



Information Sheet

Note: This information is for educational purposes. It should not be considered as medical advice. Please see your physician if you think you might have food allergies.

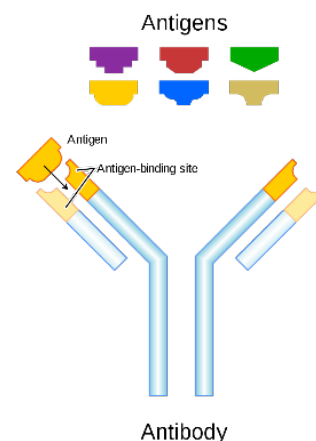
What is food allergy?

Food allergy is an allergic emergency that typically occurs within the first few minutes to two hours and can produce the sudden onset of itching, hives (urticaria), swelling of the face, tongue or back of the throat that may be accompanied by difficulty breathing and/or light headedness and hypotension.

The common mechanism leading to various food allergies is the lack of immunologic and clinical tolerance to an ingested food, which results in immediate or acute reactions mediated by specific antibodies, namely immunoglobulin-E (IgE), or delayed clinical disorders through specific immune cells.

Sensitization (making IgE antibodies) to food allergens can occur through the gastrointestinal tract, the skin, and, less commonly, the respiratory tract. Currently, the "dual-allergen exposure hypothesis" suggests that allergic sensitization to food occurs through low-dose skin sensitization, especially when skin barriers are defective, whereas early eating of food protein induces oral tolerance.

Pollen-food syndrome (formerly called oral allergy syndrome) is a specific kind of food reaction which



occurs in some patients with allergic rhinitis. Allergens present in pollens also can be found in foods. For example, fresh apples contain allergens present in birch pollen. The primary sensitization is to the pollen. The reaction is usually mild: on eating the food there may be a local itching reaction in the mouth and throat, occasionally this can be more severe with gastrointestinal symptoms or, very rarely, anaphylaxis. Usually, the food is tolerated if it is cooked such as in apple sauce. Some nut reactions are due to this syndrome, rather than to primary food allergy to the nut itself and this needs to be properly evaluated. The increasing use of molecular allergy – where IgE to allergen fragments is identified – is proving helpful in this regard.

“Food allergy” should not be confused with “food intolerance”, which is due to non-immunologic reactions to food including metabolic, pharmacologic, toxic, or undefined mechanisms but can sometimes mimic reactions typical of an immunologic response. An example is lactose intolerance where milk sugar is not digested effectively because of the missing enzyme, lactase. Patients experience gas, diarrhea, bloating, nausea and an uncomfortable after drinking milk of consuming foods with cow’s milk. They can tolerate almond or soy milk without symptoms.

Epidemiology of food allergy

There are extensive data to suggest that food allergies are common (up to 10% affected) and have been increasing in prevalence in the last two to three decades. Estimates of food allergy prevalence are highest when based on parent- or self-report rather than physician-diagnosed food allergy using standardized tests. There is a high co-occurrence of food allergy with other atopic diseases, including atopic dermatitis, asthma, and allergic rhinitis.



The foods causing most of the significant allergic reactions include peanut, tree nuts, finned fish, shellfish, milk, egg, wheat, soy, and seeds (commonly sesame). Allergy to foods other than shellfish and fruits and vegetables is more common in children than in adults. This includes milk, egg, wheat, and soy allergies.

Food allergy is a global problem



The prevalence of food allergy has been increasing, taking us to what is being termed as the “second wave of the allergy epidemic”. Not only does an increase in prevalence exist but complexity of food allergy is increasing as is the severity of anaphylaxis resulting in more hospital admissions for anaphylaxis over the last decade.

Food allergy has an impact on the quality of life of those who are allergic and their families. It is a significant public health issue and a considerable financial burden on affected individuals and families who require ongoing medical care, often for several allergic disease states.

The nutritional impact is also important. It is well documented that patients with food allergies have more growth deficiencies, malnutrition and micronutrient deficiencies, and this sometimes could be secondary to extensive elimination diets.

The prevalence and patterns of food allergy are highly variable in different parts of the world. In some developed economies 1 in 10 infants now have challenge-proven IgE mediated food allergy. Although there is lack of large studies in the developing world, similar trends are anticipated from the currently published data. A complex interplay of genetic and epigenetic characteristics, climate, infant feeding practices and migration, may influence mechanisms of food allergy in various populations at a global level.

There are important gaps concerning the elemental management of individuals with food allergy around the world, in terms of inequities in pediatric allergy services, availability of adrenaline auto-injectors, standardized national anaphylaxis action plans, understanding of everyday life management, and food allergen warning labeling requirements.

Despite efforts in the scientific community, increased health consequences and associated costs of food allergy, this chronic disease has not yet reached the level of societal attention that it warrants.

Quality of life with food allergy

Stress, anxiety and fear are common concerns among individuals and families who live with food allergies. Children may be bullied in school or by siblings and relatives.



Eating at restaurants, attending school and participating in social activities as well as grocery shopping and preparing meals all are situations that can increase emotional stress for individuals with food allergy and their families.

It is critical that individuals and their caregivers understand how to manage food allergy, can recognize an allergic reaction and know how to respond to anaphylaxis and administer an adrenaline/epinephrine autoinjector, as they follow the emergency response plan. Education and planning are key to helping ease the stress of a food allergy diagnosis.

It is necessary to engage a multidisciplinary team that includes allergists, dieticians, mental health professionals, social workers and dietitians in order to improve quality of life of individuals with food allergies and their families.

Clinical presentation in food allergy



Itchy skin reactions to foods are some of the most common presentations. These include acute reactions such as hives (urticaria), swelling of the skin and lips (angioedema), flushing and itching, by chronic disorders such as contact dermatitis and dermatitis herpetiformis, which is characterized by blisters. Atopic dermatitis is a chronic allergic skin disorder characterized by relapsing course and mediated through both specific IgE and immune cells; it may be exacerbated by food allergies. It is important, always present in anaphylaxis presentations.

Gastrointestinal reactions are also a frequent manifestation of food allergy. Vomiting or acute diarrhea are among the most common acute or immediate reactions. Reactions also can include chronic diseases such as food protein-induced enterocolitis syndrome (FPIES), which is characterized by chronic vomiting and diarrhea with failure to thrive, or food protein-induced proctocolitis (streaks of blood in the stool in an otherwise healthy infant). Eosinophilic esophagitis is caused by mixed immunological reactions and results in chronic vomiting and hard to treat reflux symptoms.

Food allergy is an extremely uncommon cause of chronic respiratory symptoms of the upper (rhinitis) and/or lower (asthma) airways. However, acute respiratory symptoms such as stridor and

wheezing are usually strong indicators of food-induced anaphylaxis. Anaphylaxis is a potentially life threatening unpredictable allergic disorder that is caused within minutes or a few hours after ingestion of the food allergen. Foods are the most common trigger of anaphylaxis in children, teens and young adults. Anaphylaxis symptoms can involve a combination of skin, respiratory, gastrointestinal, circulatory and/or neurological symptoms.

Diagnosis of food allergy

Diagnosing food allergy depends on the medical history, physical examination, elimination diets, skin prick tests (SPT), blood tests (measuring serum specific IgE, or sIgE, assays to particular foods), and in some individuals oral food challenges (OFC). The latter is considered the gold standard for diagnosing food allergy.



It should also be appreciated that diagnosis is not generally based on a single test. A stepped approach is usually used, in which history can lead to test selection, and the result of that test (such as SPT and/or blood test) can be used to determine whether an OFC is indicated, especially if the individual's clinical symptoms are unclear.

The presence of allergen sIgE to food allergens without having clinical symptoms after exposure to those foods does not diagnose food allergy, so random testing of multiple food allergens in asymptomatic individuals is unhelpful.

The diagnosis of non-IgE mediated food allergy is based on a combination of clinical signs and symptoms consistent with true food allergy occurring repeatedly on exposure to a food, resolution of those signs and symptoms with specific food avoidance, and, in some cases, biopsy results (in particular esophageal biopsy) consistent with allergic disorder that resolves with food avoidance.

Course of food allergy



Some food allergies have a high rate of resolution, or growing out of them, in childhood, such as milk (>50% by age 5-10 years), egg (approximately 50% by ages 2-9 years), wheat (50% by age 7 years), and soy (45% by age 6 years).

Other food allergies typically persist or have low rates of childhood resolution: peanut allergy (approximately 20% by age 4 years), tree nut allergy (approximately 10%), and allergy to seeds, fish, and shellfish are also considered persistent.

More rarely food allergies appear in adult life. Tolerance appears to have been broken by reducing gastric acidity (Proton Pump Inhibitors) or via the respiratory tract with a cross-reacting allergen.

When to refer to an allergist

The primary care physician or the pediatrician can diagnose and manage food allergy, however, there are situations for which we recommend referral to the allergist:



- Suspected anaphylaxis
- Suspected food allergy and failure to thrive
- Multiple food allergies
- Other significant co-existent allergic diseases (such as a child with significant

eczema and food allergy or with uncontrolled asthma and food allergy)

- To perform an oral food challenge (OFC) or a reintroduction of food in IgE mediated food allergies
- Discordance between clinical history and food allergy tests

Management and treatment of food allergy



Management

Standard therapy for food allergy is strict avoidance of ingesting the specific allergen or allergens. Minimum food avoidance is required for a better quality of life of individuals and their caregivers.

Many children can develop tolerance with age. Allergists evaluate tolerance to a food through oral food challenges that are performed in medical clinics with resuscitation available. Even though some individuals' blood test or skin prick test may indicate a decrease in allergy and possible tolerance, life threatening emergencies do occur.

Individuals with food allergy and their caregivers should be educated on how to avoid the foods that trigger the allergic reactions.

In several countries, food-labeling laws require food manufacturers to declare on the food packaging whether the common allergens are included as ingredients. However, many other countries do not have similar laws. (This is an unmet need.) Some countries also have legislation protecting consumers who eat out at restaurants. If a consumer with food allergy asks for allergen content, they must, by law be given the

Ingredients: Granola (whole grain rolled oats, brown sugar, crisp rice [rice flour, grain rolled wheat, soybean oil, whole wheat flour, sodium bicarbonate, soy lecithin], rice crisp [whole grain brown rice, sugar, malted barley flour, salt], peanut butter syrup, semisweet chocolate chips (sugar, chocolate liquor, cocoa butter, soy lecithin), sugar, palm kernel and palm oil, partially defatted peanut flour, lactose, dry whey salt, vanillin [artificial flavor]), oligofructose, polydextrose, glycerin, water. Contains: sugar, calcium carbonate, salt, soybean oil, natural and artificial flavor, sucralose. **CONTAINS WHEAT, PEANUT, SOY AND MILK INGREDIENTS. MAY CONTAIN TRACES OF TREE NUTS.**

*Sugar Content (on 40 gram basis): Regular Peanut Butter Chocolate Chip Quaker Chewy Granola

information and if they are served food containing the allergen, the food service is legally liable.

Most individuals often experience accidental ingestion of a food allergen. Most allergic reactions occur as a result of food eaten away from home such as at school, in a restaurant, on school camp or at the home of a relative or friend. Having emergency action plans to assess symptoms and treat allergic reactions are essential, especially when the food allergen might cause anaphylaxis.

Individuals who have risk factors for anaphylaxis from food allergens should have a prescription for epinephrine autoinjectors. Risk factors include: having poorly controlled asthma, allergy to peanut or tree nuts, milk or egg allergy, or a history of anaphylaxis to other allergenic foods.

Treatment for allergic reactions

- Allergic reactions induced by ingesting food range in severity from mild to life-threatening. Therefore, pharmacological treatments are needed when exposed to food allergens.
- Appropriate assessment of symptom severity is necessary in order to promptly treat the reactions.
- H1-antihistamines often are used when non-life-threatening symptoms occur (such as mild itching, or urticaria). However, there is weak evidence for their effectiveness and they certainly are not life-saving. When severe allergic reactions develop, the first-line treatment is intramuscular adrenaline injection. There is a general misconception that antihistamines will help prevent anaphylaxis from occurring. More needs to be done to discourage use of antihistamine and asthma preventers as first line treatment of anaphylaxis.

Can food allergy be prevented?

Maternal diet

There is insufficient evidence to support an intervention for maternal dietary restrictions during pregnancy or lactation in preventing food allergies. Mothers are advised to eat all foods in moderation.



Birth method

A nationwide Swedish cohort study of over 1 million children showed that children delivered by C-section had a 21 percent higher risk of developing food allergies than those born by vaginal delivery. Previous studies have shown an increased likelihood of milk allergies and asthma in C- section babies, compared to those delivered naturally via the vagina. The microbiome (bacterial flora) of the vagina colonizes the baby as it passes through from its formerly sterile environment. It is thought that bacterial exposure, especially in the gut, directs the development of the immune system. The C- section baby must pick up its bacteria from the operating room and is likely to have more Clostridium difficile. Efforts to replace the normal flora using maternal vaginal secretions have proved ineffective. The use of probiotics is under investigation.

Breastfeeding and formula

- Previous reports concluded that there were no short- or long-term benefits for exclusive breastfeeding beyond three to four months for preventing atopic disease, however other health benefits are well defined. There are insufficient data

regarding a direct relationship of breastfeeding on the onset of food allergy.

- There is no evidence yet that the role of partially or extensively hydrolyzed formula prevents the onset of specific food allergies.
- One study suggested that introduction of regular cow's milk formula in the first 14 days of life reduced the onset of cow's milk allergy. However, similar benefits have not been seen yet in other trials.

Complementary foods

- There is no evidence yet of benefits in delaying the introduction of allergenic foods beyond four to six month of age for the prevention of atopic disease, including peanuts, eggs, and fish.
- In high-risk infants (with severe eczema, egg allergy, or both), early introduction of peanuts may prevent peanut allergy, resulting in the recommendation to introduce peanut protein as early as between four and six months, under the supervision of the allergist.
- Although previous reports supporting an advantage of early egg introduction is less clear, a randomized trial using heated egg suggested that introduction of egg is likely to prevent egg allergy in infants with eczema.

Research

From the moment that food allergies appear to have increased in prevalence, not only treatment but also prevention strategies became of great importance. A landmark study on primary prevention, the Learning Early About Peanut Allergy (LEAP) study, has targeted peanut allergy by promoting an early introduction of peanut in infants at high risk (for example, those children with atopic dermatitis and egg allergy who are 4-11 months of age), and argues strongly for the early introduction of other allergenic foods, to prevent the development of food allergy.



Since food allergy derives from a defect in immune tolerance mechanisms which are modulated by gut microbiota function and structure, gut microbiome has been a target for innovative preventive strategies. New experimental tools and technologies have provided information regarding the role of metabolites generated from dietary nutrients and selected probiotic strains that could have a role in food allergy inception and be the target of interventions able to modulate the “diet-gut microbiome-immune system axis” to fight food allergy.

Currently, the only way to manage food allergy is avoidance of the food. Research continues in the hope of finding safe and effective options. Allergen immunotherapy for food (oral, sublingual, and epicutaneous) has been studied in clinical trials. Under the care of the allergist, immunotherapy may increase the threshold dose and induce desensitization to offending foods, but there is a risk of adverse reactions during the therapy. Currently, allergen immunotherapy to treat for food allergy is not recommended in general practice. Immunotherapy with anti-IgE, probiotics and Chinese Herbal Formulas may reduce side effects and be well tolerated. Several biological therapies that target molecules known to be involved in food allergy are being researched and tested across the globe.

These and other innovations will be included in new food allergy guidelines or in updated guidelines such as the World Allergy Organization (WAO) Diagnosis and Rationale Against Cow's Milk Allergy (DRACMA) guidelines, which are in development.

References

- Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D, Nadeau K, et al. Food allergy: A practice parameter update—2014. *J Allergy Clin Immunol*. 2014 Nov;134(5):1016-25.
- Sicherer S H, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol* 2018;141:41-58.
- Savage J, Sicherer S, Wood R. The natural history of food allergy. *J Allergy Clin Immunol Pract* 2016;4:196-203.
- Fiocchi A, Fierro V. “Food Allergy”, Disease Summary, in Allergic Diseases Resource Center, World Allergy Organization. Updated: March 2017. <https://www.worldallergy.org/education-and-programs/education/allergic-disease-resource-center/professionals/food-allergy>
- Tham EH, Leung DYM. How different parts of the world provide new insights into food allergy. *Allergy Asthma & Immunology Research* 2018;10(4):290-9.
- Prescott SL, Pawankar R, Allen KJ, Campbell DE, Sinn JKH, Fiocchi A, Ebisawa M, Sampson HA, Beyer K, Lee BW. A global survey of changing patterns of food allergy burden in children. *World Allergy Organization Journal* 2013;6(1):21.
- National Academies of Sciences, Engineering, and Medicine. Finding a Path to Safety in Food Allergy: Assessment of Global Burden, Causes, Prevention, Management, and Public Policy. Washington, DC: The National Academies Press; 2017.
- Nocerino R, Leone L, Cosenza L, Berni Canani R. Increasing rate of hospitalizations for food-induced anaphylaxis in Italian children: An analysis of the Italian Ministry of Health database. *J Allergy Clin Immunol*. 2015 Mar;135(3):833-5.
- Gupta RS, Warren CM, Smith BM, Blumenstock JA et al. The Public Health Impact of Parent-Reported Childhood Food Allergies in the United States. *Pediatrics*. 2018 Dec;142(6).

- Walkner M, Warren C, Gupta RS. Quality of life in food allergy patients and their families. *Pediatr Clin North Am*. 2015 Dec;62(6):1453-61.
- Patel N, Herbert L, Green TD. The emotional, social and financial burden on food allergies on children and their families. *Allergy Asthma Proc*. 2017. 1;38(2):88-91
- Dowling PJ. Food allergy: practical considerations for primary care. *Mo Med*. 2011. 108(5): 344-349
- Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, Bindslev-Jensen C, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy*. 2014;69(8):1008-25.
- Burks AW, Tang M, Sicherer S, Muraro A, Eigenmann PA, Ebisawa M, et al. ICON: food allergy. *J Allergy Clin Immunol*. 2012;129(4):906-20.
- Sampath V, Sindher SB, Zhan W, Nadeau KC. New treatment directions in food allergy. *Ann Allergy Asthma Immunol* 2018;120 (3): 254-262.
- Greer FR, Sicherer SH, Burks AW, Committee On N, Section On A, Immunology. The Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Hydrolyzed Formulas, and Timing of Introduction of Allergenic Complementary Foods. *Pediatrics*. 2019; March 18.
- Bird JA, Parrish C, Patel K, Shih JA, Vickery BP. Prevention of food allergy: Beyond peanut. *J Allergy Clin Immunol*. 2019;143(2):545-7.
- Du Toit G, Sampson HA, Plaut M, Burks AW, Akdis CA, Lack G. Food allergy: Update on prevention and tolerance. *J Allergy Clin Immunol*. 2018;141(1):30-40.
- Horimukai K, Morita K, Narita M, Kondo M, Kitazawa H, Nozaki M, et al. Application of moisturizer to neonates prevents development of atopic dermatitis. *J Allergy Clin Immunol*. 2014;134(4):824-30 e6.
- Agyemang A, Sicherer S. The importance of early peanut ingestion in the prevention of peanut allergy. *Expert Rev Clin Immunol*. 2019 Feb 14:1-9.
- Berni Canani R, Paparo L, Nocerino R, Di Scala C, Della Gatta G, Maddalena Y, Buono A, Bruno C, Voto L, Ercolini D. Gut Microbiome as Target for Innovative Strategies Against Food Allergy. *Front Immunol*. 2019 Feb 15;10:191.
- Fiocchi A, Artesani MC, Riccardi C, Mennini M, Pecora V, Fierro V, Calandrelli V, Dahdah L, Valluzzi RL. Impact of Omalizumab on Food Allergy in Patients Treated for Asthma: A Real-Life Study. *J Allergy Clin Immunol Pract*. 2019 Feb 20. pii: S2213-2198(19)30076-5. doi: 10.1016/j.jaip.2019.01.023. [Epub ahead of print]
- De Jong NW. Epicutaneous immunotherapy: the next step for food allergy desensitization. *Expert Rev Clin Immunol*. 2018 Dec;14(12):977-978.
- Dahdah L, Fierro V, Mennini M, Arasi S, Fiocchi A. What's next for DRACMA? *Expert Rev Clin Immunol*. 2018 Aug;14(8):649-651.