

# Food Allergies: Overview

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## Abstract

Food allergy is defined as an adverse immune-mediated response, which arises on exposure to a given food and is absent during prevention. The prevalence of food allergies has been increasing in the past twenty years and it represents a major public health problem in industrialized countries. Management of food allergy includes allergen avoidance or emergency treatment. An increasing appearance of allergies and atopic disorders, such as asthma, dermatitis, and rhinitis, has been observed in recent decades. Epidemiological studies show a global increase in the prevalence of food allergy all over the world and manifestations of food allergy appear increasingly frequent also in elderly subjects. Henceforth, food allergy has become an increasing concern for families, clinicians, and policymakers. Several healthcare surveys, and results from longitudinal cohort studies around the globe indicate that food allergy imposes a growing burden to the world.

**Keywords:** Allergy, food allergy, immune response, diagnosis, prevention.

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## INTRODUCTION

Food allergy has become a significant health burden as prevalence continues to increase, affecting 6%-13% of the global population and it has been increasing in occurrence ever since [29]. The symptoms have been found to vary from mild to severe, and can lead to anaphylaxis in extreme cases of food allergy, which is a life-threatening allergic reaction. Currently, there is no cure for food allergy. The eight most common food allergens are eggs, milk, peanuts, tree nuts, soy, wheat, crustacean shellfish, and fish, all of which are frequently taken around the world [31]. The mechanisms of these disorders remain unclear, and therefore the development of novel therapies is limited. Current treatments are often symptomatic, nonspecific, or may have severe side effects [37].

Food allergy presents in all ages and has a significant impact on an individual's quality of life. Some of the food allergies that start in childhood remain into adulthood and new-onset allergies can occur at any point of life [22]. A diagnosis of food allergy requires evidence of sensitization and specific symptoms on exposure to a particular food. The mechanism that leads to food allergies is the lack of immunologic and clinical tolerance to food allergens [6]. Environmental and nutritional changes have partly changed the epidemiology of allergic reactions to foods and new food allergic syndromes have emerged in

recent years [8, 9]. Food allergy imposes significant costs to multiple stakeholders and largely impact families at the household level. Recent studies reveal the need to balance the household management of food allergy with the efficient use of health resources [10-12]. Urticaria is a common presenting problem with the primary care provider. Acute urticaria lasts less than 6 weeks due to drug or food allergens. Chronic urticaria lasts more than 6 weeks is often associated without a known underlying cause [16]. Various *in-vitro* and *in-vivo* diagnostic tools are available for allergy detection. Skin prick tests are useful for aero-allergies whereas oral challenge tests are best for identifying suspected food allergies [17]. Composition of the microbiome in the fetal and neonatal period plays a key role in the development of the immune system: vaginal delivery, breastfeeding, childhood spent in rural environments and/or in contact with animals result in a greater biodiversity of the microbiome with the presence of protective species that reduce the activation of Th2 lymphocytes, involved in allergic reactions [23].

Adverse reactions to foods can be broadly divided into those with an immune basis – food allergies and celiac disease, or those without an immune basis – termed food intolerances. These non-allergic food reactions do not involve the immune system. Immunologic studies have described changes in the T-cell compartment, serum and salivary immunoglobulin profile, and mast cell and basophil degranulation status

in response to allergens [33]. Food allergy can be classified based on immune response. It could be IgE-mediated, non-IgE-mediated and could be a mixture of both. IgE-mediated food allergy involves food allergen sensitization, and secondly the development of signs and symptoms on exposure to that food. In IgE-mediated food allergy, there may be proof of an underlying immune process due to eosinophilic inflammation of the gastrointestinal tract. Incidence of food allergy is common in relation to allergy or intolerance. Also, if antimicrobial residues are present in food-producing animals it will lead to harmful effects on the consumer and may cause issues in food transformation (i.e., cheese, yogurts production) [15]. Among prevalent food allergies, cow milk allergy (CMA) is most common and may persist throughout the life. The allergic individuals are exposed to a constant threat due to milk proteins' presence in uncounted food products like yogurt, cheese, and bakery items [24].

### **IgE-MEDIATED FOOD ALLERGY**

Allergic responses are mainly caused by IgE, which is often located on the cell surface. To avoid allergic reactions due to excessive penetration of antigens into the intestinal lamina propria, the vulnerable gut mucosa is supported by specialized anti-inflammatory immune defenses, including secretory IgA (SIgA) antibodies and hyporesponsiveness to innocuous agents, particularly dietary antigens and the commensal gut microbiota [36]. The current diagnostic method detects both allergen-specific IgE and total IgE levels, but a number of allergic patients have a normal serum IgE level, which is a poor clinical correlate for allergy [27].

Recent developments representing the role of allergies, the utility of allergy testing, and the role of the allergist in eosinophilic esophagitis (EoE) patients also have concurrent atopic disorders including food anaphylaxis, asthma, allergic rhinitis, and eczema [39]. Globally, Australia has been reported to have the highest prevalence of IgE-mediated food allergy, with 10% of infants demonstrating challenge-confirmed allergies to one or more foods; by contrast, other developed areas such as Europe and the United States have prevalence estimates of 1–5% [7, 19, 25]. In terms of translational research, recent technological advances have enabled investigators to map IgE-binding 'allergenic' epitopes on different food allergens [32].

Lifestyle factors and dietary habits play an important role in causing the onset of food allergies, including qualitative and quantitative composition of the microbiota. These factors seem to have the greatest influence early in life, an observation that has led to the explanation of the food allergy epidemic, including the dual-allergen exposure hypothesis [28]. The very nature of the gut requires that its large mucosal surface is continually vulnerable to foreign substances, from food proteins to commensal bacteria and pathogens. The

mucosal immune system is required to mount protective responses against pathogenic organisms and toxins, whilst not responding excessively to harmless bacteria and food components. In health, the physical properties of the gut, including gastric acid, digestive enzymes, mucosal integrity and mucus secretion reduce the penetration of ingested pathogens and food proteins. The innate immune system targets molecules common to many pathogens.

Although for identification of immunoglobulin E (IgE)-mediated food allergy is an oral food challenge, clinically relevant biomarkers of IgE sensitization, including serum-specific IgE and skin prick testing can aid in diagnosis [20]. Irritable bowel syndrome (IBS) is a functional gastrointestinal disease and the most common cause of prolonged abdominal pain and bowel disturbances in the developed world. While initially thought to be functional or psychosomatic in nature, IBS is now recognized as a heterogeneous group of conditions. A subset of IBS patients and patients with allergic diseases share some characteristic inflammatory features. In fact, atopic children show an increased likelihood of developing IBS as adults [21].

Interplay of factors determines whether there will be a mucosal IgA secretion response, a systemic immune response, or local and systemic tolerance upon re-exposure. The mechanisms leading to food protein tolerance are not fully understood but tolerance involves an active regulatory response mediated by regulator T (TReg) cells, and clonal deletion which removes T cells with undesirable targets. Food and other proteins enter the body by ingestion, inhalation and skin penetration. They are taken up by antigen presenting cells and presented to T Helper cells. The resulting cytokine release determines whether there is a predominant TH1 or TH2 response. The TH1 response is the cell-mediated response, effective against intracellular bacteria and protozoa. In contrast the TH2 response targets parasites such as helminths with stimulation of eosinophils, basophils and mast cells, along with IgE-producing B cells. When food proteins inappropriately trigger a TH2 predominant response the result is Type 1 hypersensitivity and IgE-mediated food allergy [35]. Anaphylaxis is another systemic response initiated by binding of antigen to membrane-associated IgE on mast cells and basophils. This causes the release of inflammatory mediators, including histamine, tryptase and chemo-attractants. Injected histamine can reproduce most of the features of anaphylaxis in animals, where it leads to smooth muscle spasm, eosinophil activation and increased vascular permeability [18].

### **DIAGNOSIS OF FOOD ALLERGIES**

Accuracy of diagnosing an allergic reaction needs complete blood test to diagnose allergies against certain range of food items. Clinical history and examination are the first-line approach in diagnosing

food allergy. This skin testing is helpful to verify the absence of an IgE-mediated food allergy [34, 38]. Serum IgE testing is an important adjunct tool in accurate recognition of causal food allergens [14, 26]. Testing to large panels of food allergens is not compulsory, as it may generate false positive results leading to unnecessary dietary elimination of safe food, and unfair nutritional deficiencies [13]. Thereby, selecting *in vitro* testing for sensitization to food should be based on medical history. Other tests detecting sensitization include the basophil activation test (BAT), which evaluates the *in vitro* basophilic activation by specific allergens. According to a recently published study, BAT effectively discriminates between allergy and tolerance in peanut-sensitized children, showing 97% accuracy, 95% positive predictive value, and 98% negative predictive value [13]. Therefore, BAT assures to bring real improvement in diagnosing food allergy. There are no well-accepted criteria for diagnosing food allergies so far. Numerous diagnostic tests have been proposed as useful additions to the clinical history for diagnosis. The most commonly studied are serum food specific IgE determinations, and atopy patch testing (APT). The evaluation of a patient with suspected food allergy begins with obtaining a thorough clinical history that considers the symptoms indicative of allergic reactions to food. The clinical presentation of food allergy reactions varies within wide ranges and provides information about the incriminated mechanism.

Epigenetic marks, especially DNA methylation, possess a diagnostic potential for atopic sensitization, asthma, allergic rhinitis, and food allergy and can be used as a predictor of clinical responses in controlled allergen challenges, including oral food challenges [3].

## MANAGEMENT OF FOOD ALLERGIES

Several studies have suggested prevention of food allergies [1, 2, 4, 5]. Elimination diets have been considered as first alternative in the management of food allergies, as well as a part of evaluation for food allergy, and refer avoiding incriminated food. Henceforth, elimination diets focus on diverse aspects in clinical practice: patient is advised to remove one or several suspect food from diet; diet in which food causing allergic reactions is removed temporarily from the diet especially in patients with chronic conditions, such as atopic dermatitis or chronic urticaria; elemental diets, like extensively-hydrolyzed or amino acid-based diets are used to evaluate disorders associated with multiple food sensitivities, such as eosinophilic esophagitis. Such diets should be given with great caution, particularly in infants and children, to avoid nutritional deficiencies. Although elimination diets are used as an adjunctive mean of diagnosing food allergy, they cannot confirm the diagnosis on their own.

Recently, a useful tool like peptide microarray technology has been proposed for diagnosing food

allergy as diagnostic and prognostic performance [30]. Although desensitization can be obtained for the majority of individuals with food allergy through immunotherapy, there is a need for continued ingestion of allergen to maintain desensitization in patients.

## CONCLUSION

Allergies related to food have become a common health problem leading to a significant socioeconomic impact on human population. Treatment and diagnostic tools are crucial to avoid the exclusion diets and to make recommendations for personalized diet chart. With current advancement in science considerable progress has been made in the diagnostic algorithm in food allergy. The future of food allergy treatment shows potential with a number of clinical trials in progress. Taken together, the recent advances in various areas and fields of basic, translational and clinical food allergy research give hope for the next level of improved diagnostics, treatment and prevention.

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