

The Spectrum of Allergic Reactions to Foods

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KEY CONCEPTS

- Immunoglobulin E-mediated food allergy is the most common and well-recognized form of food hypersensitivity.
- Allergic reactions to food range from mild to life threatening.
- Risk factors for life-threatening anaphylaxis are important to recognize.
- Atopic dermatitis and asthma are allergic conditions in which hypersensitivity to a food(s) may play a role in disease activity.
- A subset of patients with eosinophilic gastrointestinal disorders may have food allergy-induced symptoms.

Introduction

An *adverse food reaction* is a general term that can be applied to a clinically abnormal response to an ingested food or food additive. Adverse food reactions are common and often assumed by patients to be allergic in nature. Food allergies are most prevalent during the first years of life, affecting about 6% of infants younger than 3 years [1–5]. About 2.5% of newborn infants have hypersensitivity reactions to cow's milk in the first year of life, with about 80% "outgrowing" the allergy by their fifth birthday [6]. Immunoglobulin E (IgE)-mediated reactions account for about 60% of milk-allergic reactions; about 25% of these infants retain their sensitivity into the second decade of life, and 35% go on to acquire other food allergies. About 1.5% of young children are allergic to eggs and 0.5% to peanuts. Some evidence suggests that the prevalence of peanut allergy has been increasing during the past two decades [7,8]. Children with atopic disorders tend to have a higher prevalence of food allergy; about 35% of children with moderate to severe atopic dermatitis (AD) have IgE-mediated food allergy [9], and about 6% of children with asthma have food-induced wheezing [10]. Adverse reactions to food additives also have been demonstrated to affect 0.5–1% of children [11–13]. Food allergy appears to be less common in adults, although

adequate epidemiologic studies are lacking. A survey in the United States indicated that peanut and tree nut allergies together affect 1.1% of American adults [7]. Overall, it is estimated that about 2% of adults in the United States are affected by food allergies [6]. Adverse reactions to foods are classified as either *food hypersensitivity (allergy)* or *food intolerance* [1,14].

Food allergy

Food hypersensitivity (allergy) is due to an immunologic reaction resulting from the ingestion of a food or food additive. This reaction occurs only in some patients, may occur after only a small amount of the substance is ingested, and is unrelated to any physiologic effect of the food or food additive. Food allergy occurs due to an immune response that typically involves the IgE mechanism, of which anaphylaxis is the best example. Adverse reactions to food additives are rare [11,12,15]. Several other food hypersensitivity disorders involve cell-mediated immune responses that are mixed with IgE-mediated mechanisms or may be entirely unrelated to IgE-mediated responses (Table 8.1).

Food intolerance

Food intolerance is a general term describing an abnormal physiologic response to an ingested food or food additive. This reaction has not been proven to be immunologic in nature, which distinguishes these reactions from those occurring as a result of food allergy. Food intolerance may be caused by many factors including toxic contaminants

Table 8.1 Food allergy disorders mediated by IgE and mixed IgE and cellular mechanisms

Immune mechanism	Disorders
<i>IgE mediated</i>	
Cutaneous	Urticaria
	Angioedema
	Morbiliform rashes
	Flushing/pruritus
Respiratory	Rhinoconjunctivitis
	Laryngospasm
	Wheezing/bronchospasm
Gastrointestinal	Oral allergy syndrome
	Gastrointestinal anaphylaxis
Multi-system	Generalized anaphylaxis
	Food and exercise-induced anaphylaxis
<i>Mixed IgE and cell mediated</i>	
Cutaneous	Atopic dermatitis
Respiratory	Asthma
Gastrointestinal	Eosinophilic esophagitis
	Eosinophilic gastroenteritis

(e.g. histamine in scromboid fish poisoning, toxins secreted by infectious agents such as Salmonella, Shigella, and Campylobacter), pharmacologic properties of the food (e.g. caffeine in coffee, tyramine in aged cheeses, sulfites in red wine), characteristics of the host such as metabolic disorders (e.g. lactase deficiency), and idiosyncratic responses.

Spectrum of food-allergic responses

The spectrum of food-allergic responses can best be understood by categorizing reactions based on the types of primary immune mechanisms responsible for these adverse reactions. The spectrum of food-induced reactions ranges from benign manifestations of disease, such as flushing or rhinorrhea, to life-threatening symptoms such as anaphylaxis or enterocolitis syndrome. In this chapter, we will examine adverse food reactions that are based on the following immune-mediated mechanisms: (1) IgE-mediated, (2) non-IgE-mediated, (3) eosinophilic disorders, and (4) allergic responses due to combinations of immune mechanisms.

IgE-mediated reactions

IgE-mediated food-allergic reactions are rapid in onset (usually within minutes to 2 hours) and are the most widely known reactions associated with foods. Symptoms are believed to be caused by preformed mediator release from tissue mast cells and circulating basophils that have been previously sensitized to a specific food antigen [14]. Specific

manifestations of IgE-mediated food hypersensitivity reactions can involve any system within the human body. These reactions frequently involve the skin, respiratory tract, gastrointestinal tract, and cardiovascular system. More severe symptoms and those involving multiple systems are defined by the term “generalized anaphylaxis” and are often life threatening. Two additional distinct presentations of IgE-mediated food-allergic reactions are the oral allergy syndrome and food-dependent, exercise-induced anaphylaxis.

Cutaneous responses

The *skin* is the most common target organ in IgE-mediated food hypersensitivity reactions, and cutaneous symptoms occur in >80% of allergic reactions to foods [16]. The ingestion of food allergens can lead either to immediate cutaneous symptoms or exacerbate chronic conditions such as AD. Acute *urticaria* and *angioedema* are the most common cutaneous manifestation of food hypersensitivity reactions, generally appearing within minutes of ingestion of the food allergen. Food allergy may account for 20% of cases of acute urticaria [17,18]. By comparison, food allergies underlying chronic urticaria and angioedema (defined as symptoms >6 weeks duration) appear to be uncommon. In adult patients with chronic urticaria evaluated by placebo-controlled food challenge, <10% of symptoms were associated with food allergy despite the perception of food involvement in as many as 50% of patients [19].

Flushing, pruritus, and morbiliform rash are other acute cutaneous manifestations that commonly occur during allergic reactions to foods. These early symptoms often precede the development of urticaria, angioedema, or more serious adverse symptoms. Food can also cause acute contact urticaria. In this condition, urticarial lesions develop only on the area of skin that is in direct contact with the food. Raw meats, seafood, raw vegetables and fruits, milk, egg, mustard, rice, and beer are among the foods that have been implicated in this form of food allergy [20–22].

Respiratory and ocular responses

Upper respiratory symptoms such as rhinorrhea, sneezing, nasal congestion, and pruritus are frequently experienced during allergic reactions to foods. Nasal symptoms typically occur in conjunction with other organ system involvement [3]. *Ocular* symptoms commonly occur concurrently with respiratory manifestations of IgE-mediated reactions to foods [14,23]. Symptoms may include periocular erythema, pruritus, conjunctival erythema, and tearing. Isolated symptoms of rhinitis and/or conjunctivitis in response to food-allergen ingestion are rare.

Lower respiratory symptoms are potentially life-threatening manifestations of IgE-mediated reactions to foods [14,24]. Symptoms can include laryngospasm, cough, and wheezing and require prompt medical intervention. In a retrospective chart review of 253 failed oral food challenges, Perry and

colleagues found that 26% of participants experienced lower respiratory symptoms, and each of the tested foods carried a similar risk for eliciting lower respiratory symptoms [16]. Although lower respiratory symptoms can occur in any person experiencing anaphylaxis to foods, patients with underlying asthma are at increased risk of severe symptoms. Lower respiratory symptoms due to food allergy are temporally related to ingestion and are typically accompanied by other organ system involvement. It is rare that chronic lower respiratory symptoms or poorly controlled asthma are sole manifestations of food allergy [25,26].

These points are illustrated by a large study of 480 patients with a history of an adverse food reaction undergoing double-blind placebo-controlled oral food challenges (DBPCFCs). Positive reactions were observed in 185 patients, 39% of whom had respiratory and ocular symptoms [3]. Symptoms included combinations of periocular erythema, pruritus, and tearing; nasal congestion, pruritus, sneezing, and rhinorrhea; and coughing, voice changes, and wheezing. Isolated respiratory symptoms occurred in only 5%. One area of exception involves occupational exposure to potential food allergens. Adults working in the food processing and packing industries may develop occupational food allergies and present with rhinoconjunctivitis, with or without asthma [27–30].

Gastrointestinal responses

The signs and symptoms of food-induced IgE-mediated gastrointestinal allergy are most commonly seen as immediate gastrointestinal hypersensitivity but can also be manifested as oral allergy syndrome [23].

Immediate gastrointestinal hypersensitivity is a form of IgE-mediated food allergy, which may accompany allergic manifestations in other target organs [15,24,31,32]. The symptoms vary and may include nausea, abdominal pain or cramping, vomiting, and/or diarrhea. The onset of upper gastrointestinal symptoms (nausea, vomiting, pain) is generally minutes to 2 hours after ingestion of the offending food but lower gastrointestinal symptoms, such as diarrhea, may begin immediately or may be delayed for 2–6 hours after ingestion. Symptoms may be severe and protracted resulting in the need for fluid or electrolyte replacement.

The *oral allergy syndrome or pollen–food related syndrome* is considered to be a form of contact urticaria that is confined almost exclusively to the oropharynx and rarely involves the lower respiratory tract or other target organs [33,34]. Oral allergy syndrome is manifested by the rapid onset of pruritus and angioedema of the lips, tongue, palate, and throat. This syndrome has been reported in up to 50% of patients with pollen-induced rhinoconjunctivitis and is most commonly associated with the ingestion of fresh fruits and vegetables. For example, patients with ragweed allergy may experience symptoms following contact with melons (e.g. watermelons, cantaloupe, honeydew) and bananas.

Birch pollen-sensitive patients often have symptoms following the ingestion of raw potatoes, carrots, celery, apples, pears, cherries, and hazelnuts. Mugwort-allergic patients may react to celery or mustard. Symptoms typically resolve spontaneously within minutes after ingestion ceases. Although symptoms rarely progress to involve other organ systems, progression to systemic involvement has been noted in approximately 10% of patients with anaphylaxis reported in not more than 1–2% [33,35,36]. Tree nuts and peanuts causing oral symptoms are best avoided because of the frequency with which these foods cause more severe reactions. Peanut and tree nut associated oral symptoms are not usually defined as part of the oral allergy symptom, rather serve as a precursor “warning sign” for more advanced symptoms to follow [37].

Generalized anaphylaxis

Anaphylaxis is defined as a “severe, potentially fatal, systemic-allergic reaction that occurs suddenly after contact with an allergy-causing substance [38].” Food-induced generalized anaphylaxis involves multiple organ systems and has been estimated to account for 30–50% of all anaphylaxis treated in emergency department settings [24,39,40]. Peanuts, tree nuts, fish, and shellfish account for more anaphylactic reactions than any other foods. In generalized anaphylaxis, the onset of symptoms is abrupt, often occurring within minutes of ingestion. Symptoms are due to the effects of potent intracellular mediators such as histamine, tryptase, and leukotrienes that are released from mast cells and basophils during an allergic reaction and can involve any organ system. Severe or life-threatening anaphylactic reactions involving the respiratory and cardiovascular systems can culminate in respiratory failure, hypotension, cardiac dysrhythmias, shock, and death if left untreated. In 25–30% of cases of food-induced anaphylaxis, a biphasic course is noted with a recurrence of symptoms hours after the initial onset. This second phase may follow a quiescent, asymptomatic interval [24,37].

Fatal and near-fatal reactions to foods have been described [37,41,42]. Peanuts and tree nuts are the most common allergens reported in such cases. Risk factors associated with fatal food-induced anaphylaxis include adolescent or young adult age group, co-existent asthma, history of previous serious reaction, delayed administration of epinephrine, and absence of skin symptoms. In a series of 13 children with fatal or near-fatal anaphylactic reactions to food, all were known to have food allergies and had accidentally ingested peanuts (four patients), nuts (six patients), eggs (one patient), or milk (two patients) [37]. Twelve of the 13 had asthma that was well controlled. Six patients died, with only two of those receiving epinephrine within the first hour. By comparison, six of the seven survivors received epinephrine within 30 minutes. The correlation between absence of skin findings and fatal anaphylaxis has not been

systematically studied, although it is postulated to result from the rapid development of hypotension, resulting in poor skin perfusion and minimal skin symptoms. An alternative explanation may be that patients lacking skin symptoms are not recognized as having anaphylaxis as quickly, leading to a delay in treatment and consequently poor outcome.

Food-associated, exercise-induced anaphylaxis

There have been increasingly more reports of patients with anaphylaxis that occur only when the ingestion of food is coupled with exercise within a 2–4 hour time interval. This syndrome is known as food-associated, exercise-induced anaphylaxis [43–47]. It appears to be most prevalent in adolescents and young adults, although there have been reports in middle aged patients as well. Most patients react to one or two specific foods. Common causative foods include wheat, celery, and seafood [44–47]. Classically, the food can be ingested in the absence of exercise without development of symptoms. Alternatively, patients may exercise without eating the specific food without induction of symptoms. The coupling of specific food ingestion and exercise, however, produces a potential life-threatening anaphylaxis.

Non-IgE-mediated reactions

Non-IgE-mediated food allergies typically present with more subacute or chronic symptoms isolated to the gastrointestinal tract that present within hours or days of food ingestion. Affected patients commonly present with a classic constellation of features that are consistent with well-described clinical disorders. These disorders include food protein-induced enterocolitis, food protein-induced proctocolitis, food protein-induced gastroenteropathy, food-induced contact dermatitis, celiac disease with or without dermatitis herpetiformis (DH), and food-induced pulmonary hemosiderosis. Although the precise immune mechanisms have not been described, evidence suggests a cell-mediated hypersensitivity response associated with all of these disorders (Table 8.2).

Cutaneous responses

Food-induced contact dermatitis has been reported in individuals without IgE antibodies to the causal food [48]. This

reaction typically occurs in food handlers and can be confirmed by patch testing, thus indicating a cell-mediated immune response. Implicated foods frequently include fish, shellfish, meats, and eggs [20–22,24].

DH is a skin manifestation of celiac disease (gluten-sensitive enteropathy). DH is a chronic blistering skin rash characterized by chronic, pruritic papulovesicular lesions that are symmetrically distributed over the extensor surfaces of the extremities and on the buttocks [49–51]. Gastrointestinal symptoms and histopathologic findings within the gut mucosa are generally milder than those seen in patients presenting with primary gastrointestinal disease. Elimination of gluten from the diet typically results in resolution of skin and gastrointestinal lesions.

Gastrointestinal responses

Food protein-induced enterocolitis syndrome (FPIES) is a disorder which presents most commonly in early infancy [52]. Acute symptoms are typically isolated to the gastrointestinal tract and consist of profuse, repetitive vomiting, and not infrequently diarrhea. Symptoms are often severe and may cause dehydration and shock, often leading to an erroneous diagnosis of sepsis. Cow’s milk and/or soy protein in infant formulas or maternal breast milk are most often responsible for induction of symptoms, although FPIES due to solid food (e.g. rice) is being reported more frequently [52,53]. Objective findings on stool examination consist of gross or occult blood, polymorphonuclear neutrophils, eosinophils, Charcot–Leyden crystals, and positive reducing substances. IgE testing for food proteins is characteristically negative. Jejunal biopsies often reveal flattened villi, edema, and increased numbers of lymphocytes, eosinophils, and mast cells. A food challenge with the responsible protein generally results in vomiting and occasionally diarrhea within minutes to several hours, and occasionally leads to shock [15,23,54].

Infants and children with FPIES are often allergic to both cow’s milk and soy protein. Approximately 50% of children with cow’s milk allergy will have concomitant soy allergy, therefore it is recommended that infants with FPIES due to cow’s milk also avoid soy products during the first year of life [23,52,55]. Elimination of the offending allergen generally results in resolution of the symptoms within 72 hours although secondary disaccharidase deficiency may persist longer. This disorder tends to subside by 18–24 months of age.

Food protein-induced enteropathy is characterized by diarrhea, vomiting, malabsorption, and poor weight gain [56]. It is clinically distinguishable from FPIES due to the presence of non-bloody stools. Vomiting is often less prominent, and re-exposure does not elicit acute symptoms after a period of avoidance. Onset of symptoms is typically delayed for days to weeks and may require continual feeding of the culprit food protein. Other clinical features include abdominal pain and distension, hypoproteinemia, and edema. Patients

Table 8.2 Food allergies mediated by cellular (non-IgE) mechanisms

Cutaneous	Contact dermatitis Dermatitis herpetiformis
Respiratory	Food-induced pulmonary hemosiderosis (Heiner’s syndrome)
Gastrointestinal	Celiac disease Food protein enterocolitis Food protein-induced enteropathy Food protein-induced proctocolitis

typically present in the first year of life. The most common causal food is cow's milk although other foods such as soy, egg, and grains have been associated with food protein-induced enteropathy. Histologic examination reveals patchy villous atrophy, mononuclear cell infiltrates, and few eosinophils. Symptoms typically resolve within 72 hours after dietary elimination and is usually outgrown within 12–24 months of dietary-allergen avoidance.

Food protein-induced proctocolitis generally presents in the first few months of life and, like FPIES, is often secondary to cow's milk and/or soy protein hypersensitivity [23,31]. Infants with this disorder often do not appear ill and generally present with bloody stools. Other distinguishing features include normal growth and absence of vomiting. Gastrointestinal lesions are usually confined to the rectum but can involve the entire large bowel and consist of eosinophilic infiltrates (5–20 eosinophils per HPF), or eosinophilic abscesses in the epithelium and lamina propria. If lesions are severe with crypt destruction, polymorphonuclear leukocytes (PMNs) are also prominent in this disorder [57]. Food protein-induced proctocolitis typically resolves after 6–12 months of dietary-allergen avoidance. Elimination of the offending food allergen leads to resolution of hematochezia within 72 hours, but the mucosal lesions may take up to 1 month to disappear and range from patchy mucosal injection to severe friability with small aphthoid ulcerations and bleeding.

Celiac disease (or gluten-sensitive enteropathy) is an extensive enteropathy leading to malabsorption [58]. Total villous atrophy and an extensive cellular infiltrate are associated with sensitivity to gliadin, the alcohol-soluble portion of gluten found in wheat, rye, and barley. Celiac disease is almost exclusively limited to genetically predisposed individuals who express the HLA-DQ2 and/or HLA-DQ8 heterodimers [59,60]. Patients often have presenting symptoms of diarrhea or frank steatorrhea, abdominal distention and flatulence, failure to thrive, and occasionally nausea and vomiting. Oral ulcers and other extra-intestinal symptoms secondary to malabsorption are sometimes associated. Serologic testing aids in the diagnosis and includes measurement of anti-IgA antibodies to human tissue transglutaminase (TTG) and anti-endomysial (EMA) [58]. Serologic testing to rule out low total serum IgA (IgA deficiency) is essential for the diagnosis of celiac disease. Confirmation with endoscopic biopsies is necessary for diagnosis and reveals total villous atrophy and inflammatory infiltrates. Clinical symptoms and endoscopic findings resolve with strict dietary elimination of gluten that must be maintained for life.

Respiratory responses

Food-induced pulmonary hemosiderosis (Heiner's syndrome) is a rare syndrome in infants characterized by recurrent pneumonia with pulmonary infiltrates, hemosiderosis, gastrointestinal blood loss, iron-deficiency anemia, and failure to

thrive [61,62]. Symptoms are associated with non-IgE-mediated hypersensitivity to cow's milk with evidence of peripheral eosinophilia and the presence of cow's milk precipitins on diagnostic testing. Deposits of immunoglobulins and C3 may also be found on lung biopsy. Strict dietary elimination of milk results in reversal of symptoms.

Adverse food reactions associated with eosinophilic disease

Allergic eosinophilic gastroenteropathies are a group of disorders characterized by symptoms of post-prandial gastrointestinal dysfunction associated with eosinophilic infiltration of at least one layer of the gastrointestinal tract, absence of vasculitis, and peripheral eosinophilia in about 50% of cases [2,23,55]. These disorders are defined by the site(s) of involvement and include eosinophilic esophagitis (EE) and eosinophilic gastroenteritis. Symptoms for each of these syndromes are related to the specific anatomical site of involvement. The pathogenesis of these disorders likely involves both IgE-mediated and cellular immune mechanisms.

Eosinophilic esophagitis

EE is characterized by severe or refractory gastrointestinal symptoms that are suggestive of gastroesophageal reflux disease (GERD) and include dysphagia, epigastric pain, and post-prandial nausea and vomiting [63]. This disorder should be considered in patients of any age presenting with esophageal symptoms, especially when recalcitrant to symptomatic treatment, such as antacids or anti-reflux medications. Very young children may present with feeding disorders; whereas, older children and adults present with dysphagia, vomiting, and abdominal pain. A history of food impaction is common.

Many patients with EE have other atopic diseases. In a series of 103 children with EE, rhinoconjunctivitis was present in 57% and wheezing was noted in 37%, while possible food allergy was cited in 46% [64]. In a retrospective review of 381 children with EE, the most commonly implicated foods were cow's milk, egg, soy, corn, wheat, and beef. Most patients with evidence of food sensitivity tested positive for multiple foods [63]. Elimination of these foods or the use of elemental diets typically results in clinical and histologic improvement. However, the pathophysiologic relationship between EE and allergens, such as foods or aeroallergens, remains unclear.

Eosinophils are not normally found in the esophageal mucosa and symptoms are likely due to the release of eosinophilic mediators. EE is clinically distinguishable from GERD due to its feature of being refractory to aggressive management with antacids, protein pump inhibitors (PPI), and pro-motility medications that are typically effective in the treatment of GERD. Other distinguishing characteristics include normal pH probe results, the presence of patient

or family history of atopy, and peripheral eosinophilia. On endoscopy, EE patients may have visually normal-appearing esophageal mucosa although esophageal furrowing and rings have been reported [65]. On histologic examination, esophageal biopsies in patients with EE typically contain >20 eosinophils per HPF as compared with <5 eosinophils per HPF in patients with GERD. Proximal and mid-esophageal lesions are common in EE whereas reactive eosinophilic infiltrates due to GERD are mainly limited to the distal esophagus [66].

Eosinophilic gastroenteritis

Eosinophilic gastroenteritis can present at any age with abdominal pain, nausea, diarrhea, malabsorption, and weight loss. In infants, it may present as outlet obstruction with postprandial projectile vomiting. In adolescents and adults, it can mimic irritable bowel syndrome [67]. Approximately one-half of patients have allergic disease, such as defined food allergies, asthma, eczema, or rhinitis [68]. However, in contrast to EE, avoidance of implicated foods may have limited value [69,70]. Eosinophilic gastroenteritis is characterized by eosinophilic infiltration of the stomach, small intestine, or both with variable involvement of the large intestine [71]. Symptoms may include vomiting, abdominal pain, diarrhea, malabsorption, and failure to thrive. Severe symptoms can mimic pyloric stenosis or other forms of gastric outlet obstruction when duodenal involvement is present. Since eosinophils may normally be found in the stomach and intestine, endoscopic findings are more difficult to interpret as compared to EE. In addition, multiple sites may need to be biopsied to effectively exclude eosinophilic gastroenteritis due to the patchy nature of eosinophilic infiltration. Biopsies in eosinophilic gastroenteritis will typically show 20–40 eosinophils per HPF. Treatment may involve elimination of the potential offending food(s) or institution of an elemental diet with slow addition of foods. Similar to EE, eosinophilic gastroenteritis usually follows a prolonged course requiring protracted therapy and dietary intervention for months to years. After dietary restriction, foods can be re-introduced slowly after avoidance and based on endoscopic and clinical evidence of disease resolution.

Conditions associated with multiple immune mechanisms

Asthma

Asthma alone is an infrequent manifestation of food allergy. Although ingestion of food allergens is rarely the main aggravating factor in chronic asthma, there is some evidence to suggest that food antigens can provoke bronchial hyperreactivity [25,26]. An exception is occupational asthma (often with accompanying rhinitis) in food-industry workers. “Baker’s asthma,” caused by IgE-mediated allergy to inhaled wheat proteins, is an example [72]. Patients with these

conditions may not react to the food upon ingestion, rather only with inhalation exposure. More typically, asthma is seen as a component of more generalized, IgE-mediated reactions. Asthmatic reactions secondary to airborne food allergens have been reported in cases where susceptible individuals are exposed to vapors or steam emitted from cooking food (e.g. fish, mollusks, crustacea, eggs, and garbanzo beans) [27–30].

Another relationship between food allergy and asthma is that co-existing asthma is a significant risk factor for death from food-induced anaphylaxis. Conversely, substantially higher rates of food allergy are noted among children requiring intubation for asthma compared to a control group of asthmatic children [73].

Atopic dermatitis

Atopic dermatitis (AD) is a chronic skin disorder that generally begins in early infancy and is characterized by typical distribution, extreme pruritus, chronically relapsing course, and association with asthma and allergic rhinitis [9]. Food allergy has been correlated with the development and persistence of AD, especially during infancy and early childhood. In children <5 years old, 35–40% will be allergic to at least one food [9,74–76]. These patients typically fail to respond to conventional medical therapy or may have frequent exacerbations of underlying skin disease if causal foods are not strictly avoided. The most common foods associated with AD include cow’s milk, egg, peanut, soy, wheat, fish, and tree nuts. Due to the chronicity of symptoms, a trial of dietary elimination of the suspected food allergen and the use of diagnostic food challenges may be warranted to aid in the accurate diagnosis of food allergy in these children. Dietary elimination of relevant food allergens may result in clearing of the skin. However, some patients continue to have ongoing skin disease due to concomitant sensitization to aeroallergens or due to non-allergic triggers.

In one well-designed report, 113 patients with marked AD underwent DBPCFC [76]. Among the 101 positive food challenges observed in 63 children skin, gastrointestinal, and respiratory symptoms were observed in 84%, 52%, and 32% oral food challenges, respectively. Some patients were subsequently placed on elimination diets based on these findings, with most exhibiting significant clinical improvement in skin symptoms. Although egg, peanut, and milk were responsible for most reactions, it was difficult to predict the patients with food allergy based on history and laboratory information alone.

In a single center’s experience evaluating over 2000 food challenges in 600 children with AD, approximately 40% of the DBPCFCs were positive [74]. Nearly 75% of the positive tests included cutaneous manifestations, principally consisting of macular, morbiliform, and/or pruritic rashes located in areas commonly affected by AD. Approximately 30% of positive tests consisted of skin rashes alone.

Summary

The ingestion of food represents the greatest foreign antigenic load confronting the human immune system. In the vast majority of individuals, tolerance develops to food antigens, which are constantly gaining access to the body proper. However, when tolerance fails to develop, the immune system responds with a hypersensitivity reaction. Inadvertent ingestion of food allergens may provoke various cutaneous, respiratory, gastrointestinal symptoms, and/or systemic anaphylaxis with shock. Investigations in the past have characterized the food hypersensitivity disorders, but our understanding of the basic immunopathologic mechanisms is incomplete and requires further investigation in order to provide target sites for therapeutic interventions.

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