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Food Allergy

by Olaitan A. Adeniji and Jack A. DiPalma

Food allergies are non-toxic adverse reactions to food that are mediated by immune mechanisms. These are different from food intolerances, which refer to adverse reactions to food that are not immune mediated. The rate of "perceived" food allergy in the general population is high but the prevalence of "true" food allergy is lower. It is more common in infants and children but most outgrow their hypersensitivity. The majority of food allergies are caused by a few foods such as milk, eggs, soybean, peanuts, fish, and wheat. Several physiologic changes are provoked in the gastrointestinal tract after the ingestion of a food allergen. Strict avoidance of the offending food is essential for a good clinical outcome.

INTRODUCTION

Foods can induce toxic and non-toxic reactions. Most toxic reactions affect all individuals alike but certain foods produce non-toxic immune mediated reactions in susceptible individuals while others are unaffected. These are termed food allergies. Food allergy is different from food intolerance, which refers to adverse reactions that are not immune mediated. Food allergy is associated with immunoglobin E (IgE mediated) and can be classified based on the pathogenic mechanism involved as seen in Figure 1 (1). Certain disorders can be classified as "definitely related to food allergy" as evidenced by double-blind, placebo-controlled food challenge evaluation (2).

EPIDEMIOLOGY

The rate of perceived food allergy in the general population is high (20%) but the prevalence of true food allergy as documented by a double-blind, placebo-controlled food challenge study to eight foods performed in the United Kingdom was 1.4% (3). It is more common in infants and children but most outgrow their hypersensitivity. A small number of foods account for the majority of reactions. Common causes of food allergy include egg, milk, soy, wheat, peanut, fish, and tree nut, with cow's milk being the most common food allergen (4, 5).

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PATHOPHYSIOLOGY

The normal immune response to ingested foods is the development of oral tolerance. Oral tolerance is a form of peripheral tolerance in which mature lymphocytes are rendered hyporesponsive after prior administration of the antigen (6). Humans normally develop tolerance to food proteins with time. A breakdown in the development of oral tolerance may occur during early childhood, when the alimentary immune mechanisms are immature, leading to IgE sensitization to food proteins. Later in life, patients with pollen respiratory allergy may also produce IgE antibodies to food proteins that cross-react with respiratory pollen allergens because of their homologous molecular structure. Thus, excessive production of food-specific IgE antibodies occurs. These antibodies bind high-affinity receptors on mast cells and basophils, as well as low-affinity receptors on macrophages, monocytes, lymphocytes, eosinophils, and platelets. After penetration of mucosal barriers, food allergens bind to IgE antibodies on mast cells or basophils to release mediators such as histamine, prostaglandins and leukotrienes, resulting in induction of smooth muscle contraction, mucous secretion and

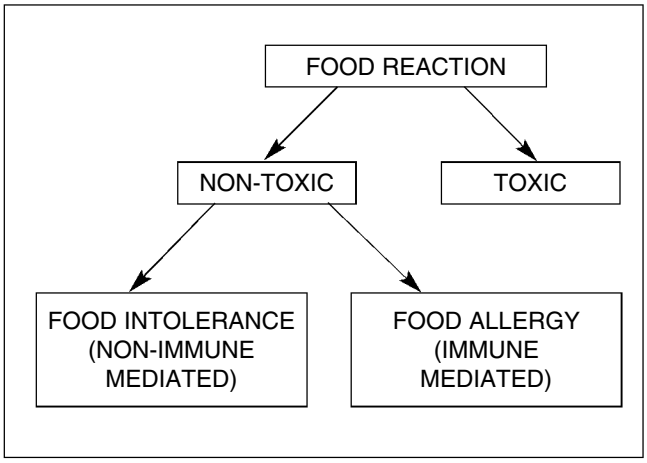

Figure 1. Reactions to food.

vasodilation responsible for the symptoms of immediate hypersensitivity reaction. Non-IgE-mediated food hypersensitivity reactions also occur but the exact pathogenesis is not known although cytokines secreted by antigen-presenting cells or T-cells may be involved. Both antigen-antibody complex and cell-mediated reactions are presumed to be responsible (7,8,9).

Table 1
Disorders Related to Food Allergy

Generalized reaction
- Anaphylaxis

Respiratory Reaction
- Asthma
- Rhinoconjunctivitis
- Laryngeal edema

Cutaneous Reactions
- Dermatitis herpetiformis
- Urticarial angioedema
- Atopic dermatitis

Specific Gastrointestinal Syndromes
- Oral allergy syndrome
- Gastrointestinal anaphylaxis
- Allergic eosinophilic gastroenteritis
- Food protein-induced proctocolitis
- Food protein-induced enteropathy
- Food protein-induced enterocolitis syndrome
- Celiac Disease

CLINICAL FEATURES

The symptoms of food allergy vary from just an acute urticaria to fatal anaphylaxis. Table 1 lists disorders related to food allergy. Respiratory reactions include upper and lower airway problems including asthma, rhinoconjunctivitis and laryngeal edema. The respiratory symptoms include profuse rhinorrhea, ocular pruritus and tearing, sneezing, nasal congestion, laryngeal pruritus and tightness, repetitive deep cough, wheezing, shortness of breath and chest tightness. Cutaneous reactions include dermatitis herpetiformis, urticarial angioedema and atopic dermatitis (10). Gastrointestinal tract symptoms such as nausea, vomiting, abdominal pain, diarrhea, abdominal distention, flatus and oropharyngeal pruritus occur.

SPECIFIC GASTROINTESTINAL SYNDROMES

Several physiologic changes are provoked in the gastrointestinal tract after the ingestion of a food allergen. Studies of intragastric provocation under endoscopic control revealed evidence of gastric mucosal hyperemia, edema, and scattered petechiae resulting in gastric hypotonia and retention of the allergen test meal, prominent pylorospasm, and altered peristaltic intestinal activity (7,11).

Oral Allergy Syndrome

The oral allergy syndrome is a contact allergy exclusively involving the oropharynx resulting in rapid onset of pruritus and angioedema of the lips, tongue, palate and throat, followed by a rapid resolution of symptoms. They occur after ingestion of fresh fruits and vegetables. Patients with pollen allergy are usually affected due to the presence of cross-reacting proteins. For example, patients with ragweed allergy may experience oral symptoms after contact with watermelon, cantaloupe, honeydew or bananas. Likewise, birch pollen-allergic patients may have symptoms after ingesting raw potatoes, carrots, celery, apples, hazelnuts, or kiwi. The proteins are usually heat labile and cooking the fruits or vegetables does not produce the same reaction. The diagnosis can be established by patient history and simply pricking the fruit with a needle and then pricking the skin of the patient with the same needle (7,12).

Gastrointestinal Anaphylaxis

Gastrointestinal anaphylaxis often follows IgE mediated hypersensitivity reactions in other organs. It occurs usually within minutes to 2 hours of exposure to offending food resulting in nausea, vomiting, diarrhea and abdominal pain. Avoidance of the offending food for about two weeks will usually result in resolution of symptoms and this can help in the diagnosis along with skin prick testing. Re-introduction of the allergen after complete avoidance for 2 weeks will induce the same symptoms (13).

Allergic Eosinophilic Gastroenteritis

Allergic eosinophilic gastroenteritis is an IgE-mediated disorder associated with eosinophilic infiltration of the gastrointestinal wall and peripheral eosinophilia without the presence of vasculitis. Eosinophilia occurs in about 50% of patients and they present with nausea, vomiting, diarrhea, abdominal pain and weight loss. The infiltration of the gastrointestinal wall may involve any layer resulting in several complications including protein losing enteropathy, ascites, obstruction and anemia. Multiple biopsies should be obtained because of the tendency towards patchy involvement of the gastrointestinal wall. Other causes of eosinophilia should be investigated. The diagnosis can be supported by a positive skin prick test or radioallergosorbent tests (RASTs) to foods. Cessation of the offending food will result in resolution of symptoms but histologic improvement may lag by up to 3 months (14). Eosinophilic esophagitis is associated with the presence of large amounts of intraepithelial eosinophils, more than that seen in gastroesophageal reflux. Patients generally do not respond to acid reducing medication and endoscopic examination is usually benign. The use of anti-inflammatory drugs (e.g. steroids) may be beneficial (15).

Food Protein-Induced Proctocolitis

Food protein allergy may induce proctitis or colitis with associated spotty hematochezia in infants. The infant is usually asymptomatic otherwise and the presence of other features should raise the possibility of a different diagnosis. Endoscopy may reveal mild erythema or loss of vascularity. The use of cow's milk or soy formula is usually implicated but the syndrome has also been described in breast fed infants and those on protein hydrolysate formulas. The symptoms usually resolve if cow's milk, eggs, or soy is withdrawn from the mother's diet. The use of amino-acid based formula will result in improvement of symptoms.

Food Protein-Induced Enteropathy

Food Protein-Induced Enteropathy is a non-IgE mediated cow's milk induced allergy manifested by vomiting, diarrhea, weight loss and malabsorption primarily in infants. Symptoms appear within a few weeks after the introduction of cow's milk-containing supplements into the infants diet. Jejunal biopsy specimen will reveal villous atrophy and crypt hyperplasia with cellular infiltrate both intraepithelially and in the lamina propria similar to that seen in celiac disease but less pronounced. Diagnosis is based on typical biopsy findings, improvement with allergen withdrawal and worsening with challenge. Increased fecal fat and abnormal D-xylose absorption is common. Patients lose their hypersensitivity to cow's milk at an early age. Other foods have also been implicated in association with a similar syndrome (16).

Food Protein-Induced Enterocolitis Syndrome (FPIES)

Food Protein-Induced Enterocolitis Syndrome (FPIES) is a symptom complex of severe vomiting and diarrhea caused by non-IgE-mediated allergy to cow's milk and/or soy in infants affecting both the small and large bowel. Although similar to Food Protein-Induced Enteropathy, it is generally more severe and should be differentiated from it. The child presents with severe vomiting generally occurring 1 to 3 hours after feeding, and diarrhea develops 5 to 8 hours later. Malabsorption and failure to thrive progressing to acidemia and methemoglobinemia has been described (17). Specific diagnostic criteria have been proposed (18). The syndrome is confirmed by a negative search for other causes, a positive oral challenge, presence of markers of inflammation in the stool, leucocytosis, and the improvement of symptoms with exclusion of the offending food. The skin prick tests or RASTs to the cow's milk or soy protein is negative. Most children become tolerant to the offending protein within 1 to 2 years and can be re-introduced to it later.

Celiac Disease

Celiac disease can be described as a type of an allergic reaction to food protein (gluten). It is more common in North America than previously thought with a prevalence of about 1:300, similar to that in Europe. Most patients are clinically silent. Diarrhea is usually present at diagnosis and is associated with abdominal pain, weight loss, angular stomatitis, glossitis, cheilosis, and anemia. Extra-intestinal manifestations also occur with time including dermatitis herpetiformis. The exact pathophysiology of celiac disease is unknown but the high titers of circulating antibodies to gluten and subsequent decline on a gluten-free diet support an immune-mediated mechanism. The concordance rates for identical twins are 70% to 100% compared with those of 30% for non-identical twins, supporting a genetic etiology. Patients develop small bowel mucosal abnormality with loss of normal villous architecture and increased intraepithelial lymphocytes on biopsy. Small bowel biopsy remains the gold standard in a patient with positive serology. The antitissue transglutaminase antibody test may become the cost-effective initial serologic test of choice. Most patients improve with gluten-free diet but other medications may be required for severe and complicated cases. Dapsone is effective for dermatitis herpetiformis but has no effect on the intestinal manifestations (19,20).

DIAGNOSIS OF FOOD ALLERGY

The majority of food allergies are caused by foods such as milk, eggs, soybean, peanuts, fish, and wheat. When the reaction is acute, such as with urticarial reaction to shrimp, the diagnosis is obvious. However, a detailed history is required for chronic disorders like atopic dermatitis and the diagnosis will depend on double-blind, placebo- controlled food challenge (DBPCFC). The history should include: the name of the food suspected to have caused the reaction and the quantity ingested; how long after the ingestion of the food did the symptoms develop and how severe was the reaction.

Elimination of the suspected food from the diet for 1 to 2 weeks should lead to resolution of symptoms and prompt recurrence occurs upon resumption of the particular food. The patient may also attempt to keep a diary of food consumed and symptoms experienced over a period of time in an effort to uncover an otherwise unrecognized association. There are different types of elimination diets depending on the clinical situation. A type of elimination diet involves the avoidance of one particular food or several foods with the continuation of others. Another method involves the elimination of all foods except a defined group. A third way is the elimination of all foods and the use of amino acid-based elemental formula diet.

Specific IgE Antibody Test

This test is done by placing a food extract on the skin and using a lancet or similar device to pierce through it and puncture the skin. A wheal-and flare reaction is elicited. This skin prick test is positive if the wheal is greater than 3mm and indicates the presence of specific IgE antibody. Although, a positive test has a low positive predictive value (<50%), a negative test is more important because of its high negative predictive value (>95%). Positive skin test in infants is more likely to be a true positive because it is harder to detect IgE in this age group (21,22,23). In patients with a possible history of food induced anaphylaxis, a diluted extract may be used first to reduce the likelihood of a systemic reaction. Intradermal injection for food hypersensitivity is no longer done because of its low specificity and the possibility of severe anaphylactic reaction in sensitive patients (24).

Radioallergosorbent tests (RASTs) are in vitro tests for the evaluation of specific IgE-mediated food allergy. They are as sensitive as the prick skin test in detecting food-specific IgE in serum against water-soluble food antigens (25). Specific IgE antibody testing is more likely to be positive in patients with other atopic disorders such as atopic dermatitis, asthma, family history of atopic diseases and a personal prior history of acute food allergic reaction, especially close to the ingestion of a particular food.

Although not specific to food allergy, other tests may be done to aid in the diagnosis such as endoscopy with biopsy, tests of malabsorption, stool studies and esophageal pH study.

Oral Challenge

When patients respond to elimination diet by avoiding several foods and test positive for food specific IgE, oral challenge can be helpful in identifying specific sensitivi-

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ties. This will help streamline the possible offending food and expands the patients diet. The double-blind placebo-controlled food challenge is regarded as the "gold standard." Neither the physician nor the patient is aware of which challenge contains the test food. The amount of food is slowly increased depending on the nature of the patient's illness and specific symptoms are noted during the food challenge. The challenge should be stopped once a reaction is obvious. It may be necessary at times to give medications to resuscitate the patient such as antihistamines, intravenous fluids or steroids, especially in patients with food protein induced enterocolitis syndrome.

Single-blind food challenge can be helpful in screening multiple foods. This method can be employed in patients with vague symptoms to reduce patient bias during oral challenge. An open oral food challenge can be done to eliminate foods when the physician is sure that the patient's bias will not affect the result of the test. After a negative blinded challenge, an open feeding with larger, meal-sized portions of food should be done under physician supervision (26).

MANAGEMENT

Once the diagnosis of food allergy has been established, strict avoidance of the offending food and minimal accidental ingestion is important for a good clinical outcome. Most patients will outgrow their allergy at an early age. Proper patient and family education will ensure compliance. Involvement of a dietician knowledgeable in food allergy is helpful. The patient can also be directed to the Food Allergy Network, a nonprofit organization.

Patients with classic food allergy should also avoid cooked or processed forms of the particular food because minute amounts could be enough to trigger symptoms. However, those with oral allergy syndrome can usually tolerate cooked or processed forms of the food.

Proper management of anaphylactic reaction begins with early recognition by patient and family members and should involve a clear action plan. Resuscitative medications such as antihistamine and epinephrine should be readily available. The medication of choice for anaphylaxis is injection epinephrine, therefore, patients with IgE-mediated food allergy should carry one at all times (27). ■

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