic, papulovesicular rash symmetrically distributed over the extensor surfaces of the extremities and the buttocks associated with gluten ingestion and often with gluten-sensitive enteropathy. Direct immunofluorescence or specific immunologic assays may be helpful in making the diagnosis. (B)
83. Cow's milk-induced pulmonary hemosiderosis (Heiner syndrome) is an extremely rare condition in infants and toddlers that also may be related to egg or pork hypersensitivity and for which the immunopathology is poorly understood. It is characterized clinically by recurrent episodes of pneumonia associated with pulmonary infiltrates, hemosiderosis, gastrointestinal blood loss, iron-deficiency anemia, and failure to thrive. The presence of precipitating antibodies to the responsible antigen is necessary but not sufficient to make the diagnosis. (C)
84. Toxic food reactions, bacterial contamination of food, and pharmacologic food reactions may mimic IgE-mediated reactions and should be considered early in the differential diagnosis because of the serious nature of such reactions. (C)
85. Pharmacologic adverse food reactions occur after ingestion of foods with pharmacologically active substances, such as vasoactive amines, in particular histamine (scombroid poisoning), and produce a wide range of clinical manifestations, especially gastrointestinal and central nervous system in nature. Patients may present with flushing, sweating, nausea, vomiting, diarrhea, headache, palpitations, dizziness, swelling of the face and tongue, respiratory distress, and shock. (C)
86. Enzymatic food reactions are caused by the ingestion of normal dietary amounts of foods in individuals susceptible to such reactions because of medications, disease states, malnutrition, or inborn errors of metabolism (e.g., lactose intolerance). (C)
87. Reactions not related to specific food ingestion but due to the act of eating that can be misdiagnosed as reactions to foods include gustatory or

vasomotor rhinitis, carcinoid syndrome, idiopathic anaphylaxis, systemic mastocytosis, inflammatory bowel disease, and irritable bowel syndrome. (C)

88. Conditions incorrectly identified as being related to food ingestion include multiple sclerosis, attention-deficit disorder, autism and other behavioral conditions, chronic fatigue syndrome, and the "yeast connection." (C)

General Management of Food Allergy

89. The key to the management of patients with food allergy is avoidance of foods known to have or suspected of having caused a reaction. (F)
90. Since elimination diets may lead to malnutrition or other serious adverse effects (e.g., personality change), every effort should be made to ensure that the dietary needs of the patient are met and that the patient and/or caregiver(s) are fully educated in dietary management. Once the diagnosis of food allergy is confirmed, the patient should be advised to avoid eating the food. (D)
91. In some cases, severe allergic reactions may be seen in patients who only inhale or come in contact with food allergens, thereby making avoidance even more difficult. (D)
92. The successful avoidance of food allergens relies on (1) identification in each patient of the specific food that caused the reaction; (2) recognition of cross-reacting allergens in other foods; (3) education of the patient and/or caregiver about avoidance measures, with particular emphasis on hidden food allergens or additives; and (4) willingness of the educated patient and/or caregiver to read labels carefully, inquire at restaurants, and take other measures to prevent inadvertent exposure to known or suspected allergens. (D)
93. In selected cases, reevaluation of patients with food allergy may be important to determine if food allergy has been lost over time. (F)
94. If there is a history of suspected or proven IgE-mediated systemic reactions to foods, injectable epinephrine should be given to patients and/or caregivers to carry with them and they should be instructed in its use. (F)
95. Prophylactic medications have not been shown to be effective in consistently preventing severe, life-threatening reactions to foods and may mask a less severe IgE-mediated reaction to a food, knowledge of which could prevent a more severe reaction to that food in the future. (D)

Management in Special Settings and Circumstances

96. Fatal and near-fatal food anaphylactic reactions tend to occur away from home after an unintentional ingestion of a food allergen by individuals with a known allergy to the same food. (C)
97. Delay in the administration of injectable epinephrine is a common feature of fatal food allergic reactions. (C)
98. Peanut and tree nuts account for most fatal and near-fatal food allergic reactions in the United States. (C)
99. Allergic reactions that result from direct skin contact with food allergens are generally less severe than reactions due to allergen ingestion. Reactions that result from inhalation of food allergens are generally less frequent and less severe than reactions caused by either direct skin contact or ingestion. Exceptions to these generalizations are more likely in occupational

environments and other settings in which food allergen sensitization occurred via either inhalation or skin contact. (B)

100. Schools and childcare centers should have policies for facilitating food allergen avoidance, including staff education regarding label reading and cross-contamination, prohibition of food or utensil sharing, and increased staff supervision during student meals. (D)
101. Schools and childcare centers should have policies ensuring prompt treatment of food anaphylaxis, including a requirement for physician-prescribed treatment protocols for food allergic students, staff education regarding recognition and treatment of anaphylaxis, and the ready availability of injectable epinephrine. (D)
102. It is important to inform workers in a restaurant or other food establishment about a history of a systemic food allergic reaction, although this does not ensure that the meal will be free of the offending food. (C)
103. Allograft transplant recipients may acquire specific food allergic sensitivities from organ donors. (B)
104. Patients with latex allergy have an increased risk of experiencing IgE-mediated food-induced symptoms, including anaphylaxis, particularly when ingesting banana, avocado, kiwi, or chestnut. (C)

Definitions:

Category of Evidence

Ia Evidence from meta-analysis of randomized controlled trials

Ib Evidence from at least one randomized controlled trial

IIa Evidence from at least one controlled study without randomization

IIb Evidence from at least one other type of quasi-experimental study

III Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV Evidence from expert committee reports, opinions or clinical experiences of respected authorities, or both

LB Evidence from laboratory-based studies

Strength of Recommendation

A. Directly based on category I evidence
B. Directly based on category II evidence or extrapolated recommendation from category I evidence
C. Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D. Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
E. Directly based on category LB evidence
F. Based on consensus of the Joint Task Force on Practice Parameters

CLINICAL ALGORITHM(S)

"Algorithm for Diagnosis and Management of Food Allergy" is provided in the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each summary statement (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved quality of care in the prevention, diagnosis, and management of food allergies
- Reduced morbidity and mortality related to food allergy or misdiagnosis of food allergy

POTENTIAL HARMS

Elimination diets may lead to malnutrition or other serious adverse effects (e.g., personality change). Every effort should be made to ensure that the dietary needs of the patient are met and that the patient and/or caregiver(s) are fully educated in dietary management.

QUALIFYING STATEMENTS

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- This is a complete and comprehensive document at the current time. These clinical guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients and are not intended to replace a clinician's judgment or establish a protocol for all patients. The medical environment is a changing environment and not all recommendations will be appropriate for all patients. Because this document incorporated the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provide an official American Academy of Allergy, Asthma and Immunology (AAAAI) or American College of Allergy, Asthma and Immunology (ACAAI) interpretation of these practice parameters. Any request for information about or an interpretation of these practice parameters by the AAAAI or the ACAAI should be directed to the Executive Offices of the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma and

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- This parameter was edited by Dr. Nicklas in his private capacity and not in his capacity as a medical officer with the Food and Drug Administration. No official support or endorsement by the Food and Drug Administration is intended or should be inferred.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American College of Allergy, Asthma, & Immunology. Food allergy: a practice parameter. Ann Allergy Asthma Immunol 2006 Mar;96(3 Suppl 2):S1-68. [682 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

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GUIDELINE COMMITTEE

Joint Task Force on Practice Parameters

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Chief Editors: Jean A. Chapman, MD, Cape Girardeau, MO; I. Leonard Bernstein, MD, Departments of Medicine & Environmental Health, University of Cincinnati College of Medicine, Cincinnati, OH; Rufus E. Lee, MD, Dothan, AL; John Oppenheimer, MD, Department of Medicine, UMDNJ-New Jersey Medical School, New Brunswick, NJ

Associate Editors: Richard A. Nicklas, MD, Department of Medicine, George Washington Medical Center, Washington, DC; Diane E. Schuller, MD, Department of Pediatrics, Pennsylvania State University, Milton S. Hershey Medical College, Hershey, PA; Sheldon L. Spector, MD, Department of Medicine, University of California, Los Angeles; David Lang, MD, Allergy/Immunology Section, Division of Medicine, and Allergy/ Immunology Fellowship Training Program, Cleveland Clinic Foundation, Cleveland, OH; Ronald A. Simon, MD, Division of Allergy, Asthma and Immunology, Scripps Clinic and Research Foundation, La Jolla, CA; David Kahn, MD, Department of Internal Medicine, Division of Allergy & Immunology, University of Texas Southwestern Medical Center, Dallas, TX; Jay M. Portnoy, MD, Section of Allergy, Asthma & Immunology, The Children's Mercy Hospital, Professor of Pediatrics, University of Missouri-Kansas City, School of Medicine, Kansas City, MO; Stephen A. Tilles, MD, Department of Medicine, University of Washington School of Medicine, Seattle, WA; Joann Blessing-Moore, MD, Department of Medicine & Pediatrics, Stanford University Medical Center, Palo Alto, CA; Scott H. Sicherer, MD, Department of Pediatrics, Jaffe Food Allergy Institute, Mount Sinai School of Medicine, New York, NY: Dana V. Wallace, MD, Nova Southeastern University, Davie, FL; Suzanne S. Teuber, MD, Department of Medicine, Training Program Director, Allergy and Immunology, University of California -- Davis, School of Medicine, Division of Rheumatology, Allergy and Clinical Immunology, Genome and Biomedical Sciences Facility, Davis, CA

Reviewers: Eyassu Abegaz, MD; Sami Bahna, MD, Shreveport, LA; Wesley Burks, MD, Durham, NC; Nugyek Camara, MD, Hinsdale, IL; Alessandro Fiocchi, MD, Milan, Italy; Marianne Frieri, East Meadow, NY; Raif Geha, Boston, MA; Paul Hannaway, MD, Salem, MA; John Kelso, MD, San Diego, CA; Myngoc T. Nguyen, MD, Piedmont, CA; Barbara E. Magera, MD, PharmD, Charleston, SC; Hugh A. Sampson, MD, New York, NY; Jonathan Spergel, MD, Philadelphia, PA; and Robert S. Zeiger, MD, PhD, San Diego, CA

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Joint Council of Allergy, Asthma, and Immunology (JCAAI) Web site.

Print copies: Available from JCAAI, 50 N. Brockway, Ste 3-3 Palatine, IL 60067

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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