

# Food Allergens and Anaphylaxis

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## Introduction

When one considers the very broad range of foods and food additives in the typical North American diet, it is astonishing that foods do not cause adverse reactions more often than they do. In point of fact, intolerances to foods and food additives are distinctly uncommon, and the food supply in North America is much safer than a generation ago (1). However, people often mistakenly attribute non-specific symptoms experienced to foods ingested and consequently have the perception that foods are responsible for many symptoms. These false perceptions are often reinforced by the media, practitioners of alternative or complimentary medicine and others. In spite of the fact that these false beliefs are not evidence-based, they often become axiomatic and difficult to deconstruct. This article will explore the range of adverse reactions to foods, including toxic, pharmacologic and immunologic food reactions. Characteristics of common food allergens will be discussed and manifestations, investigation and management of food allergies will be reviewed.

### Classification of adverse reactions to foods

Foods may cause adverse reactions in many different ways. In the broadest terms, these reactions may be thought of as either immunologic or non-immunologic. Non-immunologic reactions may be further subclassified as either toxic/pharmacologic or nontoxic/intolerance. Examples of toxic reactions to foods would include bacterial food poisoning (e.g. botulism, salmonella, staphylococcal exotoxins), heavy metal poisoning (e.g. mercury, lead), tetrodotoxin in blowfish and scombroid fish poisoning. Scombroid fish poisoning is a situation in which an enzyme in the flesh of the fish of the scombroidae family (e.g. tuna, mackerel, swordfish) is activated when the fish is not fresh. This enzyme, histidine decarboxylase, converts histidine to histamine. Ingestion of fish with high levels of histamine gives rise to a toxic reaction, which resembles manifestations of an allergic reaction to fish. The physiologic manifestations of food poisoning are a predictable outcome of the known actions of the specific toxins involved.

Many foods exert pharmacologic effects due to the chemical constituents of the specific foods. For example, alcohol causes intoxication because of its ability to intercalate into the cell membrane, causing changes in phospholipid packing density. Caffeine in coffee and tea has predictable effects on the cardiovascular and central nervous systems.

In contrast, nontoxic/intolerance-type reactions to foods are exemplified by lactase deficiency resulting in lactose intolerance, galactosemia, pancreatic insufficiency, gustatory rhinitis and gallbladder disease.

On the other hand, foods may give rise to manifestations by way of immunologic mechanisms. These may range from IgE-mediated (or immediate hypersensitivity) reactions to a wide spectrum of non-IgE mediated reactions. Examples of immediate hypersensitivity reactions include acute anaphylaxis, hives due to foods and oral allergy syndrome. The latter is a form of contact hypersensitivity to fresh fruits, vegetables and nuts as a result of cross-reactivity with allergens in tree, grass, and ragweed pollens.

Non-IgE mediated reactions to foods tend to be delayed, require higher levels of exposure and are generally not immediately life-threatening. Non-IgE mediated immunologic mechanisms are involved in the pathogenesis of milk-induced enterocolitis, protein-induced enteropathy, dermatitis herpetiformis, and celiac disease. Some allergic conditions caused by foods, such as atopic dermatitis, are caused by both IgE-mediated and non-IgE mediated reactions to foods.



## Food Allergens

With very few exceptions, food allergens are proteins rather than carbohydrate or fat molecules. Typically, allergenic proteins from foods are glycosylated. This is a metabolic process whereby a carbohydrate moiety is chemically bound to the food molecule. The resultant glycoprotein is highly resistant to degradation by heating or processing and to the digestive effects of gastric acid and digestive enzymes. Most food allergens, with the exception of fresh fruits and vegetables, are highly stable proteins of moderate molecular weight (between 10 – 70 kD). Because of the relative stability of most food allergens, allergenic portions of these proteins (peptides) will remain intact in spite of processing, storage, cooking and digestion. These intact food peptides are capable of triggering allergic reactions after passage into the bloodstream.

Fruit and vegetable protein allergens tend to be exceptions to the rule. These proteins are often quite labile and are rapidly degraded by heating or cooking as well as by digestive processes. For this reason, fresh fruits and raw vegetables will tend to trigger more severe reactions than their cooked counterparts. There are notable exceptions to this general rule.

Eight foods are responsible for the majority of food-related allergic reactions in North America. These are milk, egg, soy, wheat, peanut, tree nut, fish, and shellfish. All of these food allergies are typically acquired in childhood but only allergies to peanut, tree nut, fish and shellfish tend to persist into adult life. Most individuals are allergic to only a single food whereas only a minority of individuals are allergic to two or more foods. Peanut, tree nut and shellfish-induced reactions tend to be more severe and are responsible for the bulk of anaphylactic fatalities. Approximately 150 deaths per year are attributable to food-induced anaphylaxis (2). The major risk factors for fatal anaphylaxis to foods include a history of previous severe reactions, co-existent or underlying asthma, delayed administration of epinephrine during an acute reaction and a tendency to minimize or deny the potential severity of food allergy. The latter risk factor is especially problematic among teenagers.

### Clinical course of anaphylaxis

Most allergic reactions to foods will occur within 1 hour of ingestion of the food, but occasionally, onset of symptoms may be delayed by as much as 2 hours. In most individuals, the acute manifestations of an allergic reaction will subside either spontaneously or with treatment with no further recurrences. However, in 5% to 15% of instances, symptoms may recur between 2 to 8 hours after the initial symptoms. These recurrent symptoms are termed a biphasic reaction. The biphasic symptoms may be as severe as, or even more severe than, the initial acute phase.

Anaphylactic reactions, or multisystem allergic reactions, may typically involve the skin, respiratory tract, gastrointestinal tract, cardiovascular system, or genitourinary system in any combination. However, hives are present in approximately 85% of cases of anaphylaxis. Importantly, hives tend to be absent during the clinical course of anaphylaxis in the most severe cases, particularly during life-threatening reactions. IgE-mediated reactions exhibit a characteristic constellation of signs and symptoms (Table 1). In contrast, there is little evidence to implicate immunologic reactions as the cause of migraine headaches, behavioural or developmental disorders, arthritis, seizures, multiple sclerosis, and inflammatory bowel disease.

TABLE 1: Clinical Manifestations of Acute Anaphylactic Reactions

Organ System Involved	Manifestations
1. Skin	Itching, hives, flushing, swelling
2. Respiratory tract	
a. Upper respiratory tract	Itchy, watery eyes, runny or stuffy nose, sneezing
b. Upper airway	Throat constriction, difficulty swallowing, change in voice
c. Lower airway	Wheezing, cough, tightness in chest, shortness of breath
3. Cardiovascular system	Dizziness, lightheadedness, loss of consciousness, chest pain
4. Gastrointestinal system	Nausea, vomiting, crampy abdominal pain, diarrhea
5. Genitourinary system	Uterine cramps, miscarriage in pregnancy

The public at large will self-report a high prevalence of food allergy. In surveys of North American population, the self-reported prevalence of food allergy ranges from 20% to 25%. However, true food allergy, confirmed by double-blind placebo-controlled oral challenge, is present in 6% to 8% of children and 1% to 2% of adults. Eight foods, including milk, egg, soy, wheat, fish, shellfish, peanut and tree nut, account for over 90% of all food allergies in North America although more than 200 foods have been reported to cause allergic reactions. The actual prevalence of any given food allergy depends in large part upon the dietary habits of a given population. Cow's milk allergy is present in approximately 2.5% of infants and allergy to peanut and tree nuts is present in approximately 1.1% of the general North American population. Allergy to sesame seed is an emerging problem whereas allergy to pine nut, an uncommon food in North America, is still rare. While allergic reactions are often attributed to food preservatives or coloring agents, true allergies to food additives are rare (3).

Foods have been documented to cause between 30% to 50% of all anaphylactic reactions. Specific foods will also cause flares in atopic dermatitis (eczema) in 30% to 50% of children. In contrast, foods rarely contribute to worsening atopic dermatitis in adults. Food allergies have been implicated in about 20% of cases of acute urticaria, that is, hives lasting for hours to several days. However, foods rarely contribute to hives that recur daily for weeks or months. Food allergies manifest with asthmatic symptoms in 5% to 6% of food-allergic children but seldom manifest with nasal rhinorrhea or congestion. (4,5).

### Diagnosis: History and Physical Examination

Important elements on history which point to food allergy include characteristic symptoms, timing of a reaction with respect to food ingestion, and reproducibility of symptoms on repeated challenge. Often the cause can be ascertained on the basis of a detailed dietary history, particularly if a symptom diary has been kept in conjunction with details of ingested foods. However, hidden ingredients as a cause of reactions may not be evident from a food diary.

Physical examination will seldom contribute very much to the evaluation of food allergies although other allergic disorders such as asthma and atopic dermatitis are known to contribute to the severity of allergic reactions to foods. There are some clinical conditions that can mimic anaphylaxis, such as systemic mastocytosis. Systemic mastocytosis is a condition in which the bone marrow produces an abnormally large number of mast cells, the cells containing chemical mediators of anaphylaxis. Episodic release of these mediators produces typical manifestations of anaphylaxis. There may be typical physical findings of systemic mastocytosis on examination that may clarify the diagnosis.

## Laboratory Investigations

With IgE-mediated immunologic reactions to foods, prick skin tests will typically be positive to the suspect food (Figure 1). Alternatively, blood tests (known as CAP-RAST tests) for food-specific IgE antibodies may be utilized either in place of prick skin testing or for confirmation of skin test results. In addition, the levels of food-specific IgE may yield additional information on the risk of anaphylaxis in patients.

FIGURE 1:



Where the history is more compatible with a non-IgE mediated mechanism, biopsy of the gut or skin may provide valuable information.

Positive prick skin tests or blood tests for specific IgE indicate the presence of IgE antibody but do not make a diagnosis of clinical allergy to a specific food. The positive skin test or blood test must be interpreted in the context of evidence for clinical reactions since false positive tests are frequently encountered with foods. In contrast, negative prick skin tests and negative blood tests for specific IgE are very accurate at ruling out food allergy. A negative prick test or blood test will reliably exclude immediate hypersensitivity to food in over 95% of cases (6).

Numerous tests have been devised by practitioners of alternative medicine by which to diagnose food allergy. These include Vega testing, IgG4 subclass analysis, provocation/neutralization testing, applied kinesiology, hair analysis and cytotoxic testing. These methods have been subjected to rigorous scientific analysis and have been shown to be useless in some instances and potentially harmful in others.

## Oligoantigenic Diets and Food Challenges

When history, physical examination and diagnostic testing point to a specific food as a potential cause of reactions, elimination of that food from the diet should bring about resolution of symptoms. Reintroduction of the food will lead to recurrent symptoms. However, when symptoms are severe, challenge with a suspect food is undertaken in a supervised medical setting with resuscitation facilities at hand. Oral challenge may be conducted in a number of different ways. The challenge may be open, such that both the physician and patient know that the suspect food is being administered. Alternatively, the challenge may be single blind. The physician may administer either the suspect food or a placebo to the patient. The patient will be unaware of the order of administration of either the food or placebo and will be asked to report symptoms. This is more reliable than an open challenge and removes an element of subjectivity on the part of the patient. The most reliable approach, the “gold standard,” is the double-blind, placebo-controlled food challenge. With this approach, neither the supervising physician nor the patient knows the order of administration of placebo or suspect food, and this minimizes the element of subjectivity.

## Treatment: Long-term Dietary Elimination

Currently, there are no means by which to “desensitize” food-allergic individuals. The sole effective approach to treatment is elimination of the causative food allergen from the diet. This requires considerable education of the patient, family members, and caregivers. In numerous studies of accidental anaphylaxis and particularly fatal anaphylaxis, common themes have arisen. One problem has been failure of the patient to recognize terminology on labels indicating the presence of a food allergen. For example, milk protein may be denoted as artificial butter flavour, casein, lactalbumin, nougat, pudding, whey, or yogurt on labels. A milk-allergic individual may not appreciate that all of these ingredients represent milk protein which is highly allergenic to that individual.

Foods prepared in restaurants, bakeries and other establishments in which ingredients are not listed represent yet another challenge to the food allergic individual. Certain ingredients may be hidden in other foods. Peanut is often used in sauces to flavour or thicken the sauce. It has been used in chili and pasta sauce and has triggered reactions in unsuspecting individuals. Similarly, peanut butter is often used to “glue” the ends of egg rolls and may be another source of exposure.

Cross-contamination of foods, either in a manufacturing facility, in the sale of bulk foods in retail outlets or in restaurants during preparation of meals may pose a hazard to allergic individuals. Oriental restaurants are often problematic for peanut or shellfish-allergic individuals. Buffets often pose a hazard because of the high risk of cross-contamination.

While large manufacturers in North America adhere to good manufacturing practices and generally provide reliable and accurate information on labels, this is not always the case with imported foods. We have found that chocolates imported from Eastern Europe frequently contain undeclared peanut protein in high levels, which may trigger reactions in unsuspecting individuals. Occasionally, though, undeclared allergens make their way into manufactured foods when suppliers of ingredients are changed or manufacturing processes are altered. These foods are subject to recalls initiated by the Canadian Food Inspection Agency. Information on product recalls may be obtained from the CFIA website or from Anaphylaxis Canada. The latter organization will issue e-mail alerts to registered members.

## Summary

Individuals with suspect food allergies must undergo appropriate evaluation in order to identify the causative food allergen by means of history, physical examination, and laboratory diagnostic testing. An appropriate elimination diet must be prescribed by a doctor and devised by a registered dietician with emphasis on education to minimize the likelihood of exposure to food allergens. An action plan for management of acute reactions should be developed in conjunction with family members and caregivers. A rigorous approach to management of food allergies should minimize the likelihood of reactions resulting from accidental exposure, and a rapid and efficient response to an acute reaction will lessen the ensuing potential for morbidity and mortality.

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Health Canada has identified a list of foods and ingredients that can cause adverse reactions in hypersensitive individuals. This list includes milk, eggs, fish, shellfish, soy, wheat, peanuts, tree nuts (e.g. almonds, walnuts, pecans), sesame seeds, and sulphites. Although this list represents the foods causing the most common and serious reactions, a wide variety of other foods have been reported to cause adverse reactions in certain individuals.

Most food manufacturers are aware of the seriousness of food allergies and follow Good Manufacturing Practices, an industry standard, and have policies and procedures in place with respect to preventing allergen cross-contamination of those allergens. Manufacturers must ensure they declare the presence of these food allergens on the ingredient list. Although, currently there is no mandatory allergen labelling regulations in place, the responsibility is on the manufacturer to identify allergens in products. Consumers with food allergies are advised to contact the manufacturer of a particular product to enquire about the ingredients used.

Based on the guiding principles of the Good Manufacturing Practices, new food allergen labelling

regulations are being developed that will require all food manufacturers to label commonly known food allergens in a consistent manner.

Kellogg Canada has a long history of maintaining a comprehensive allergy control and awareness program to deal with food allergens. As a dietitian when looking at a Kellogg label you will always know if the food contains one of the major food allergens. You will find a bolded precautionary labelling statement at the end of the ingredient list on products that may inadvertently contain one of the major food allergens. Kellogg Canada uses two types of precautionary labelling statements beginning with either "Contains traces" or "May contain" and alerts the consumer to the risk of cross contamination due to manufacturing or farming practices.

Kellogg Canada is committed to providing accurate and consistent information about our products to food allergic consumers. We also work closely with scientific organizations and allergy associations to ensure that our practices are consistent with scientific developments and meet consumer needs.

The following are a list of some recognized allergy and anaphylaxis resources. They provide a wealth of allergen awareness information for consumers and health professionals alike.

The Canadian Food Inspection Agency (CFIA) Food Recalls/ Allergy Alerts are available on their website or you can sign up to receive them by email.

Visit: [www.inspection.gc.ca](http://www.inspection.gc.ca), click on your language preference, then click on Food Recalls / Allergy Alerts or Rappels des aliments / Alertes à l'allergie.



Fondée en 1990, Association québécoise des allergies alimentaires a pour mission d'offrir du support et de l'information, de promouvoir l'éducation et la prévention, ainsi que d'encourager la recherche sur les allergies alimentaires et l'anaphylaxie.

La population désireuse de se renseigner peut composer le (514) 990-2575 ou consulter le site Internet [www.aqaa.qc.ca](http://www.aqaa.qc.ca).



Anaphylaxis Canada is a national registered charity dedicated to improving awareness and understanding of life-threatening allergies. Anaphylaxis Canada provides information and support to people living with anaphylaxis and conducts and supports research related to anaphylaxis. Anaphylaxis Canada also works with industry, government, the medical community, educators, and others to develop programs to protect people at risk for anaphylaxis.

For more information, or to join the Anaphylaxis Canada Registry, visit [www.anaphylaxis.ca](http://www.anaphylaxis.ca) or call 1-866-785-5660 (toll-free) or 416 785-5666 (local).

Anaphylaxis Canada

Helping people live with deadly allergies

Founded in 1964, the Allergy/Asthma Information Association is a registered Canadian charity dedicated to helping allergic individuals and their families cope with everything from the sniffles and sneezes of hayfever to life-threatening food allergies and asthma.

For more information, please call 1-888-250-2298 or 1-866-694-0679 (français) or visit the website at [www.aaia.ca](http://www.aaia.ca)



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