AMERICAN GASTROENTEROLOGICAL ASSOCIATION

American Gastroenterological Association Medical Position Statement: Guidelines for the Evaluation of Food Allergies

This document presents the official recommendations of the American Gastroenterological Association (AGA) on the evaluation of food allergies. It was approved by the Clinical Practice and Practice Economics Committee on September 23, 2000, and by the AGA Governing Board on November 12, 2000.

The term *food allergy* refers to an adverse immunologic response to the protein in foods. Food allergy is to be distinguished from other, more common, adverse reactions to foods that are designated as food intolerance. Adverse reactions caused by food intolerance may result from particular constituents of foods, such as toxins (e.g., food poisoning) or pharmacologic agents (e.g., caffeine or tyramine), or from host factors, such as metabolic disorders (i.e., lactase deficiency). Food allergy is not one particular disorder, but rather immunopathophysiologic mechanisms underlying a number of defined or poorly defined gastrointestinal disorders/symptom complexes. Identification and elimination of the causal allergenic food protein from the diet can lead to resolution of symptoms.

The purpose of these guidelines is to provide a rational basis for the evaluation of food allergy in gastrointestinal disorders. Because food allergy is more common in children than in adults, more emphasis is placed on this age group. Although these guidelines include information that is useful for primary caregivers (dietary therapy, radioallergosorbent tests [RAST], and low-risk oral food challenges), some of the evaluations (skin testing, endoscopy, and high-risk food challenges) may require specialists (gastroenterologists or allergists) and tertiary care centers.

Recommendations

In consideration of the above points, a recent consensus workshop (Workshop on the Classification of Gastrointestinal Diseases of Infants and Children, November 1998, Washington, D.C.) concluded that the diagnosis of food allergy is made on the basis of one or more elements listed in Table 1. The selection of patients who may benefit from an evaluation for food allergy also should take into consideration a number of epidemiologic factors that suggest an increased probability of underlying food allergy. Epidemiologic factors that may be helpful in assigning a priori risk for food allergy are listed in Table 2. Of primary importance is the fact that food allergy is rarely confirmed in adults.

In addition to considering the above elements, food allergy should be considered as a potential immunopathophysiologic mechanism in a number of defined gastrointestinal disorders that have clearly been linked with food allergy, at least in a subset of patients. These particular disorders and symptom complexes are listed in Table 3. It is clear that in many disorders, a lack of response to treatments other than food elimination, and even a successful response to medical or surgical treatment, does not necessarily exclude food allergy as a cause for the condition.

The type of evaluation used for particular disorders is specific for each disorder and beyond the scope of these guidelines. However, an evaluation for food allergies may be undertaken initially, concomitantly with other diagnostic tests, or following failure to discern other causes, depending on the particular disorder and clinical history. In some cases, a particular finding during the evaluation may provide information that then prompts an evaluation for food allergy (i.e., >7 eosinophils per high-power field on esophageal biopsy).

Even without performing adjunctive laboratory tests, "formula changes" are commonly undertaken by pediatricians and families as a test of intolerance or allergy. There have been no specific guidelines concerning these formula changes. It is helpful to know that only a small proportion of infants with immunoglobulin (Ig) E–mediated cow's milk allergy (14%) will react to soy. In contrast, those with non–IgE-mediated cow's milk allergy are frequently ($>50\%$) reactive to soy protein. For these infants, a switch to extensively hydrolyzed cow's milk–based formula is the treatment of choice. For a small proportion of infants with symptoms that continue on hydrolysate, amino-acid based formula may be required. Breastfeeding is clearly cost-effective compared with infant

Table 1. Elements Suggesting Food Allergy as a Cause of Gastrointestinal Disease

History of an allergic, or allergic-like, reaction to a food ingestion
Exclusion of anatomic, functional, metabolic, or infectious causes
Pathologic findings consistent with an allergic cause (usually eosinophilia)
Confirmation of a relationship between ingestion of the specific dietary protein and symptoms by clinical challenges or repeated, inadvertent, exposures
Evidence of the food-specific IgE antibody in settings of IgE-mediated disease
Failure to respond to conventional therapies aimed at anatomic, functional, metabolic, or infectious causes
Improvement in symptoms with elimination of the causal dietary protein(s)
Clinical response to treatments of allergic inflammation (i.e., corticosteroids)
Similarities to clinical syndromes either proven or presumed to be caused by immunologic mechanisms
Lack of other explanations for the clinical allergic-like reaction

formula, but maternally ingested protein can elicit allergic symptoms in the breast-fed infant. Maternal dietary manipulation (e.g., avoidance of milk protein) can be undertaken for treatment in breast-fed infants, but with multiple food-allergic infants it may be difficult, and substitution with infant formulas may be needed.

The laboratory testing undertaken in the evaluation of food allergy includes both tests that are specific for food allergy and ancillary tests that are performed in the diagnostic evaluation of gastrointestinal symptoms, as listed in Table 4. The table also lists tests that are unproven and should not be used. Two factors that may guide the use of tests for food-specific IgE antibody are the chronicity of symptoms and the association of atopic diseases (asthma, atopic dermatitis, and anaphylaxis to foods). In patients with acute reactions associated with particular food ingestions and those with chronic gastrointestinal symptoms who have other manifestations of atopic disease, tests for specific IgE antibody (RASTs or skin-prick tests) are likely to be useful adjuncts for diagnosis, although the false-positive rate for predicting clinical symptoms of these tests is high. Similarly, for some of the disorders

Table 2. Factors That Increase the Chance That Food Allergy Is a Cause of Gastrointestinal Disease

Young age of patient (<3 yr)
History of acute reaction proximate to ingestion of a particular food
Associated atopic diseases
Atopic dermatitis (eczema)
Acute food allergic reactions
Asthma
Family history of atopic diseases

Table 3. Specific Disorders and Symptom Complexes in Which Food Allergy Is a Potential Cause

Clear relationship, high risk
Acute, severe (sometime multisystem) gastrointestinal reaction immediately after ingestion ("gastrointestinal anaphylaxis")[a]
Oral allergy syndrome (oral/perioral pruritus associated with food-specific IgE)[a]
Dietary protein proctitis/proctocolitis of infancy[b]
Dietary protein–induced enteropathy of infancy[b]
Celiac disease[b]
Dietary protein–induced enterocolitis of infancy[b]
Occult blood loss from the gastrointestinal tract of milk-fed infants[b]
Subset with food allergy, evaluation often warranted
Gastroesophageal reflux in infants[c]
Eosinophilic esophagitis, any age group[c]
Eosinophilic gastroenteritis[c]
Enteropathy/malabsorption, any age group[b]
Possible relationship in subset, not well studied
Constipation in early childhood
Infantile colic

[a]Associated with positive tests for food-specific IgE antibody.
[b]Characteristically not associated with positive tests for food-specific IgE antibody.
[c]Subtypes may be associated with positive tests for food-specific IgE antibody.

(eosinophilic gastroenteritis or eosinophilic esophagitis), a subset of patients may have positive tests for IgE antibody. Lastly, tests for specific IgE antibody may be needed to rule out the potential for severe acute reactions before conducting oral challenges in settings where patients have atopic diseases or possible history of acute reactions. In chronic disorders not associated with atopic disease, tests for food-specific IgE are typically negative.

Ultimately, the diagnosis of food allergy rests on both the evidence of elements listed in Table 1 and confirmation of reactivity/association determined by

Table 4. Laboratory Tests Used in the Evaluation of Food Allergy in Gastrointestinal Disorders

Primary tests for specific IgE antibody to particular foods, as indicated
RAST
Prick/puncture skin tests
Adjunctive tests
Endoscopy/biopsy
Absorption studies
Stool analysis (heme, leukocytes, eosinophils)
pH probe
Tests of no value/contraindicated
Intradermal skin tests with foods
Provocation/neutralization
Cytotoxicity
Applied kinesiology
IgG_4 antibody

NOTE. Tests are selected based on individual disorders/symptom complexes.

Table 5. Types of Elimination Diets

Elimination of one or several specific foods associated with symptoms
Useful for acute reactions, IgE-positive foods, or high-suspicion food(s)
Oligoantigenic diet–specified foods allowed in the diet selected for generally low-risk for food allergy
Useful when a large number of foods are associated with symptoms
Can result in false-negative result if correct foods not eliminated
Elemental diet–hypoallergenic formula (i.e., amino acid–based formula) serves as total nutrition, may allow a few "safe" solids
Useful when large number of foods is suspected or for infants on no or few solids
Poor compliance outside of infancy

(1) resolution of symptoms with an elimination diet and (2) recurrence of symptoms after oral challenge (if challenge is appropriate in the particular setting). Three approaches to dietary elimination are detailed in Table 5. The choice of dietary approach will depend on the specific history, whether a few or multiple foods are suspected, and likelihood of patient compliance. In identifying potential food allergens, it is useful to bear in mind that a rather short list of foods accounts for 85%–90% of significant reactions (Table 6), although any food can provoke a reaction. Elimination of the causal protein should result in resolution of symptoms, although the time to resolution may be prolonged in some disorders (weeks in eosinophilic esophagitis). In some cases, adjunctive tests such as endoscopy/biopsy may be helpful to show resolution of pathology.

A general approach to the diagnosis of food allergy incorporating history, diagnostic tests, elimination diets, and challenge (Table 7) is outlined in Figure 1, but a variety of adjustments in approach may be warranted for particular disorders/symptom complexes as described in the accompanying technical review and as mentioned above for infants. Specific information concerning procedures for performing oral food challenges is given in the accompanying technical review.

Table 6. Foods Responsible for Majority of Significant Food Allergy in Infants, Children, and Adults

Infants	Children	Adults
Cows' milk	Cows' milk	Peanut
Soy	Egg	Tree nuts
	Peanut	Fish
	Soy	Shellfish
	Wheat	
	Tree nuts (walnut, hazel, etc.)	
	Fish	
	Shellfish	

Table 7. Modalities for Oral Food Challenge

Type of challenge
Open challenge (food protein given in usual form): useful for screening reactivity, highest level of bias (false-positive)
Single-blind (food substance hidden in capsules or another food): useful for screening reactivity, less bias, more labor intensive
Double-blind, placebo-controlled: removes bias, most labor-intensive, important for research studies
Challenge administration
Timing: individualized depending on history (acute/subacute or chronic)
Division of doses: quantity individualized based on prior history
IgE-positive patient: 8–10 g given in gradually increasing divided doses over 90 min, followed by larger, meal-sized portion 3 h later
Monitoring/treatments
Monitor for gastrointestinal symptoms (also respiratory, skin symptoms in some cases)
Stool analysis as indicated
Biopsy in some cases (enteropathy, eosinophilia)
Emergency treatments as indicated (epinephrine, antihistamines, intravenous fluids, corticosteroids, etc.)
See text regarding enterocolitis syndrome

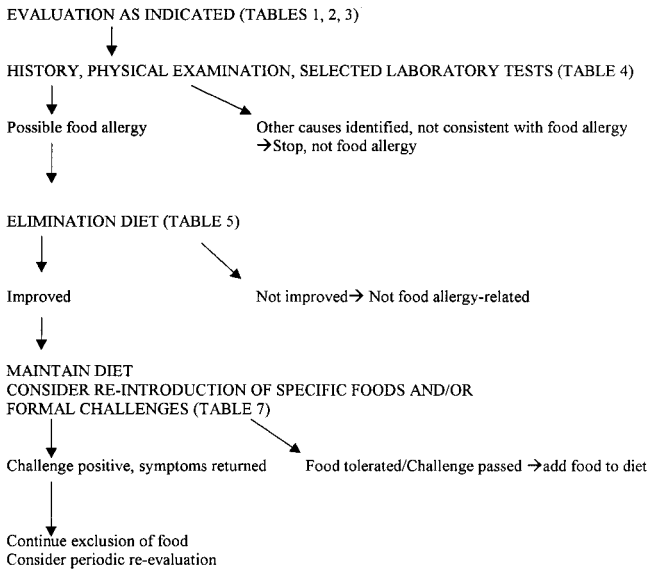

Figure 1. General scheme for evaluating the role of food allergy in gastrointestinal disorders. See text for evaluation of food allergy in infants.

Address requests for reprints to: Chair, Clinical Practice and Practice Economics Committee, AGA National Office, c/o Membership Department, 7910 Woodmont Avenue, 7th Floor, Bethesda, Maryland 20814. Fax: (301) 654-5920.

The Clinical Practice and Practice Economics Committee acknowledges the following individuals whose critiques of this review paper provided valuable guidance to the authors: Lisa Gangarosa, M.D.; Fergus Shanahan, M.D.; Nicholas J. Talley, M.D.; Stephen Targan, M.D.; and Harland Winter, M.D.

© 2001 by the American Gastroenterological Association

0016-5085/01/$35.00
doi:10.1053/gast.2001.23417