

AN OVERVIEW OF FOOD ALLERGIES

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Abstract: The prevalence of food allergies has been rising globally, affecting both children and adults. Misunderstanding food allergies can lead to unnecessary dietary restrictions or, in some cases, life-threatening consequences. This overview aims to describe food allergies, distinguish it from other forms of food sensitivity, and discuss its symptoms, diagnosis, and treatment. The literature source consists of relevant journals and books from the search engines PubMed and Google Scholar. When an individual with a food allergies consumes a particular allergen, their immune system produces IgE antibodies against that allergen. Upon subsequent exposure, these antibodies trigger the release of histamines and other inflammatory mediators from mast cells and basophils, resulting in allergic symptoms. The classic symptoms of a food allergies can range from mild to severe and include skin reactions (hives, eczema, or itching), gastrointestinal symptoms (nausea, vomiting, diarrhea, or abdominal pain), respiratory issues (sneezing, runny nose, coughing, or difficulty breathing) or systemic reactions (anaphylaxis). The combination of of medical history, physical examination, and diagnostic tests in some cases can provide enough diagnostic reliability to make the diagnosis of a food allergies. Oral antihistamines may relief for mild allergic symptoms, whereas systemic corticosteroids may be prescribed for severe acute reactions or persistent inflammatory symptoms. Patients with systemic reactions should receive intramuscular epinephrine (adrenaline) during anaphylaxis.

Keywords: Food Allergies, Pathophysiology, Symptoms, Diagnosis, Treatment.

I. INTRODUCTION

Food allergies may significantly affect an individual's social and psychological well-being. Among the adverse consequences associated with food allergies is anxiety concerning potential allergic reactions. These concerns can restrict social interactions and travel activities, ultimately diminishing overall quality of life.¹

The first well-documented case histories of patients with food allergies appeared in the early twentieth century; however, food allergies were largely overlooked until more recent years. Adverse reactions to foods are not a new phenomenon and have been described for over two thousand years. The ancient Greek physician Hippocrates documented a reaction to milk in the first century. Anaphylactic reactions to egg and fish have been reported as early as the sixteenth and seventeenth centuries.²

Food allergies are currently recognized as a major public health concern, with its prevalence increasing significantly over the past two decades worldwide, particularly in Westernized and industrialized countries. Similar trends are being observed in developing nations as their economies expand and their populations increasingly adopt Westernized lifestyles. Overall, Food allergies are estimated to affect approximately 5% of adults and 8% of children.^{3,4} This rising prevalence has been accompanied by an increase in hospitalizations for food-induced anaphylaxis, reflecting what has been described as the "second wave of the allergy epidemic," following the earlier rise in asthma and respiratory allergies. Pouessel et al. reported that foods accounted for 37% of intensive care unit (ICU) admissions due to anaphylaxis and 79% of recurrent anaphylaxis cases. Furthermore, self-reported FA appears to be even more common and is often associated with a substantial yet underrecognized impact.^{5,6,7}

The epidemiology of food allergy is influenced by genetic, cultural, and geographical dietary factors. Severe and potentially fatal reactions may occur at any age; however, the highest risk is observed among adolescents and young adults with asthma and a confirmed food allergy to peanuts, tree nuts, fruits, milk, wine, vegetables, and/or seafood.²

Misunderstanding food allergies can lead to unnecessary dietary restrictions or, in some cases, life-threatening consequences. Therefore, it is essential to have an accurate understanding of this condition. This overview aims to describe food allergies, distinguish it from other forms of food sensitivity, and discuss its symptoms, diagnosis, and treatment.

II. MATERIALS AND METHODS

For this review, literature sources such as scientific journals on search engines (PubMed and Google Scholar) and relevant national books were searched. The keywords used were “Food Allergies”, “Pathophysiology”, “Clinical symptoms”, “Diagnosis”, and “Treatment”. Inclusion criteria were all reviews on Food Allergies. Exclusion criteria were literature published more than 10 years ago. Information was collected, recorded and analysed to assess the validity and reliability of the literature.

III. RESULTS AND DISCUSSION

An adverse food reaction is a broad term that encompasses any abnormal clinical response associated with the ingestion of food. Such reactions are generally classified as either food intolerance or food allergy/ food hypersensitivity, based on the underlying pathophysiological mechanisms. Food intolerance refers to an adverse physiologic response to a food and may be due to inherent properties of the food (i.e. toxic contaminant, pharmacologic active component) or to characteristics of the host (i.e. metabolic disorders, idiosyncratic responses, psychological disorder), they may not be reproducible, and they are often dose dependent. In contrast, food allergy is defined as an abnormal immunological response to food occurring in a susceptible individual. Allergic reactions are typically reproducible upon each exposure to the offending food and are frequently not dose-dependent.²

Several types of adverse immune-mediated reactions contribute to the body’s defense against disease. In food allergies, the mechanism of “immediate hypersensitivity” involves three principal components: food allergens, immunoglobulin E (IgE), and effector cells, namely mast cells and basophils. A food allergen is the specific component of a food that triggers an immune response in sensitized individuals. A single food may contain multiple allergens, the majority of which are proteins rather than carbohydrates or lipids. Individuals with food allergies produce elevated levels of IgE, a class of antibodies involved in immune defense. Upon exposure to a specific food allergen, the immune system generates allergen-specific IgE antibodies. These IgE molecules circulate in the bloodstream and bind to high-affinity IgE receptors on basophils and mast cells. Basophils are phagocytic white blood cells, or cells that engulf and absorb foreign bodies in the bloodstream. Mast cells are found in tissues primarily at sites in the body that come in contact with the environment – such as the skin, lungs and gastrointestinal tract. Both cell types play central roles in the pathophysiology of allergic reactions. Upon interaction with food antigens, IgE becomes cross-linked and binds to mast cells and basophils via the high-affinity receptor. This process activates these cells, leading to the release of granules that contain preformed inflammatory mediators (eg, histamine), as well as de novo synthesis and/or release of inflammatory mediators (eg, leukotrienes), proteases (eg, tryptase), inflammatory cytokines (eg, IL4), and chemotactic molecules. Mast cells and basophils are activated within a few minutes of IgE cross-linking, therefore this process is called an immediate allergic reaction; symptoms occur shortly after allergen contact.^{8,9}

Based on the immunological mechanism involved, food allergies may be further classified in a) IgE-mediated, which are mediated by antibodies belonging to the Immunoglobulin E (IgE) and are the best characterized food allergy reactions; b) Non IgE-mediated, which are mediated when the cell component of the immune system is responsible of the food allergy and mostly involve the gastrointestinal tract; c) mixed IgE mediated-cell mediated when both IgE and immune cells are involved in the reaction.²

Table 1. Classification dan Clinical Symptoms of Food Allergies

Type of Food Allergies	Clinical Symptoms
IgE-mediated	Skin: Urticaria Angioedema Erythematous morbilliform rash Flushing Respiratory: Allergic rhinoconjunctivitis

	Acute bronchospasm Gastrointestinal: Oral Allergy Syndrome Acute gastrointestinal spasm Cardiovascular: Dizziness & fainting Anaphylaxis Food-associated exercise induced anaphylaxis Miscellaneous: Uterine cramping & contractions Feeling of “pending doom”
Non IgE-mediated	Skin: Atopic dermatitis Respiratory: Asthma Gastrointestinal: Eosinophilic esophagitis (EOE) Eosinophilic gastritis Eosinophilic gastroenteritis
Mixed IgE and Non IgE-mediated	Skin: Dermatitis herpetiformis Dermatitis contact Respiratory: Food-induced pulmonary hemosiderosis (Heiner's Syndrome) Gastrointestinal: Food protein-induced entero-colitis syndrome (FPIES) Food protein-induced procto-colitis syndrome (FPIPS) Food protein-induced enteropathy syndrome Celiac disease

Pathophysiology of Food Allergies

When an individual with a food allergies consumes a particular allergen, their immune system produces IgE antibodies against that allergen. Upon subsequent exposure, these antibodies trigger the release of histamines and other inflammatory mediators from mast cells and basophils, resulting in allergic symptoms.¹⁰ Factors that contribute to the type and severity of reactions include the amount of ingested allergen, the stability of the allergen against digestion, and the permeability of the epithelial barrier. The immediate allergic reaction leads to intense inflammation that can become life-threatening. The release of vasoactive mediators into the circulation can lead to vascular collapse and anaphylactic shock.¹¹

IgE-mediated food allergy is characterized by immediate clinical manifestations, due to the release of mediators triggered by the bonding of IgE antibodies, mast cells and basophils. Once produced, IgE bind to its high-affinity receptor on the surface of mast cells and basophils, therefore arming these cells for activation on re-exposure to the antigen. The second contact with the antigen activates and makes these cells degranulate, resulting in performed mediators release (histamine, tryptase, platelet activating factor, prostaglandin and leukotrienes) and can lead to local and systemic manifestations.³

Several hypotheses have been proposed to explain the rising prevalence of food allergy. One of the most widely discussed is the hygiene hypothesis, which suggests that reduced exposure to microbes and infections during early childhood may increase susceptibility to allergic diseases. This effect is thought to occur through altered immune system development, characterized by an imbalance in immune responses favoring a T-helper 2 (Th2) lymphocyte profile over a T-helper 1 (Th1) response. Observational studies further indicate that factors associated with greater microbial exposure, such as contact with household pets, attendance at childcare facilities, vaginal delivery, and the presence of older siblings, may exert protective effects against the development of food allergies. The second proposed explanation is the dual-allergen exposure hypothesis. Evidence from both animal and human studies suggests that impaired skin barrier function in infants with eczema may promote allergen sensitization through environmental exposure via the cutaneous route rather than the oral route.¹² This

hypothesis further proposes that exposure to food antigens through the skin is more likely to result in allergic sensitization, whereas early oral exposure is more likely to induce immune tolerance.¹³ Food allergies are therefore thought to arise from the interplay between cutaneous and gastrointestinal exposure to food antigens, with a greater propensity for sensitization when the initial exposure occurs through the skin. The Vitamin D hypothesis, Vitamin D possesses well-recognized immunoregulatory and tolerogenic properties, and its deficiency has been proposed as a potential risk factor for the development of food allergies.¹⁴ The association between vitamin D and the prevention of food allergies were first suggested by evidence showing that infants with serum vitamin D levels <50 nmol/L at 1 year of age had an 11-fold increased risk of peanut allergy—confirmed by oral food challenge—compared with infants whose vitamin D levels were >50 nmol/L. Accumulating evidence further indicates that vitamin D plays an important role in regulating T helper (Th) cell differentiation and in promoting the induction of regulatory T (Treg) cells.¹⁵ Moreover, Th2-skewed immune responses have been shown to be favored under conditions of low or deficient vitamin D status.¹⁶ According to the microbiota hypothesis, the presence of specific bacterial strains as well as dietary substrate and their metabolites, could influence food allergy development.^{17,18}

Clinical Symptoms of Food Allergies

Several foods are well-known triggers for allergic reactions, include:^{19,20}

Table 2. Big Eight of Food Allergens

The most common food allergens	
Milk	: One of the most common allergens in infants and young children, milk allergy is often outgrown by age three
Eggs	: Particularly in children, with many outgrowing the allergy by age five
Peanuts	: Known for its potential to cause severe reactions, peanut allergies can persist into adulthood
Tree Nuts	: Includes almonds, walnuts, and cashews, which can cause reactions similar to those of peanuts
Soy	: Commonly affects infants and young children, with many outgrowing it by age three
Wheat	: Often associated with both allergies and intolerances, such as celiac disease
Fish	: Typically causes lifelong allergies, often starting in adulthood
Shellfish	: Includes crustaceans and mollusks, and is usually a lifelong allergy

When an offending food enters the stomach, nausea, vomiting, cramping and diarrhea may occur. The classic symptoms of a food allergies can range from mild to severe and include:^{10, 21}

1. Skin reactions: hives, eczema, or itching
2. Gastrointestinal symptoms: nausea, vomiting, diarrhea, or abdominal pain
3. Respiratory issues: sneezing, runny nose, coughing, or difficulty breathing
4. Systemic reactions: anaphylaxis (a severe, life-threatening reaction requiring immediate medical attention)

Symptoms of food allergy are highly individualistic, varying in terms of degree, time of onset, location and amount of food eaten. Symptoms can vary within the same person as well as among populations, can occur alone or in combination, with more than one symptom occurring at one time; and in some cases there can be generalized anaphylaxis.^{2,21} The type and severity of symptoms changes from one subject to another, and in the same subject from one reaction to another, in accordance with food and with the same food depending on the sensitizing molecule. In both IgE-mediated and non IgE-mediated food allergies, symptoms most frequently affect the skin, gastrointestinal tract, respiratory and cardiovascular system, in either isolation or in association. The short period of time (usually < 2 hours) between ingesting a food and the appearance of symptoms leads to a suspicion of a mediated IgE reaction, except for food dependent exercise anaphylaxis (FDEIA) and of delayed anaphylaxis to red meat. Anaphylaxis is a rare but potentially fatal condition in which several different parts of the body experience food allergic reactions at the same time. Symptoms may progress rapidly and may include severe itching, hives, sweating, swelling of the throat, breathing difficulties, lowered blood pressure, unconsciousness and can even lead to death.²²

Diagnosis of Food Allergies

The diagnosis of food allergies is not simple because of its multiple clinical symptoms and because diagnostic tests are not always enough to offer diagnostic certainty. The combination of medical history, physical examination, and diagnostic tests in some cases (e.g anaphylaxis or in children with a clinical history suggestive of allergy and positive results in skin tests or specific IgE), can provide enough diagnostic reliability to make the diagnosis of a food allergies without conducting an oral food challenge (OFC)²³

1. Medical History

Diagnosing a food allergy begins with a thorough medical history to identify the suspected food; the amount eaten to cause a reaction (to determine the severity of the sensitivity); the amount of time between food consumption and development of symptoms; how often the reaction occurs; and other detailed information. The goal of medical history is also to identify the possible immunological mechanism underlying the food allergies.

2. Physical examination

A complete physical examination and selected laboratory tests are conducted to rule out underlying medical conditions not related to food allergies.²¹

3. Diagnostic Test

Several tests are available to determine if a person's immune system is sensitized to a specific food.

- Skin Prick Tests (SPT), a diluted extract of the suspected food is placed on the skin, which is then scratched or punctured. If no reaction at the site occurs, then the skin test is negative and allergy to the food is unlikely. If a bump surrounded by redness forms within 15 minutes, similar to a mosquito bite, then the skin test is positive and the person may be allergic to the tested food.
- Blood tests using the radio allergosorbent test (RAST) or the enzyme linked immunosorbent assay (ELISA) to measures the level of IgE antibodies (serum-specific IgE/ sIgE) specific to certain allergens, can provide similar information to that obtained by the skin test.²¹
- Oral Food Challenge

If the medical history, physical examination and skin or laboratory tests suggest a food allergies, and if the reactions to the food are not severe, then the doctor may conduct a food challenge. In a oral food challenge, increasing doses of the suspected food are given until the individual develops symptoms or tolerates a normal portion under medical supervision to confirm a diagnosis.

- Allergen component-resolved diagnostics (CRD) are proposed as a more accurate method of diagnosis, because instead of using crude allergen extracts, which consist of both allergenic and non-allergenic components, CRD measures sIgE to individual allergen proteins

Skin prick tests (SPT) and serum-specific IgE (sIgE) are routinely used in clinical practice and are relatively safe and inexpensive to perform. However, the conventional positive results ($SPT \geq 3$ mm or $sIgE \geq 0.35$ kU/L) have poor specificity to clinical food allergies, with approximately half of sensitized individuals able to tolerate the food without reaction. As increasing magnitude of these tests correlates with a higher risk of reaction, many studies have defined thresholds for these tests with 95% positive predictive value (PPV) to food allergies. Although SPT and sIgE thresholds with 95% PPV to food allergies are routinely used to minimize the need for diagnostic food challenges, a proportion of children remain in the immunologic grey area; that is, they are food-sensitized but below the 95% PPV threshold.^{5,10,21}

Treatment of Food Allergies

Once a diagnosis of food allergy has been established, strict avoidance of the identified allergen remains the only evidence-based management strategy. Individuals with food allergy should be provided with a comprehensive emergency action plan to manage accidental exposures, as allergic reactions may be unpredictable and, in some cases, fatal. The use of medical alert identification devices, such as bracelets or necklaces, is recommended to facilitate rapid recognition and appropriate intervention by healthcare professionals or caregivers in the event that the individual is found unconscious. Fatalities associated with food-induced anaphylaxis frequently occur in situations in which affected individuals mistakenly believe they are not at risk. Evidence suggests that fatal outcomes often arise when individuals are unprepared to recognize and promptly manage severe reactions, highlighting the critical importance of education and preparedness.²¹

At present, no pharmacological agents have been shown to modify the long-term natural history of food allergy. Oral antihistamines may provide symptomatic relief for mild allergic manifestations, whereas systemic corticosteroids may be prescribed for severe acute reactions or persistent inflammatory symptoms. Patients with a history of significant or systemic reactions should receive thorough instruction in the timely administration of intramuscular epinephrine (adrenaline), which acts by supporting cardiovascular function and promoting bronchodilation during anaphylaxis. Emerging immunomodulatory approaches, including Oral Immunotherapy (OIT) and Sublingual Immunotherapy (SLIT), aim to induce desensitization through controlled allergen exposure. OIT involves the supervised ingestion of gradually increasing quantities of the allergen to promote immune tolerance, while SLIT entails the administration of allergen extracts sublingually to reduce immunologic sensitivity over time. Although these therapies show promise, their long-term efficacy and safety profiles continue to be evaluated.²⁴

IV. CONCLUSION

The prevalence of food allergies has been rising globally, affecting both children and adults. Food allergy can be a significant impact on one's daily life and can even affect the 'lifestyle' of an entire family. Understanding the definition, recognizing common allergens, the pathophysiology and employing effective treatment are essential for improving the quality of life for those affected by food allergies.

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