Eur Arch Otorhinolaryngol (2010) 267:1327–1335
DOI 10.1007/s00405-010-1280-5

REVIEW ARTICLE

Allergic rhinitis caused by food allergies

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Received: 18 March 2010 / Accepted: 5 May 2010 / Published online: 20 May 2010

Abstract Food allergies occur in 1–2% of adults and in 8% of children under 6 years of age. Food-induced allergies are immunological reactions that cause a variety of symptoms affecting the skin, gastrointestinal tract, and respiratory tract. The reactions are mediated by both IgE- and non-IgE-dependent (cellular) mechanisms. Isolated food-induced allergic rhinitis is not common as it frequently occurs together with other food allergy symptoms such as asthma, eczema, oral allergic manifestations, urticaria, and gastrointestinal symptoms. The present paper provides an overview of food allergies and food-induced allergic rhinitis.

Keywords Food allergy · Allergic rhinitis · IgE mediated · Peanut allergy · Urticaria · Anaphylaxis

Introduction

Adverse food reactions have been recognised for centuries; the ancient Greek physician Hippocrates noted that cow's milk could cause gastric upset and hives. An adverse reaction to food is an abnormal condition that occurs after the ingestion of some foods. Two categories of adverse food reactions exist: food allergy and food intolerance (Table 1). A food-induced allergic reaction, or food allergy, is an immunological reaction that can affect the skin, gastrointestinal tract, and respiratory tract. It is mediated by both IgE- and non-IgE-dependent, i.e. cellular, mechanisms. IgE-mediated reactions include anaphylaxis, urticaria, angioedema, oral allergy syndrome, acute rhinitis, and acute asthma. Non-IgE-mediated reactions consist of contact dermatitis, dermatitis herpetiformis, coeliac disease, and Heiner Syndrome. Mixed reactions produce atopic dermatitis, allergic eosinophilic esophagitis (AEE), and allergic eosinophilic gastroenteritis (AEG) [1–3].

Food intolerance is a non-immunological reaction to ingested food, and may be caused by metabolic deficiencies (e.g. lactase or fructase deficiency), pharmacological intolerance (e.g. caffeine or tyramine in aged cheese), toxicity (e.g. bacterial or contaminants such as histamine in scombroid poisoning), or psychological disorders [1–5]. These classifications are shown in Table 1.

The majority of adverse food reactions are caused by food intolerance rather than food allergies; thus, many people believe that they or a family member has a food allergy, when the actual cause of the adverse reaction is food intolerance. It is important to identify true food allergies because allergic reactions such as anaphylaxis can be severe and potentially life threatening. A detailed medical history, laboratory tests, elimination diets, and food challenges are necessary to diagnose food allergies.

Epidemiology

The prevalence of food allergies varies according to age, culture, and population, and the true prevalence is not

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Table 1 Classification of adverse food reactions

Food intolerance
Metabolic (lactase or fructase deficiency, galactosemia)
Pharmacologic (caffeine, tyramine, alcohol, and histamine)
Toxins (bacterial food poisoning and scombroid fish poisoning)
Food allergy
IgE mediated (anaphylaxis, urticaria, angioedema, acute rhinitis, and acute asthma)
Non-IgE mediated (contact dermatitis, dermatitis herpetiformis, proctocolitis, coeliac, and Heiner syndrome)
Mixed (atopic dermatitis, eosinophilic esophagitis, and eosinophilic enteritis)

known because most patient histories have not been confirmed by clinical studies. Food allergy occurs in 1–2% of adults and in 8% of children under 6 years of age [2, 4, 6]. The prevalence of food allergies in early childhood is high, and it decreases slightly with age. The most common food allergies in young children are cow's milk (2.5%), eggs (1.3%), peanut (0.8%), wheat (0.4%), soy (0.4%), tree nuts (0.2%), fish (0.1%), and shellfish (0.1%). Half of the infants who have an IgE-mediated cow's milk allergy develop sensitivity to other foods [7, 8]. Allergies to milk, soy, eggs, and wheat are likely to resolve in adulthood. However, other food allergies are more likely to persist [2], and adults are frequently allergic to shellfish (2%), peanuts (0.6%), tree nuts (0.5%), and fish (0.4%) [7].

In Russia, Estonia, and Lithuania, the most common food allergies are citrus fruit, chocolate, apples, hazelnuts, strawberries, fish, tomato, eggs, and milk; in Sweden and Denmark, allergies to tree nuts, apples, pears, kiwi fruit, stone fruits, and carrots are most common [9]. In the United States, the most common food allergies among children are cow's milk, eggs, peanuts, tree nuts, soy, wheat, and fish, and allergies to shellfish, peanuts, tree nuts, and fish are most common among adults [10].

Food allergies have increased in recent years for unknown reasons. For example, the rate of peanut allergies has doubled in young children during the past decade. Although the cause is not well understood, environmental and genetic factors are likely to be involved [11, 12]. Food allergies are a serious problem worldwide. They are the most common cause of anaphylaxis in children, and are the reason for an increasing number of visits to accident and emergency departments for allergic reactions [13].

Pathogenesis

Allergic reactions to food are mediated by IgE-, non-IgE-dependent, or mixed mechanisms. Food allergens are typically glycoproteins of 10–70 kDa that bind to high-affinity IgE receptors (FcΣRI and FcΣRII). Specific antigen exposure induces cross-linking of food allergen-specific IgE and FcΣRI on mast cells and basophils [3, 14]. The cells then degranulate and release histamine, prostaglandins, and leukotrienes, which produce clinical symptoms. Mast cells were thought to be the primary effector cells, but studies have shown that basophils also play a major role in acute food allergy symptoms [15]. The glycoproteins are usually water soluble and resistant to denaturation by heat and degradation by proteases [2]. Several food allergens have been purified and well characterised (Table 2).

Table 2 Class-1 food allergens

Food	Allergens
Cod fish	Gad C1 (Parvalbumin)
Shrimp	Tropomyosin (Pen a1, Pen il, Met e1)
Peanut	Ara h1
	Ara h
	Ara h3
Soyabean	Trypsin inhibitor
	Thiol protease
	Conglycinin
Egg	Gal d1 (ovomucoid)
	Gal d2 (ovalbumin)
	Gal d3 (ovotransferrin)
	Gal d4 (lyzozyme)
Milk	Bos d8 (α casein)
	Bos d5 (β lactoglobulin)
	Bos d4 (α lactalbumin)
Brazil nut	Ber M 1
Rice	Ory S 1 (α intibitor)
Mustard	Sin a 1
	Bra j 1
Apple	Mal d 3
Corn	Zea m 14
Peach	Pru p1, Pru p2, Pru p3

The gastrointestinal mucosal immune system is exposed to numerous antigens. Thus, an intact and immunologically active gastrointestinal barrier is critical to suppress immune reactivity to foreign antigens and to protect the gastrointestinal tract against pathogens. The gut contains epithelial cells joined by tight junctions, a thick mucus layer, lumenal and brush border enzymes, bile salts, and extreme pH conditions. In the gut, the innate immune system (natural killer cells, polymorphonuclear leucocytes, macrophages, epithelial cells, and toll-like receptors) works together with the adaptive immune system (intraepithelial and lamina propria lymphocytes, Peyer's patches, IgA, and cytokines) to provide an active barrier to foreign antigens [2, 5, 16]. Nevertheless, the

Table 3 Class-2 food allergens

Food allergen	Cross-reacting foods	Homologous allergen
Birch Bet V1	Apple (Mald1)	Bet v1
	Carrot (Dau d)	Bet v1
	Celery (Api g1)	Bet v1
Birch Bet V2	Latex (Hev b8)	Profilin
	Celery (Api g4)	Profilin
	Potato	
Protein group 2	Latex (Hev b2)	1,3 gluconase
	Banana, kiwi	
Protein group 3	Latex (Hev b6.02)	Chitinase
	Avocado (Pers a1)	Endochitinase

prevalence of gastrointestinal infections and food allergies is high during the first few years of life, because the gut barrier and immune system are not fully developed [17]. Sensitisation in infants probably occurs as a result of the high permeability of their intestinal mucosa and early exposure to food antigens [17, 18]. Furthermore, infants have an immature secretory immunoglobulin A (SIgA) system and insufficient enzymatic activity [7, 18].

Two percent of the food antigens that are absorbed and transported throughout the body do not cause clinical symptoms because of oral tolerance, which may result from T cell anergy. Intraepithelial cells are inefficient antigen-presenting cells; they present allergens on the major histocompatibility complex as the first signal to T cells, but they lack the second signals (CD-28 and ICAM-1) needed to stimulate an active immune response. Consequently, the partially activated T cells become anergic or tolerant [6, 19]. Furthermore, dendritic cells in Peyer's patches express interleukin IL-10 and IL-4, which favour the generation of tolerance, and regulatory T cells secret the immunosuppressive cytokines IL-10 and tumour necrosis factor-beta, which are also important for oral tolerance [2, 6, 7, 16, 19]. Several types of regulatory T cells contribute to the development of oral tolerance: Th3 cells, which are a population of CD4+ cells that secrete transforming growth factor-beta; Tr1 cells, which secrete IL-10; CD4+ CD25+ regulatory T cells, which express the transcription factor FoxP3; CD8+ suppressor T cells; and gamma-delta T cells [5, 7, 19].

Under normal conditions, antigen presentation should suppress a further immune response; however, an allergic response occurs in sensitised individuals. The release of cytokines causes a loosening of the tight junctions between the intestinal epithelial cells and subsequent paracellular allergen inflow; dendritic cells in the gut carry this allergen to the gut-associated lymphoid organs. Non-GI manifestations tend to be mediated by IgE. Helper T cells activate B cells, which in turn, secrete allergen-specific IgE. The antibody circulates and becomes stationed on mast cells throughout the body, preparing the mast cells to be triggered by the allergen [2].

Gut bacteria at a density of 10^{12}–10^{14} cells per gram in the colonic tissue are important for the mucosal immune response and development of oral tolerance [18]. The bacterial population in the gut is determined by the maternal flora and the local environment. Studies have shown that lactation can prevent food allergies and that probiotics (Lactobacillus GG) can induce oral tolerance and prevent atopic dermatitis [7].

Food allergens

The two types of sensitisation to food allergens are class-1, which occurs in the gastrointestinal tract, and class-2, which occurs in the skin or respiratory tract [20]. Class-1 allergens are water-soluble glycoproteins, 10–70 kDa in size, and are stable to heat, acid, and proteases. Examples include caseins in milk, vicillins in peanuts, ovomucoid in eggs, and non-specific lipid transfer proteins in apples (Mal d 3) or corn (Zea m 14) [11, 20] (Table 2). Class-2 allergens are heat labile, susceptible to enzymatic degradation, and difficult to isolate. A limited number of these allergens have been identified: the Cupin superfamily, the Prolamin superfamily, and the pathogenesis-related proteins of the plant defence system [20] (Table 3).

In pollen food syndrome, also known as oral allergy syndrome, a cross-reaction occurs between a pollen allergen and a homologous protein allergen in raw fruits or vegetables (e.g. birch pollen protein Bet v 1 and the homologous Mal d 1 protein in apple or Dau d 1 in carrot). The initial route of sensitisation is respiratory exposure to the pollen proteins. Oral exposure to the food proteins is usually well tolerated because they are unstable in the presence of digestive enzymes. Heating food may either reduce or enhance allergenicity [5, 20]. The epicutaneous application of food proteins such as those in peanut skin creams may result in strong allergic sensitisation and TH2 inflammation [21].

Clinical disorders

Cutaneous reactions

Food can cause a variety of cutaneous hypersensitivity disorders via IgE-, non-IgE-mediated, and mixed reaction mechanisms. Cutaneous reactions are the most common clinical manifestations of an allergic reaction to a food or food additive [2]. Symptoms range from urticaria and angioedema to exacerbation of atopic dermatitis (Table 4). Acute urticaria and angioedema are mediated by IgE specific to a food protein. The condition begins on the face, eyelids, and lips, and then progresses throughout the body and limbs. The reaction is pruritic as a result of histamine release, and bradykinin formation occasionally causes burning and pain. Skin contact with food allergens may cause contact urticaria. The symptoms of chronic urticaria and angioedema may persist for longer than 6 weeks [2, 3].

Atopic dermatitis is a chronic pruritic rash on the face, limbs, and body, occurring most often in infancy and early childhood [6]. Both food-specific IgE- and non-IgE-mediated mechanisms appear to be responsible for chronic eczematous inflammation. Food allergens induce skin rashes in 40% of children who have moderate to severe atopic dermatitis [22]. Infants and children who have food allergies generally have a positive skin test or allergen-specific IgE directed towards various foods; especially, eggs, milk, soy, and peanuts. Food-induced contact dermatitis is often seen among food handlers, especially those who handle raw fish, shellfish, meat, or eggs.

Dermatitis herpetiformis is a non-IgE-mediated hypersensitivity disorder related to coeliac disease. It is characterised by a chronic, intensely pruritic, papulovesicular rash that is symmetrically distributed over the extensor surfaces and buttocks [2, 7]. The skin symptoms usually resolve when gluten is eliminated from the diet.

Gastrointestinal reactions

Pollen food syndrome is an IgE-mediated allergic reaction. Patients with a history of seasonal allergic rhinitis experience symptoms more frequently during pollen season. They develop itching or tingling of the lips, tongue, palate, and throat following the ingestion of certain foods. Angioedema of the lips, tongue, and uvula may occur and, in rare instances, can lead to a severe systemic reaction such as laryngeal oedema [2, 6]. The syndrome is primarily caused by fruit and vegetable epitopes that cross-react with pollen allergens. Patients who have a ragweed allergy may react to fresh melons and bananas; those with a grass pollen allergy may experience symptoms after ingesting raw tomatoes; and patients with a birch pollen allergy may react to raw potatoes, carrots, celery, apples, pears, hazelnuts, or kiwi fruit. As the allergens responsible for these reactions are easily broken down by heat or gastric enzymes, most patients experience allergic symptoms only in the oral and pharyngeal mucosa [7, 23]. Gastrointestinal anaphylaxis, another IgE-mediated allergic reaction, typically presents as vomiting, nausea, abdominal pain, and diarrhoea after ingestion of a food allergen [17].

The AEE and AEG can be mediated by IgE- or non-IgE-dependent mechanisms. The symptoms vary according to the degree of eosinophil infiltration into the oesophagus, stomach, and intestinal walls. Approximately half of the patients have peripheral eosinophilia; however, a diagnosis cannot be made on that basis [24]. AEE may manifest as gastroesophageal reflux symptoms such as dysphagia, nausea, vomiting, and epigastric pain (heartburn), particularly in children [7, 24]. Most patients who have AEE exhibit other allergic signs such as eczema, rhinitis, or asthma. The pH probe results are generally normal. A patient with gastroesophageal reflux and a negative pH probe result should undergo endoscopy and a biopsy [6]. An elemental diet, which contains no potential allergens, or an oligoantigenic diet, which removes common allergenic foods, may be required to determine the role of food in a patient's allergy. The long-term prognosis for AEE has not been clearly delineated, but patients who are not treated appropriately may develop Barrett's esophagitis [25].

The AEG symptoms include vomiting, abdominal pain, and diarrhoea; the disorder can occur at any age, including early infancy [25]. Weight loss or failure to thrive is a hallmark of AEG. Depending on the extent and location of the inflammatory involvement, patients may present with blood in the stool, iron deficiency anaemia, and protein-losing enteropathy [25]. Increased numbers of TH2 cells have been found in the peripheral blood and infiltrated into the intestinal mucosa of patients with AEG [26].

Table 4 Cutaneous reactions

Mechanism	Disorders	Symptoms
IgE mediated	Acute urticaria and angioedema	Pruritus and hives
	Chronic urticaria and angioedema	Pruritus, hives, >6 weeks
IgE and cell mediated	Atopic dermatitis	Marked pruritus and eczematous rash
Cell mediated	Contact dermatitis	Marked pruritus and eczematous rash
	Dermatitis herpetiformis	Marked pruritus and eczematous rash

Food protein-induced proctocolitis is a non-IgE-mediated allergic reaction that occurs in infants. Cow's milk and soy protein-based formulas are usually responsible for this reaction. Mucus and blood in the stool of breastfed infants can be attributed to food allergens, primarily cow's milk, ingested by the mother. These infants typically appear healthy and grow well, but are identified as having food protein-induced proctocolitis by gross or microscopic blood in their stool. The bleeding resolves when the allergen is excluded from the mother's diet [7, 27].

Food protein-induced enterocolitis syndrome is a non-IgE-mediated allergic reaction and typically manifests in the first few months of life, with severe projectile vomiting, diarrhoea, and failure to thrive [27]. The symptoms are most commonly provoked by cow's milk or soy protein-based formulas; however, solid foods such as rice can also cause these symptoms. In adults, shellfish (e.g. shrimp, crab, and lobster) hypersensitivity may provoke a similar syndrome, with delayed onset of severe nausea, abdominal cramps, and vomiting.

Coeliac disease is a non-IgE-mediated enteropathy associated with the HLA-DQ2 serotype and sensitivity to gliadin found in wheat and rye; it causes malabsorption of nutrients from the small intestine (Table 5).

Respiratory reactions

Respiratory symptoms caused by food allergies are classified as acute or chronic. Acute reactions are generally IgE mediated, and chronic reactions are mediated by a mix of IgE mediated and cellular mechanisms (Table 6).

It is difficult to identify the true prevalence of food-induced allergic rhinitis, because it frequently occurs in association with other food allergy symptoms such as asthma, eczema, oral allergic manifestations, urticaria, and gastrointestinal symptoms. Moreover, sensitisation to inhaled pollen proteins may result in cross-reactions with homologous fruit and vegetable proteins [20, 28]. A study of egg allergy in children reported that the risk for developing rhinitis and asthma by 4 years of age was significantly increased in those who had an egg allergy as an infant [29]. Additionally, rhinitis induced by oral food challenges occurred more frequently in infancy and early childhood compared with adulthood [30]. Rhinitis with rhinorrhoea that occurs after eating hot, spicy foods and autonomic stimulation by emotional and psychosomatic factors associated with food ingestion may be responsible for non-immunological rhinitis [28].

Asthma is a rare manifestation of food-induced allergic reactions although acute bronchospasm often occurs together with food-induced symptoms [30]. Airway hyperreactivity deteriorating into life-threatening asthma may occur in sensitised patients following ingestion of a small amount of a food allergen. Vapours or steam containing proteins emitted from cooking food such as fish can induce an asthmatic reaction and anaphylaxis [17]. Food-induced asthmatic symptoms should be considered

Table 5 Gastrointestinal reactions

Mechanism	Disorder	Symptoms
IgE mediated	Pollen food allergy syndrome (oral allergy syndrome)	Pruritus, tingling, and/or angioedema of the lips, palate, tongue, or oropharynx;
	Gastrointestinal anaphylaxis	Nausea, abdominal pain, cramps, vomiting, and/or diarrhoea
IgE and/or cell mediated	Allergic eosinophilic esophagitis (AEE)	Gastroesophageal reflux or excessive emesis, dysphagia, intermittent abdominal pain, and unresponsive reflux medications
	Allergic eosinophilic gastroenteritis (AEG)	Recurrent abdominal pain, irritability, intermittent vomiting, and weight loss
Cell mediated	Food protein-induced proctocolitis	Gross or occult blood in stool, usually in first few months of life
	Food protein-induced enterocolitis	Vomiting and diarrhoea (±bloody) vomiting typically delayed 1–3 h after feeding
	Food protein-induced enteropathy (coeliac disease)	Diarrhoea or steatorrhea, abdominal distention, weight loss, ±nausea and vomiting, oral ulcers

Table 6 Respiratory reactions

Mechanism	Disorder	Symptoms
IgE mediated	Allergic rhinitis	Periocular pruritus, tearing, and conjunctival erythema, nasal congestion, rhinorrhea, and sneezing
IgE and cell mediated	Asthma	Cough, dyspnea, and wheezing
Cell mediated	Heiner's syndrome	Recurrent pneumonia, pulmonary hemosiderosis, and iron-deficiency anaemia

in patients who have refractory asthma and a history of atopic dermatitis, gastroesophageal reflux, and food allergies [7].

Heiner syndrome, a rare disorder typically caused by cow's milk, is characterised by recurrent episodes of pneumonia associated with pulmonary hemosiderosis, gastrointestinal blood loss, iron deficiency anaemia, and failure to thrive in infants [7].

Anaphylactic reactions:

Anaphylaxis is the most serious food allergy and can be life threatening. Food allergens combine rapidly with IgE antibodies present on vascular and tissue mast cells and circulating basophils, which then secrete massive amounts of histamine, platelet-activating factor, and leukotrienes, resulting in oedema, cardiovascular symptoms, and circulatory collapse or shock. Generalised anaphylaxis caused by food allergies accounts for at least one-third to one-half of all cases of anaphylaxis seen in hospital accident and emergency departments [6, 7]. Food-dependent, exercise-induced anaphylaxis can occur in a person who is sensitised to a particular food allergen, such as celery, and who exercises within 2 h after ingesting that food [6]. Omega-5 gliadin, found in wheat, has been shown to be a major cause of food-dependent, exercise-induced anaphylaxis [31].

Diagnosis

The diagnostic approach for a suspected food allergy begins with a detailed history and careful physical examination. The history should include the possible causal food or foods, the quantity of the suspected food ingested, and the duration between ingestion and the development of symptoms. Furthermore, the history should note any co-existent factors such as exercise, aspirin, or alcohol and any similar symptoms occurring after ingesting the food in the past [2]. In general, the history is more helpful for IgE-mediated disorders because these reactions occur soon after food ingestion, and multiple target organs are affected. It is more difficult to take a history for non-IgE-mediated disorders because the symptoms occur hours or days after ingestion of the allergen [5]. Diet cards are used as an adjunct to a medical history, and patients are advised to keep chronological records of all foods they have eaten. In many cases, the identification of food-specific IgE antibodies, the results of elimination diets, or the responses to oral food challenges can be sufficient to confirm a diagnosis; however, invasive testing, endoscopy, and biopsy may be necessary in other cases like AEE or AEG [11].

Laboratory tests and procedures

The skin prick test (SPT) is the most common screening test for food allergies. SPTs provide a rapid means of detecting sensitisation in IgE-mediated disorders [11, 32]. The negative predictive accuracy is generally greater than 90% although the positive predictive accuracy is often less than 50% [5]. The reliability of the results depends on multiple factors, including the use of appropriate extracts and testing techniques, the accurate interpretation of the results, and the avoidance of medications such as antihistamines, which can interfere with testing. Consideration of the clinical history and disease pathophysiology is necessary to make maximal use of the test results [11].

Certain food allergens are easily denatured; thus, fresh food must be used for the prick-to-prick method. Intradermal skin tests with foods are less specific than prick tests because it is shown that intradermal skin tests have high "clinically false-positive" results; no more diagnostic than skin prick tests and can increase the risk for anaphylaxis; thus, they should be avoided [3, 6, 11, 33].

Food-specific IgE antibodies can be quantified using in vitro laboratory methods, which are advantageous when skin testing is limited by dermatographism, generalised dermatitis, or a clinical history of severe anaphylactic reactions to a given food. Serum tests to determine food-specific IgE antibodies (e.g. radioactive allergosorbent and CAP-FEIA tests) provide another modality for evaluating IgE-mediated food allergy [34]. In the radioactive allergosorbent test or enzyme-linked immunosorbent assay, the food allergen is bound to a matrix and bathed in the patient's serum. Food allergen-bound IgE antibodies are detected using radioisotope-tagged or enzyme-tagged monoclonal anti-human IgE serum, and immunoreactivity is measured by counting the bound radioactivity or assaying the enzyme tag, usually alkaline phosphatase or horseradish peroxidase [6]. A food-specific IgE level that exceeds the diagnostic level (Table 7) for a particular food indicates a greater than 95% chance of an allergic reaction upon ingestion of that food [7, 34]. Several studies have reported that low food-specific IgE levels were associated with positive food challenge outcomes in infants and young children. For egg allergy, an IgE level $\geq$2 kUA/L had a 95% positive predictive value in children younger than 2 years of age, and a level of 5 kUA/L had a 95% positive predictive value for milk allergy in infants younger than 1 year of age.

Patch tests are performed by exposing the skin to the food allergen under occlusion for 24 h. The area is then evaluated for erythema and papules in the subsequent 24–72 h. Patch tests are typically used to diagnose delayed contact hypersensitivity reactions such as AEE, food protein-induced enterocolitis, and atopic dermatitis, in which T cells play a prominent role [2]. The atopy patch test is

Table 7 Predictive value of food allergen-specific IgE levels

Allergen	kU/L	PPV
Egg	7	98
Infants <2 years	2	95
Milk	15	95
Infants <2 years	5	95
Peanut	14	100
Fish	20	100
Soybean	30	73
Wheat	26	74

Table from Hugh A. Sampson. Update on food allergy. J Allergy Clin Immunol 2004;113:805–819

more specific than the SPT, but less sensitive. The negative predictive value is close to 90%, except for milk, which has a negative predictive value close to 60% [35]. Endoscopy and biopsy are the most important tools for diagnosing non-IgE-mediated disorders, and are critical for the diagnosis of AEE and AEG [5].

The basophil histamine-release assay is primarily used in research settings, and has not been conclusively shown to provide diagnostic results reproducible enough for the clinical setting. Plasma histamine and tryptase levels increase after a food challenge; histamine rises within minutes, but is rapidly metabolised within an hour. Plasma tryptase elevation persists for many hours to days, and may be useful in determining whether anaphylaxis caused an unexplained sudden death [6].

Food challenges typically begin by eliminating the suspected food for at least 7–14 days following the clinical history and skin test results. An elemental diet (Neocate, EleCare Nutramigen, or Pregestimil) may help patients, particularly children, avoid all protein allergens. Antihistamines and beta-adrenergic bronchodilators have a negative effect on the results and must be discontinued. If the elimination diet is successful, the diagnosis may be confirmed with food challenges. The double-blind, placebo-controlled, food challenge (DBPCFC) is the gold standard for the diagnosis of food allergies because it eliminates both patient and observer bias. The patient is given a minute quantity of food in a liquid or powdered form contained in a masking vehicle. The dose is doubled every 15–30 min until allergic symptoms or signs occur, indicating a positive reaction. If the maximum dose causes no symptoms, the test is negative and must be confirmed by open feeding under observation to rule out the rare false-negative challenge result. In a clinical setting where minimal bias is suspected, a blind food condition is often not required, and open food challenges may be preferable [2, 6, 7, 32]. These tests are administered in a controlled environment in a hospital or specialty clinic with emergency equipment and trained personnel at hand.

Treatment

Elimination diet

The only therapy for a food allergy is avoidance of the suspected food. When a food allergy is diagnosed, strict elimination of the food allergen from the diet and avoidance of any contact with the food by ingestion, skin contact, inhalation, or injection are necessary. Patients and caregivers must be informed about food allergen avoidance and the signs of anaphylaxis. If the food allergy is longstanding, significant inflammatory damage might have occurred in the gastrointestinal tract, and may take months to heal [6, 7, 32]. Clinical tolerance develops to most food allergens over time, with the exception of peanuts, nuts, and seafood [32]. Clinical tolerance develops in about 20% of young children who have a peanut allergy, but children who experience an allergic reaction after the age of 5 years are unlikely to develop clinical tolerance. Therapy for infants with a cow's milk allergy usually involves selection of a hydrolysed milk formula. Food cross-reactions occur within botanical families, and a person who is allergic to one food is likely to develop an allergy to other foods in that family [2]. Allergen avoidance is the mainstay of therapy for non-IgE-mediated food hypersensitivities. It appears that clinical tolerance eventually develops in most children, with the exception of those who have coeliac disease.

Medication

Self-injectable epinephrine and a written emergency plan for treatment in case of accidental ingestion should be provided to anyone who has a potentially severe food allergy. For patients with significant systemic symptoms, the treatment of choice is epinephrine, which is administered by intramuscular injection in the lateral thigh [36]. Activated charcoal has been shown to be useful in the treatment of accidental ingestion of a food allergen, particularly peanuts [37].

Treatment may be limited to oral antihistamines in patients who have a history of mild reactions such as urticaria and pruritus following the ingestion of a food allergen. Antihistamines alone may prevent IgE-mediated skin symptoms, but they do not block systemic reactions. Antihistamines and topical steroids are the treatment mainstays for food-induced allergic rhinitis [28].

Systemic corticosteroids are often used to treat anaphylaxis, chronic IgE-mediated disorders such as atopic dermatitis or asthma, and non-IgE-mediated gastrointestinal disorders [7]. Some studies have suggested that cromolyn sodium or leukotriene inhibitors are effective for treating AEE or AEG, but these approaches have not been confirmed in controlled trials [38].

A mixture of traditional Chinese herbs is a non-specific therapy that has shown promise in a murine model of anaphylaxis [39].

Theoretically, anti-IgE antibody therapy should protect against multiple food allergens although indefinite administration would be required to maintain the protective effect. A study of immunotherapy for a peanut allergy showed that after the treatment, a significantly greater amount of peanut protein was required to elicit allergic symptoms in patients who underwent treatment compared with control subjects [40]. Immunotherapy using conventional subcutaneously or sublingually administered cross-reacting pollen allergens has been successful for treating fruit-induced oral allergy syndrome in birch-sensitive patients [6]. Immunotherapy with peas is being evaluated to minimise peanut allergy [6].

Recombinant peptides as food allergen epitopes (e.g. peanut Ara h1, 2, or 3 coupled to a bacterial DNA CpG) are recognised by animal immune systems by initiating Th1 or Treg cell suppression [41]. Heat-killed bacteria (*Listeria monocytogenes*, *Escherichia coli*) coupled to food allergens or epitopes have alleviated allergic reactions in murine and canine models [42].

Conclusion

The true prevalence of food allergies is not known as most patient histories have not been confirmed by clinical studies. Isolated food-induced allergic rhinitis is not common; rather, it frequently occurs with other food allergy symptoms such as asthma, eczema, oral allergic manifestations, urticaria, and gastrointestinal symptoms. Antihistamines and topical steroids are used to treat food-induced allergic rhinitis. Rhinitis with no history of specific food allergies or other allergic symptoms does not require further investigation. However, patients at risk for a rare and life-threatening respiratory system reaction and those having an IgE-mediated food allergy with a risk for anaphylaxis must be identified so that testing can be performed and appropriate diets can be initiated.

Conflict of interest statement The authors declare no competing interests.

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