Food Allergies: Immune Mechanisms, Clinical Manifestations, Diagnosis, and Prevention

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Overview

Food allergies are defined as abnormal immune reactions to specific components in food, most commonly proteins. These reactions can range in severity from mild symptoms such as skin irritation and gastrointestinal upset to severe systemic manifestations like anaphylaxis. Symptoms typically emerge within minutes to a few hours following exposure and may include itching, swelling, vomiting, diarrhea, hives, difficulty breathing, or hypotension. Anaphylaxis, a potentially life-threatening condition, involves widespread immune activation and multi-organ involvement.

Food intolerances and foodborne illnesses, although often confused with allergies, are not immune-mediated and have distinct etiologies.

Common Allergenic Foods and Risk Factors

A limited number of foods are responsible for the majority of allergic reactions. These include milk, eggs, peanuts, tree nuts, soy, wheat, fish, and shellfish, commonly known as the "big eight". Sesame was later recognized as a major allergen in the U.S. under the FASTER Act of 2021 (Food Allergy Safety, Treatment, Education, and Research Act, 2021). Genetic predisposition, vitamin D deficiency, obesity, and reduced microbial exposure due to high hygiene levels have been identified as risk factors for allergy development.

Immunological Mechanisms

Most food allergies are IgE-mediated, where immunoglobulin E binds to specific food antigens and activates mast cells and basophils, leading to the release of histamine and other inflammatory mediators (Berin & Sampson, 2013). Non-IgE-mediated allergies also exist and typically cause delayed gastrointestinal or dermatological symptoms. IgE antibodies produced after initial sensitization bind to receptors on immune cells. Subsequent exposure to the allergen causes cross-linking of IgE on these cells, triggering degranulation and inflammatory response (Chinthrajah et al., 2016).

Clinical Manifestations

Symptoms vary from mild (rash, nasal congestion, gastrointestinal discomfort) to severe, such as respiratory distress, cyanosis, hypotension, or shock. Common symptoms include:

- Urticaria and angioedema
- Oral itching and swelling
- Nasal congestion or wheezing
- Nausea, vomiting, and diarrhea
- Dizziness and fainting

Anaphylaxis is particularly associated with peanut, tree nut, and shellfish allergies and is more likely in individuals with concurrent asthma.

Routes of Exposure and Sensitization

While oral ingestion is the primary exposure route, sensitization may also occur via dermal contact or inhalation. For example, exposure to airborne allergens in food processing environments or through topical products containing allergenic oils has been linked to increased allergy risk (Lack et al., 2003; Du Toit et al., 2015). Skin barrier dysfunction, especially in infants with eczema, plays a critical role in sensitization to allergens such as peanuts (Kelleher et al., 2016).

Cross-Contact and Occupational Hazards

Cross-contact refers to the unintended presence of allergens in non-allergenic foods due to shared preparation equipment or surfaces. Proper cleaning and food handling, alongside accurate allergen labeling, are essential to prevent accidental exposure (U.S. Food and Drug Administration [FDA], 2015).

Occupational allergy risks are notable in industries such as seafood processing and baking. For example, "baker's asthma" and respiratory reactions among seafood workers have been documented due to airborne protein exposure.

Diagnosis

Diagnosis is guided by clinical history, dietary elimination trials, and specific testing methods:

- **Skin prick testing** detects IgE-mediated allergies quickly and with reasonable sensitivity.
- **Serum-specific IgE testing** (e.g., RAST, CAP-RAST) quantifies allergen-specific IgE levels in blood (Hamilton, 2005).
- **Oral food challenges**, especially double-blind, placebo-controlled trials, are considered the gold standard for confirming food allergy (Sampson et al., 2014).

Patch testing is used to identify delayed-type hypersensitivity reactions affecting the skin.

Differential Diagnosis

Several non-allergic conditions can mimic food allergy symptoms:

- **Lactose intolerance** is a non-immune reaction due to lactase deficiency.
- **Celiac disease** is an autoimmune response to gluten, distinct from wheat allergy.
- **Irritable bowel syndrome (IBS)** and **hereditary angioedema** may also present with overlapping symptoms (Fasano & Catassi, 2012).

In Vivo Tests	
Elimination diet	This involves an eating plan that omits a food or group of foods believed to cause an adverse reaction. By removing certain foods for a period of time and then reintroducing them during a "challenge" period, it allows the identification of which foods are causing symptoms. The elimination of 6 foods, i.e., eggs, soy, cow's milk, wheat, seafood, and peanut/tree nuts, can be therapeutic and diagnostic in EoE.
Oral food challenge (OFC)	OFC is the gold standard for diagnosis of food allergy. It consists of administering the suspect food at established doses and observing the clinical response in a protected clinical setting.
Skin prick test (SPT)	Commercial extracts of allergen are inoculated subcutaneously to detect the presence of sIgE bound to mast cells.
Skin Prick by Prick (PbP)	PbP is similar to the SPT but is performed using fresh, cooked or raw food.
Atopy Patch Test (APT)	The suspect food is applied directly on the skin using special supports and removed after 48–72 h to study non-IgE (cell-mediated) or mixed IgE/cell-mediated responses.
In vitro Tests	
Total serum IgE (tIgE)	The total concentration of IgE in the blood is measured; this is useful for assessing the presence of an allergic background but does not identify specific triggers.
Radio allergoimmuno sorbent (RAST) detection of allergen-specific IgE (sIgEs)	Fluorescent enzyme-labeled antibody assay measures absolute sIgE levels. Values may correlate with the likelihood of clinical reaction for specific foods.
Component Resolved Diagnosis (CRD)	CRD is similar to RAST, but it utilizes purified native or recombinant allergens to detect sIgE antibodies against individual allergenic molecules.
Basophil Activation Test (BAT)	BAT measures by flow cytometry the expression of activation markers on the surface of basophils following the cross-linking of IgE bound to the high-affinity IgE receptor (FcεRI) by allergen or anti-IgE.

Pathophysiology

Food allergies involve type I hypersensitivity reactions in which allergenic proteins stimulate TH2 cell responses, leading to IL-4 mediated activation of B cells and IgE production (Muraro et al., 2014). These IgE molecules bind to mast cells and basophils. Upon re-exposure, allergen binding causes degranulation and release of mediators like histamine, resulting in allergic symptoms. A secondary late-phase response occurs in some cases, involving the infiltration of eosinophils, neutrophils, and other immune cells, leading to prolonged inflammation and tissue damage (Galli et al., 2008).

Prevention and Management

The primary strategy is avoidance of known allergens and preparedness to manage accidental exposure. Individuals should carry epinephrine auto-injectors and wear medical alert identification. Allergen-specific immunotherapy remains experimental in food allergy treatment. Recent guidelines support the early introduction of allergenic foods, such as peanuts and eggs, during infancy to prevent allergy development, especially in high-risk children. Breastfeeding for at least four months may also provide some protection against early allergic diseases.

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