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# History and physical examination in the patient with possible food allergy

Author: Wesley Burks, MD Section Editor: Scott H Sicherer, MD, FAAAAI Deputy Editor: Elizabeth TePas, MD, MS

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## INTRODUCTION

An adverse food reaction is a generic term that refers to any untoward reaction following the ingestion of a food. Adverse food reactions are common and may be secondary to food allergy or to a wide variety of other disorders.

This topic reviews the history and physical examination in patients with possible food allergy. The clinical manifestations and diagnostic testing modalities are discussed separately. (See <u>"Clinical manifestations of food allergy</u>: An overview" and <u>"Diagnostic evaluation of food allergy"</u>.)

#### **OVERVIEW**

Adverse food reactions can be subdivided into allergic and nonallergic reactions. Food allergy (or hypersensitivity) is defined broadly as an immunologic reaction to food and can be further distinguished into immunoglobulin E (IgE)-mediated mechanisms and non-IgE-mediated mechanisms. The National Institute of Allergy and Infectious Diseases (NIAID) guidelines for the diagnosis and management of food allergy in the United States define food allergy as "an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food" [1].

The history is of critical importance in the evaluation of a patient with possible food allergy [<u>1-3</u>]. Primary goals of the history are to determine if food allergy could be present and, if so, what type and which food may be responsible. The history is subsequently used to guide testing and interpret results.

**Food allergy** — Food allergy is due to an abnormal immunologic response following exposure (usually ingestion) to a food [1]. Allergy and hypersensitivity are used interchangeably in these sections to refer to these abnormal immunologic reactions. However, the term "hypersensitivity" is sometimes used more liberally

in other literature to describe all exuberant adverse reactions to food, including lactose intolerance, for example [4].

True food allergy appears to be present in only 6 to 8 percent of children and 3 to 4 percent of adults [<u>5-8</u>]. Despite a relatively low prevalence, food allergy is the primary cause of anaphylaxis presenting to emergency departments and accounts for many outpatient visits following less severe reactions [<u>9</u>]. (See <u>"Food allergy in children: Prevalence, natural history, and monitoring for resolution", section on 'Prevalence of childhood food allergy'</u> and <u>"Food-induced anaphylaxis"</u>.)

**Nonimmunologic reactions** — Nonimmunologic adverse food reactions are far more common than food allergy and, as implied by the term, arise from nonimmunologic reactions to food ingestion. Examples include lactose intolerance, auriculotemporal syndrome (or Frey syndrome, a gustatory flushing appearing on the skin below the ear and along the jaw line), and disorders resulting from anatomic abnormalities, enzymatic deficiencies, metabolic diseases, toxins, gastrointestinal infections, and a host of other processes (<u>table 1</u>) [<u>10-13</u>]. (See <u>'Differential diagnosis'</u> below.)

**Role of the history in evaluation** — The clinical history is an essential component of the evaluation of a patient with possible food allergy. This topic review discusses how the history, supported by the physical exam, is used to accomplish specific goals:

- Distinguish food allergy from a host of other adverse food reactions
- · Distinguish among different types of food allergy
- · Identify a possible culprit food

The history is also used to determine what type of testing should be performed and how that testing is interpreted, particularly for IgE-mediated food allergy. An extremely important point is that a positive result on skin testing or in vitro testing indicates sensitization (IgE antibody specific for the tested food) and is not necessarily equivalent to a clinical allergy. The information obtained from the clinical history is used to assess the patient's pretest probability of having food allergy. Testing for specific allergic conditions is then performed and interpreted in the context of this assessment.

# **TYPES OF FOOD ALLERGY**

Food allergy can be subdivided into various types, depending upon the underlying pathogenic mechanism. A primary distinction is between food allergy caused by IgE-mediated mechanisms and food allergy caused by other immunologic mechanisms. This distinction is critical because IgE-mediated reactions may progress to life-threatening anaphylaxis and must be properly identified and managed. (See <u>"Anaphylaxis: Emergency treatment"</u> and <u>"Food-induced anaphylaxis"</u>.)

**IgE-mediated allergy** — IgE-mediated reactions are characterized by stereotypical signs and symptoms that develop rapidly following exposure (usually ingestion).

**Symptoms** — IgE-mediated food allergy presents with some combination of the following signs and symptoms: nausea; vomiting; cramping; diarrhea; flushing; pruritus; urticaria; swelling of the lips, face, or throat; wheezing; lightheadedness; or syncope (<u>table 2</u>).

A patient may present with only one or two of these symptoms or virtually all of them. In children, a classic presentation is vomiting and urticaria. In adults, reactions frequently involve urticaria, angioedema of the lips and face, and abdominal symptoms. Extragastrointestinal symptoms are common and may be the only symptoms present (eg, urticaria).

A more detailed discussion of the different presentations of IgE-mediated food allergy is presented separately. (See <u>"Clinical manifestations of food allergy: An overview"</u>.)

**Timing** — IgE-mediated reactions occur rapidly after ingestion of the culprit food (ie, within seconds to minutes). Uncommonly, reactions up to two hours and beyond can also occur.

**Common culprit foods** — IgE-mediated food allergy occurs most often in association with certain foods, although any food has the potential to cause allergy. In young children, 90 percent of IgE-mediated allergies are caused by cow's milk, egg, soy, peanut, wheat, tree nuts, and fish and shellfish [14]. In adolescents and adults, the most common culprit foods causing systemic reactions are peanut, tree nuts, shellfish, and fish [14-16]. Allergies to fresh fruits and vegetables are common but usually less severe [14] (see "Clinical manifestations and diagnosis of oral allergy syndrome (pollen-food allergy syndrome)"). Allergies to various seeds (sesame, poppy, canola) appear to be increasing [14,17].

**Related allergic conditions** — Patients should be questioned about symptoms of other allergic diseases, such as eczema (atopic dermatitis), allergic rhinitis, and asthma, as patients with these conditions are more likely to have food allergy.

**Other forms of food allergy** — In contrast with IgE-mediated disorders, food allergies caused by other mechanisms present with more subacute and chronic reactions. These disorders commonly affect the gastrointestinal tract and/or skin and are most frequent in infants and children [18].

The pathogenesis of these food allergy disorders may involve antigen-antibody complex (Type III) and cellmediated (Type IV) hypersensitivity, although solid evidence supporting these mechanisms is limited [19-22]. There are several groups of disorders that are classified as non-IgE or cell-mediated food allergy:

- The eosinophilic gastrointestinal disorders, which are food related in some patients (particularly eosinophilic esophagitis in children)
- The dietary protein-induced disorders
- · Celiac disease and the associated skin disorder, dermatitis herpetiformis
- · Atopic dermatitis, which is food related in some patients

These conditions are rarely associated with severe acute reactions, with the important exception of dietary protein-induced enterocolitis of infancy, in which infants can develop dehydration, hypotension, and acidemia. Each of these disorders is presented in more detail separately. (See <u>"Food protein-induced allergic</u>"

proctocolitis of infancy" and "Clinical manifestations and diagnosis of eosinophilic esophagitis" and "Eosinophilic gastroenteritis" and "Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children" and "Role of allergy in atopic dermatitis (eczema)".)

**Symptoms** — Non-IgE-mediated food allergies usually involve isolated gastrointestinal symptoms, such as reflux, nausea, vomiting, cramping, and diarrhea. These types of food allergies should also be considered in infants in the first year of life with varying degrees of blood and mucus in the stool.

Patients with these forms of food allergy usually appear well. An exception to this statement, as mentioned previously, is seen in the infantile syndrome of dietary protein-induced enterocolitis, in which infants can present with dehydration or failure to thrive and also develop severe hypotension upon food re-exposure. (See <u>"Food protein-induced allergic proctocolitis of infancy"</u>.)

Because the symptoms of non-IgE-mediated allergic disorders are nonspecific, the history and physical alone are rarely sufficient to distinguish them from nonallergic disorders unless they present as one of several, well-recognized syndromes. Gastroenterologic tests, including blood tests, stool examinations, endoscopy, colonoscopy, and mucosal biopsy, may be required for diagnosis.

**Timing** — Non-IgE-mediated reactions have a subacute and/or chronic course and generally present hours to days after the food is ingested. (See <u>"Clinical manifestations of food allergy: An overview"</u>.)

# SPECIFIC KEY QUESTIONS

The history is of critical importance in the evaluation of a patient with suspected food allergy. A primary goal is to determine if an IgE-mediated food allergy is probable as this type of reaction can pose an immediate threat to the patient if undetected and can be identified by specific signs and symptoms in most cases. Eliciting or augmenting factors should also be sought [23].

The following specific questions should be asked when evaluating a patient for possible food allergy [<u>1-</u><u>3,19,24-27</u>]:

#### Questions related to the suspected food allergen

- What particular food was suspected to have provoked the reaction? Peanut, tree nuts, shellfish, fish, milk, egg, wheat, and soy account for the majority of serious IgE-mediated food allergies.
  - It is more likely that a food eaten rarely is the trigger of an acute allergic reaction, rather than a food that is a routine component of the diet. Questions should be directed to disclose ingredients that are uncommon in the patient's diet.
  - The possibility that a known allergen for a patient is present as a "contaminant," for example through cross-contact in preparation, should be considered in an individual with known food allergies who experiences a reaction associated with ingestion of a meal comprised of previously tolerated foods.

- How much of the suspected food was ingested? IgE-mediated reactions can be triggered by minute amounts of food proteins. However, threshold doses required to trigger a reaction vary. Some individuals are less sensitive, and larger amounts of allergen must be ingested before a reaction occurs. Other disorders (eg, lactose intolerance) more typically require larger portions to induce symptoms.
- What other foods were ingested at the time? Patients will typically recount the main dish or food eaten prior to a reaction. However, sauces, dressings, breads, beverages, and side dishes should also be reviewed.
- Are all of the ingested ingredients known? There may be hidden ingredients in commercially processed foods that will only be apparent with review of labels. Processed foods also may be mislabeled or contain undeclared allergens. Packaged meat, egg, and poultry products are exempt from the Food Allergen Labeling and Consumer Protection Act. Food labels may be vague (eg "natural flavorings"). In some cases, the patient or clinician will need to contact the manufacturer to obtain more specific information. (See <u>"Management of food allergy: Avoidance", section on 'Food labeling'</u>.)
- How was the food prepared and served? Exposure to food allergens via cross-contact should be considered (eg, deep-fried food, food served in a buffet). (See <u>"Management of food allergy: Avoidance"</u>, <u>section on 'Restaurant meals'</u> and <u>"Management of food allergy: Avoidance"</u>, <u>section on 'Home-meal</u> <u>preparation'</u>.)

#### Questions related to symptoms

- What specific symptoms were involved? The patient should be questioned about systemic, gastrointestinal, dermatologic, and respiratory symptoms. (See <u>"Clinical manifestations of food allergy:</u> <u>An overview</u>".)
- Were any of the signs and symptoms of an IgE-mediated reaction present (<u>table 2</u>)? If present, an IgEmediated allergy must be considered. If absent, other forms of food allergy or intolerance are more likely.
- Did similar symptoms develop on other occasions when the food was eaten (ie, reproducibility)? IgEmediated allergies cause symptoms with every ingestion, although there may be a threshold amount that is required. Was the food prepared in a different manner or consumed in much larger amounts? As examples, a patient may react to raw salmon in sushi but not to canned salmon or to scrambled egg but not egg in baked goods.
- Has the patient reacted with cutaneous or inhalation exposure to the suspected food allergen? Contact urticaria upon exposure to raw or lightly cooked egg is common in children with egg allergy. Respiratory symptoms may develop upon inhalation of food allergens that are aerosolized during the cooking process. Some, but not all, food allergens are aerosolized during cooking. (See <u>"Respiratory</u> <u>manifestations of food allergy"</u>.)
- How much time elapsed between ingestion of the food and the development of symptoms? Different types of food allergy have characteristic times to onset of symptoms. IgE-mediated reactions typically

occur within minutes, whereas cell-mediated reactions are more indolent and may take several hours to days to manifest. One exception is that IgE-mediated allergic reactions to meat can be relatively delayed. (See <u>"Allergy to meats"</u>.)

- Does the patient have a history of avoiding or refusing to eat the suspected food? Young children sometimes display dislike for, or refusal to ingest, foods that are later confirmed as allergens. This presumably occurs due to mild reactions that they experience when trying the food. Although young children are often picky eaters, attention should be paid to this behavior when allergies are suspected, especially when common allergenic foods (eg, peanut, egg) are rejected. However, an underlying eating disorder should be considered in patients who avoid or refuse to eat multiple foods.
- How was the reaction treated? Did it resolve spontaneously, or were medications administered that may have curtailed the development of other symptoms? How long were the medications continued, and were there any later symptoms?

#### Questions related to contributory factors

- Was the patient involved in exercise or other exertion in proximity to the reaction? Allergic reactions to food may only occur in some patients if there is exercise/exertion just after ingestion or may be more severe with exertion. (See <u>"Exercise-induced anaphylaxis: Clinical manifestations, epidemiology,</u> <u>pathogenesis, and diagnosis</u>".)
- Were any medications (including nonprescription anti-inflammatory medications) or alcohol ingested in proximity to the reaction? These agents are believed to increase the rate of allergen absorption. (See <u>"Food-induced anaphylaxis", section on 'Factors affecting presentation'</u>.)
- Are there other variables between reactions that may influence severity? Phase in the menstrual cycle, occurrence during a pollen season, or climactic conditions (especially heat and humidity) are factors that influence reactions in a small number of patients.
- Has the patient received a recent transfusion or undergone solid organ or bone marrow transplantation
  [28]? There are rare reports of patients acquiring food allergies following transfusion of a blood product
  [29-32] or after transplantation [33-47]. In the former case, the allergy is transient and is due to foodspecific IgE in the blood product. In the latter case, the potential mechanism depends upon the type of
  transplant and can range from temporary allergy due to transferred activated mast cells/basophils or
  allergen-specific IgE to longer-lasting or permanent allergy due to transfer of food allergen-specific
  lymphocytes or hematopoietic stem cells from the donor. Alternatively, an allergic reaction to a food can
  occur in an allergic patient after receiving a blood product that contains intact allergen consumed by the
  donor [48,49].

Records of acute care provided on site, in emergency departments, or in urgent care clinics should be retrieved and reviewed if needed. These can provide documentation of key physical findings, such as flushing, urticaria, wheezing, tachycardia, or hypotension, of which patients themselves may not be aware.

#### PHYSICAL EXAMINATION

The physical examination should focus on physical findings of allergic reactions if the patient is evaluated acutely or stigmata of allergic disease if the patient presents with chronic symptoms.

Acute presentation — IgE-mediated food allergic reactions are suggested by characteristic signs and symptoms, such as urticaria and angioedema, and respiratory, gastrointestinal, and/or cardiovascular symptoms that develop in minutes to an hour after food ingestion (<u>table 2</u>). Another important disorder that may present acutely with severe vomiting progressing to dehydration and hypotension, usually one to three hours after food ingestion, is dietary protein-induced enterocolitis, which is not associated with IgE antibodies. (See <u>"Food protein-induced allergic proctocolitis of infancy"</u>.)

**Chronic symptoms** — Certain symptoms of chronic disease should prompt consideration of food allergy as a cause or contributor. Atopic dermatitis is associated with food allergy in approximately 40 percent of infants/children with moderate to severe disease [50,51]. Patients who display stigmata of other allergic diseases, such as allergic rhinitis (eg, "allergic shiners," pale and swollen nasal mucosa) are more likely to have concomitant IgE-mediated food allergy.

Chronic gastrointestinal symptoms and failure to thrive can also be associated with food allergy in a subset of patients, usually infants/children. These disorders are only rarely associated with detectable IgE antibodies to foods, with the exception of eosinophilic gastrointestinal disease, in which food-specific IgE can often be demonstrated.

#### **DIFFERENTIAL DIAGNOSIS**

Nonallergic adverse food reactions can present similarly to food allergy. Since the symptoms associated with these nonallergic disorders are those of generalized gastrointestinal dysfunction, the differential diagnosis is broad and includes anatomic, toxic, metabolic, and/or infectious disorders (<u>table 1</u>). Other causes of flushing or angioedema, such as mast cell disorders and hereditary angioedema, initially may be suspected to be food allergy. (See <u>"Mastocytosis (cutaneous and systemic): Epidemiology, pathogenesis, and clinical manifestations"</u> and <u>"Mast cell disorders: An overview"</u> and <u>"Hereditary angioedema: Epidemiology, clinical manifestations, exacerbating factors, and prognosis"</u>.)

In some cases, referral to a gastroenterologist is indicated. Endoscopy (upper and lower), pH probe, absorption evaluation, gastrointestinal biopsy, radiologic studies, manometry, stool evaluation, and other techniques may be appropriate as determined by the clinical setting. (See <u>"Lactose intolerance: Clinical manifestations, diagnosis, and management"</u> and <u>"Approach to the adult with chronic diarrhea in resource-rich settings"</u>.)

#### **ROLE OF THE GENERALIST**

The generalist should attempt to discern whether an IgE-mediated allergy is present as this can pose immediate risk to the patient if not recognized. As discussed previously, the reaction should be examined for features of IgE-mediated allergy (<u>table 2</u>), and the historical information discussed above should be obtained. (See <u>'Role of the history in evaluation'</u> above.)

If an IgE-mediated allergy is suspected, then the generalist should address the following:

- Is referral indicated?
- Does the patient need an epinephrine autoinjector?
- Are there in vitro allergy tests that would be helpful, or should testing be deferred to an allergy specialist?

If IgE-mediated allergy is not suspected, then the clinician should attempt to discern whether the reaction represented some other type of food allergy or a nonallergic food reaction. (See <u>"Clinical manifestations of food allergy: An overview", section on 'Non-IgE-mediated reactions'</u> and <u>"Clinical manifestations of food allergy: An overview", section on 'Nixed IgE and non-IgE-mediated reactions'</u> and <u>'Differential diagnosis'</u> above.)

**Referral** — The patient should be referred to an allergy specialist in cases of IgE-mediated food allergy. The diagnosis and management of non-IgE-mediated food allergy often require the assistance of a gastroenterologist as well as an allergist. Patients with other adverse food reactions who require specialist evaluation may sometimes be directed to gastroenterologists. (See <u>"Clinical manifestations of food allergy: An overview"</u>.)

When the type of allergy is unclear — In some cases, the clinician cannot discern the type of reaction that is probably responsible for a patient's reaction from the history. This is most often the case for patients presenting with isolated gastrointestinal symptoms. In such instances, the clinician must arrange for further evaluation and proceed as if the reaction were IgE mediated, including equipping the patient with <u>epinephrine</u> if suspicion is sufficiently high.

**Treatment from the generalist** — Patients should be instructed to avoid the suspect food until further evaluated. Care must be taken not to impose dietary restrictions that put patients, particularly growing infants and children, at nutritional risk. Referral should be arranged without delay in such cases. Information for patients/parents on food avoidance and label reading can be obtained from <u>Food Allergy Research and Education</u>. (See <u>"Management of food allergy: Avoidance"</u> and <u>"Management of food allergy: Nutritional issues"</u>.)

Patients with suspected IgE-mediated allergy where anaphylaxis is **not** considered a risk should be instructed to have antihistamines (eg, <u>diphenhydramine</u>) available to treat mild symptoms, such as pruritus and rash. However, antihistamines are **not sufficient** for patients in whom there is any indication of more severe symptoms or anaphylaxis.

**Prescribing epinephrine** — Some patients should also be equipped with <u>epinephrine</u> autoinjectors. This topic is discussed in detail elsewhere. (See <u>"Prescribing epinephrine for anaphylaxis self-treatment"</u>.)

**Testing by the generalist** — Skin testing is the preferred method of diagnosing food allergy in most cases and **must** be performed by allergy specialists. However, in vitro tests can be ordered by the generalist if one or a few suspect foods are implicated by the history. In contrast, searching for culprit foods with panels of tests is rarely productive and should not be performed. The use and interpretation of these tests is reviewed in detail separately. (See <u>"Diagnostic evaluation of food allergy"</u>.)

In vitro tests, if performed, must be interpreted with care as patients can have positive tests to foods that do not cause actual reactions on exposure and negative tests to foods that do cause reactions. All allergy testing must be consistent with the clinical history in order to be meaningful.

Detailed discussions of the clinical manifestations and diagnosis of food allergy are presented separately. (See <u>"Clinical manifestations of food allergy: An overview"</u> and <u>"Diagnostic evaluation of food allergy"</u>.)

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See <u>"Society guideline links: Food allergy"</u>.)

#### **INFORMATION FOR PATIENTS**

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5<sup>th</sup> to 6<sup>th</sup> grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10<sup>th</sup> to 12<sup>th</sup> grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

• Beyond the Basics topics (see <u>"Patient education: Food allergy symptoms and diagnosis (Beyond the Basics)</u>" and <u>"Patient education: Food allergy treatment and avoidance (Beyond the Basics)</u>")

#### SUMMARY

• Adverse food reactions can be subdivided into allergic and nonallergic reactions. Food allergy (or hypersensitivity) is defined broadly as an immunologic reaction to food and can be further distinguished into immunoglobulin E (IgE)-mediated mechanisms and non-IgE-mediated mechanisms. IgE-mediated

reactions may progress to life-threatening anaphylaxis and must be properly identified. (See <u>'Overview'</u> above.)

- The history is of critical importance in the evaluation of a patient with possible food allergy. Primary goals
  of the history are to determine if food allergy may be present and, if so, what type of allergy and which
  food may be responsible. The history is subsequently used to guide testing and interpret results. (See
  <u>'Role of the history in evaluation'</u> above.)
- IgE-mediated reactions are characterized by stereotypical signs and symptoms that develop rapidly after food ingestion (<u>table 2</u>). Symptoms beyond the gastrointestinal tract are common and may be the only symptoms present (eg, urticaria). Combinations of the following signs and symptoms are typical: nausea; vomiting; cramping; diarrhea; flushing; pruritus; urticaria; swelling of the lips, face, or throat; wheezing; lightheadedness; or syncope. Although any food can cause IgE-mediated allergy, a few foods cause most of these reactions. (See <u>'IgE-mediated allergy'</u> above.)
- Non-IgE-mediated food allergies usually involve subacute or chronic symptoms that are isolated to the gastrointestinal tract, such as nausea, vomiting, cramping, and diarrhea. History is often not sufficient to distinguish them from nonallergic disorders unless they present as one of several well-recognized syndromes. (See <u>'Other forms of food allergy'</u> above.)
- Certain questions are particularly useful for obtaining important information about food allergy. (See <u>'Specific key questions'</u> above.)
- The physical examination should focus on physical findings of allergic reactions if the patient is evaluated acutely or stigmata of allergic disease if the patient presents with chronic symptoms. (See <u>'Physical examination'</u> above.)
- Nonallergic adverse food reactions can present similarly to food allergy and include a host of anatomic, toxic, metabolic, and/or infectious disorders (<u>table 1</u>). (See <u>'Differential diagnosis'</u> above.)
- Referral to an allergy specialist should be arranged if IgE-mediated food allergy is suspected. Skin testing is the preferred next step in most cases and should only be performed by an allergy specialist; however, in vitro tests can be ordered by the generalist if one or a few suspect foods are implicated by the history. Searching for culprit foods with panels of in vitro tests is rarely productive and should not be performed. (See <u>'Role of the generalist'</u> above.)
- The diagnosis and management of non-IgE-mediated food allergy often requires the assistance of a gastroenterologist as well as an allergist. Tests by the gastroenterologist may include blood work, stool examinations, endoscopy, colonoscopy, and mucosal biopsy. (See <u>'Referral'</u> above.)
- Immediate management for patients with suspected food allergy includes specific instructions on food avoidance and treatment of a possible reaction after an accidental exposure. If the patient has experienced a systemic reaction/anaphylaxis or is thought to be at risk for possible anaphylaxis, then <u>epinephrine</u> autoinjectors (usually two or more) should be prescribed. Epinephrine must be accompanied

by clear instructions for proper use of the specific device as well as instructions about which symptoms should prompt its use. (See <u>'Treatment from the generalist'</u> above and <u>'Information for patients'</u> above.)

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#### **GRAPHICS**

#### Nonimmunologic adverse food reactions

iastro	intestinal disorders
Nonce	liac gluten sensitivity
Gastr	oesophageal reflux
Carbo	hydrate malabsorption
-	Lactase deficiency
	Sucrose-isomaltase deficiency
Irritat	ble bowel syndrome
Intole	rance of short-chain fermentable carbohydrates (FODMAPs)
Yeast	overgrowth syndrome
Pancr	eatic insufficiency (cystic fibrosis)
Peptic	ulcer disease
Gallbl	adder disease
'oxic i	reactions
Seafo	od
	Scombroid poisoning (fresh tuna and mackerel)
-	Ciguatera poisoning (grouper, snapper)
	Saxitoxin (shellfish)
	food poisoning
	l toxins
ntole	rances
Pharm	nacologic agents
	Caffeine
	Theobromine (tea, chocolate)
	Histamine and histamine-like compounds (berries, wine, fish, sauerkraut)
	Tryptamine (tomato, plum)
	Tyramine (aged cheeses, pickled fish)
•	Serotonin (banana, tomato)
	Phenylethylamine (chocolate)
	Glycosidal alkaloid solanine (potatoes)
	Alcohol
Flavo	rings and preservatives
	Sodium metabisulfite
	Monosodium glutamate
	ogic reactions
	ulotemporal syndrome
	ologic reactions
	phobias
	aversions

#### **Accidental contaminations**

Pesticides

Antibiotics (if allergy present)

Adapted from: Sampson HA. Differential diagnosis in adverse reactions to foods. J Allergy Clin Immunol 1986; 78:212.

Graphic 51225 Version 10.0

#### **Clinical manifestations of IgE-mediated reactions**

Clinical features	
Dermatologic - Pruritus, flushing, urticaria/angioedema, diaphoresis	
Eyes - Conjunctival injection, lacrimation, periorbital edema, pruritus	
Respiratory tract - Nose/oropharynx (sneezing, rhinorrhea, nasal congestion, oral pruritus, metallic taste), upper airway (hoarseness, stridor, sense of choking, laryngeal edema), lower airway (dyspnea, tachypnea, wheezing, cough, cyanosis)	
Cardiovascular - Conduction disturbances, tachycardia, bradycardia (if severe), arrhythmias, hypotension, cardiac arrest	
Gastrointestinal - Nausea/vomiting, abdominal cramping, bloating, diarrhea	
Neurologic - Sense of impending doom, syncope, dizziness, seizures	

IgE: immunoglobulin E.

Graphic 79448 Version 5.0

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