

# Food allergy

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A **food allergy** is an abnormal immune response to food. The signs and symptoms may range from mild to severe. They may include itchiness, swelling of the tongue, vomiting, diarrhea, hives, trouble breathing, or low blood pressure. This typically occurs within minutes to several hours of exposure. When the symptoms are severe, it is known as anaphylaxis. Food intolerance and food poisoning are separate conditions.<sup>[1]</sup>

Common foods involved include cow's milk, peanuts, eggs, shellfish, tree nuts, wheat, rice, and fruit.<sup>[1][2][3]</sup> The common allergies in a region vary depending on the country.<sup>[1]</sup> Risk factors include a family history of allergies, vitamin D deficiency, obesity, and high levels of cleanliness.<sup>[1][2]</sup> Allergies occur when immunoglobulin E (IgE), part of the body's immune system, binds to food molecules.<sup>[1]</sup> A protein in the food is usually the problem.<sup>[2]</sup> This triggers the release of inflammatory chemicals such as histamine.<sup>[1]</sup> Diagnosis is usually based on a medical history, elimination diet, skin prick test, blood tests for food-specific IgE antibodies, or oral food challenge.<sup>[1][2]</sup>

Early exposure to potential allergens may be protective.<sup>[2][4]</sup> Management primarily involves avoiding the food in question and having a plan if exposure occurs.<sup>[2]</sup> This plan may include giving adrenaline (epinephrine) and wearing medical alert jewelry.<sup>[1]</sup> The benefits of allergen immunotherapy for food allergies is unclear, thus is not recommended as of 2015.<sup>[5]</sup> Some types of food allergies among children resolve with age, including that to milk, eggs, and soy; while others such as to nuts and shellfish typically do not.<sup>[2]</sup>

In the developed world, about 4% to 8% of people have at least one food allergy.<sup>[1][2]</sup> They are more common in children than adults and appear to be increasing in frequency. Male children appear to be more commonly affected than females.<sup>[2]</sup> Some allergies more commonly develop early in life, while others typically develop in later life.<sup>[1]</sup> In developed countries, a large proportion of people believe they have food allergies when they actually do not have them.<sup>[6][7][8]</sup>

**Food allergy**



Hives on the back are a common allergy symptom.

**Classification and external resources**

<b>Specialty</b>	emergency medicine
<b>ICD-10</b>	T78.0 ( <a href="http://apps.who.int/classifications/icd10/browse/2016/en#/T78.0">http://apps.who.int/classifications/icd10/browse/2016/en#/T78.0</a> )
<b>ICD-9-CM</b>	V15.01 ( <a href="http://www.icd9data.com/getICD9Code.aspx?icd9=V15.01">http://www.icd9data.com/getICD9Code.aspx?icd9=V15.01</a> )-V15.05 ( <a href="http://www.icd9data.com/getICD9Code.aspx?icd9=V15.05">http://www.icd9data.com/getICD9Code.aspx?icd9=V15.05</a> )
<b>OMIM</b>	147050 ( <a href="https://omim.org/entry/147050">https://omim.org/entry/147050</a> )
<b>MedlinePlus</b>	000817 ( <a href="https://medlineplus.gov/ency/article/000817.htm">https://medlineplus.gov/ency/article/000817.htm</a> )
<b>eMedicine</b>	med/806 ( <a href="http://www.emedicine.com/med/topic806.htm">http://www.emedicine.com/med/topic806.htm</a> )
<b>MeSH</b>	D005512 ( <a href="https://www.nlm.nih.gov/cgi/mesh/2016/MB_cgi?field=uid&amp;term=D005512">https://www.nlm.nih.gov/cgi/mesh/2016/MB_cgi?field=uid&amp;term=D005512</a> )

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## Signs and symptoms

Food allergies usually have a fast onset (from seconds to one hour) and may include:<sup>[9]</sup>

- Rash
- Hives<sup>[9]</sup>
- Itching of mouth, lips, tongue, throat, eyes, skin, or other areas<sup>[9]</sup>
- Swelling (angioedema) of lips, tongue, eyelids, or the whole face<sup>[9]</sup>
- Difficulty swallowing<sup>[9]</sup>
- Runny or congested nose<sup>[9]</sup>
- Hoarse voice<sup>[9]</sup>
- Wheezing and/or shortness of breath<sup>[9]</sup>
- Diarrhea, abdominal pain, and/or stomach cramps<sup>[9]</sup>
- Lightheadedness<sup>[9]</sup>
- Fainting<sup>[9]</sup>
- Nausea<sup>[9]</sup>
- Vomiting<sup>[9]</sup>

In some cases, however, onset of symptoms may be delayed for hours.<sup>[9]</sup>

Symptoms of allergies vary from person to person. The amount of food needed to trigger a reaction also varies from person to person.

Serious danger regarding allergies can begin when the respiratory tract or blood circulation is affected. The former can be indicated through wheezing and cyanosis. Poor blood circulation leads to a weak pulse, pale skin and fainting.<sup>[10]</sup>

A severe case of an allergic reaction, caused by symptoms affecting the respiratory tract and blood circulation, is called anaphylaxis. When symptoms are related to a drop in blood pressure, the person is said to be in anaphylactic shock. Anaphylaxis occurs when IgE antibodies are involved, and areas of the body that are not in direct contact with the food become affected and show symptoms.<sup>[11]</sup> This occurs because no nutrients are circulated throughout the body, causing the widening of blood vessels. This vasodilation causes blood pressure to decrease, which leads to the loss of consciousness. Those with asthma or an allergy to peanuts, tree nuts, or seafood are at greater risk for anaphylaxis.<sup>[12]</sup>

## Cause

Although sensitivity levels vary by country, the most common food allergies are allergies to milk, eggs, peanuts, tree nuts, seafood, shellfish, soy, and wheat.<sup>[13]</sup> These are often referred to as "the big eight".<sup>[14]</sup> Allergies to seeds — especially sesame — seem to be increasing in many countries.<sup>[15]</sup> An example an allergy more common to a particular region is that to rice in East Asia where it forms a large part of the diet.<sup>[16]</sup>

One of the most common food allergies is a sensitivity to peanuts, a member of the bean family. Peanut allergies may be severe, but children with peanut allergies sometimes outgrow them.<sup>[17]</sup> Tree nuts, including cashews, Brazil nuts, hazelnuts, macadamia nuts, pecans, pistachios, pine nuts, coconuts, and walnuts, are also common allergens. Sufferers may be sensitive to one particular tree nut or to many different ones.<sup>[18]</sup> Also, seeds, including sesame seeds and poppy seeds, contain oils where protein is present, which may elicit an allergic reaction.<sup>[18]</sup>

Egg allergies affect about one in 50 children but are frequently outgrown by children when they reach age five.<sup>[19]</sup> Typically, the sensitivity is to proteins in the white, rather than the yolk.<sup>[18]</sup>

Milk from cows, goats, or sheep is another common food allergen, and many sufferers are also unable to tolerate dairy products such as cheese. A small portion of children with a milk allergy, roughly 10%, have a reaction to beef. Beef contains a small amount of protein that is also present in cow's milk.<sup>[20]</sup>

Seafood is one of the most common sources of food allergens; people may be allergic to proteins found in fish, crustaceans, or shellfish.<sup>[21]</sup>

Other foods containing allergenic proteins include soy, wheat, fruits, vegetables, maize, spices, synthetic and natural colors, and chemical additives.

Balsam of Peru, which is in various foods, is in the "top five" allergens most commonly causing patch test reactions in people referred to dermatology clinics.<sup>[22][23][24]</sup>

## Sensitization

An Institute of Medicine report says that food proteins contained in vaccines, such as gelatin, milk, or egg can cause sensitization (development of allergy) in vaccine recipients, to those food items.<sup>[25]</sup>

## Atopy

Food allergies develop more easily in people with the atopic syndrome, a very common combination of diseases: allergic rhinitis and conjunctivitis, eczema, and asthma.<sup>[26]</sup> The syndrome has a strong inherited component; a family history of allergic diseases can be indicative of the atopic syndrome.

## Cross-reactivity

Some children who are allergic to cow's milk protein also show a cross-sensitivity to soy-based products.<sup>[27]</sup> Some infant formulas have their milk and soy proteins hydrolyzed, so when taken by infants, their immune systems do not recognize the allergen and they can safely consume the product. Hypoallergenic infant formulas can be based on proteins partially predigested to a less antigenic form. Other formulas, based on free amino acids, are the least antigenic and provide complete nutritional support in severe forms of milk allergy.

People with latex allergy often also develop allergies to bananas, kiwifruit, avocados, and some other foods.<sup>[28]</sup>

## Pathophysiology

Conditions caused by food allergies are classified into three groups according to the mechanism of the allergic response:<sup>[29]</sup>

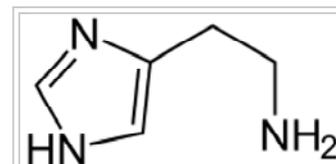
1. IgE-mediated (classic) – the most common type, occurs shortly after eating and may involve anaphylaxis.
2. Non-IgE mediated – characterized by an immune response not involving immunoglobulin E; may occur some hours after eating, complicating diagnosis
3. IgE and/or non-IgE-mediated – a hybrid of the above two types

Allergic reactions are hyperactive responses of the immune system to generally innocuous substances. When immune cells encounter the allergenic protein, IgE antibodies are produced; this is similar to the immune system's reaction to foreign pathogens. The IgE antibodies identify the allergenic proteins as harmful and initiate the allergic reaction. The harmful proteins are those that do not break down due to the strong bonds of the protein. IgE antibodies bind to a receptor on the surface of the protein, creating a tag, just as a virus or parasite becomes tagged. Why some proteins do not denature and subsequently trigger allergic reactions and hypersensitivity while others do is not entirely clear.<sup>[30]</sup>

Hypersensitivities are categorized according to the parts of the immune system that are attacked and the amount of time it takes for the response to occur. The four types of hypersensitivity reaction are: type 1, immediate IgE-mediated; type 2, cytotoxic; type 3, immune complex-mediated; and type 4, delayed cell-mediated.<sup>[31]</sup> The pathophysiology of allergic responses can be divided into two phases. The first is an acute response that occurs immediately after exposure to an allergen. This phase can either subside or progress into a "late-phase reaction" which can substantially prolong the symptoms of a response, and result in tissue damage.

Many food allergies are caused by hypersensitivities to particular proteins in different foods. Proteins have unique properties that allow them to become allergens, such as stabilizing forces in their tertiary and quaternary structures which prevent degradation during digestion. Many theoretically allergenic proteins cannot survive the destructive environment of the digestive tract, thus do not trigger hypersensitive reactions.

<sup>[32]</sup>



A histamine, the structure shown, causes a person to feel itchy during an allergic reaction. A common medication to stop this is an antihistamine, which fights the histamines in the person's system.

## Acute response

In the early stages of allergy, a type I hypersensitivity reaction against an allergen, encountered for the first time, causes a response in a type of immune cell called a  $T_H2$  lymphocyte, which belongs to a subset of T cells that produce a cytokine called interleukin-4 (IL-4). These  $T_H2$  cells interact with other lymphocytes called B cells, whose role is the production of antibodies. Coupled with signals provided by IL-4, this interaction stimulates the B cell to begin production of a large amount of a particular type of antibody known as IgE. Secreted IgE circulates in the blood and binds to an IgE-specific receptor (a kind of Fc receptor called FcεRI) on the surface of other kinds of immune cells called mast cells and basophils, which are both involved in the acute inflammatory response. The IgE-coated cells, at this stage, are sensitized to the allergen.<sup>[33]</sup>

If later exposure to the same allergen occurs, the allergen can bind to the IgE molecules held on the surface of the mast cells or basophils. Cross-linking of the IgE and Fc receptors occurs when more than one IgE-receptor complex interacts with the same allergenic molecule, and activates the sensitized cell. Activated mast cells and basophils undergo a process called degranulation, during which they release histamine and other inflammatory chemical mediators (cytokines, interleukins, leukotrienes, and prostaglandins) from their granules into the surrounding tissue causing several systemic effects, such as vasodilation, mucous secretion, nerve stimulation, and smooth-muscle contraction. This results in rhinorrhea, itchiness, dyspnea, and anaphylaxis. Depending on the individual, the allergen, and the mode of introduction, the symptoms can be system-wide (classical anaphylaxis), or localized to particular body systems; asthma is localized to the respiratory system and eczema is localized to the dermis.<sup>[33]</sup>

## Late-phase response

After the chemical mediators of the acute response subside, late-phase responses can often occur due to the migration of other leukocytes such as neutrophils, lymphocytes, eosinophils, and macrophages to the initial site. The reaction is usually seen 2–24 hours after the original reaction.<sup>[34]</sup> Cytokines from mast cells may also play a role in the persistence of long-term effects. Late-phase responses seen in asthma are slightly different from those seen in other allergic responses, although they are still caused by release of mediators from eosinophils, and are still dependent on activity of  $T_H2$  cells.<sup>[35]</sup>

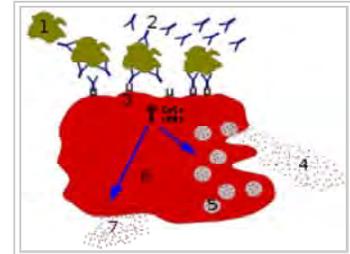
## Diagnosis

Diagnosis is usually based on a medical history, elimination diet, skin prick test, blood tests for food-specific IgE antibodies, or oral food challenge.<sup>[1][2]</sup>

- For skin-prick tests, a tiny board with protruding needles is used. The allergens are placed either on the board or directly on the skin. The board is then placed on the skin, to puncture the skin and for the allergens to enter the body. If a hive appears, the person is considered positive for the allergy. This test only works for IgE antibodies. Allergic reactions caused by other antibodies cannot be detected through skin-prick tests.<sup>[36]</sup>

Skin-prick testing is easy to do and results are available in minutes. Different allergists may use different devices for testing. Some use a "bifurcated needle", which looks like a fork with two prongs. Others use a "multitest", which may look like a small board with several pins sticking out of it. In these tests, a tiny amount of the suspected allergen is put onto the skin or into a testing device, and the device is placed on the skin to prick, or break through, the top layer of skin. This puts a small amount of the allergen under the skin. A hive will form at any spot where the person is allergic. This test generally yields a positive or negative result. It is good for quickly learning if a person is allergic to a particular food or not, because it detects IgE. Skin tests cannot predict if a reaction would occur or what kind of reaction might occur if a person ingests that particular allergen. They can, however, confirm an allergy in light of a patient's history of reactions to a particular food. Non-IgE-mediated allergies cannot be detected by this method.

- Patch testing is used to determine if a specific substance causes allergic inflammation of the skin. It tests for delayed food reactions.<sup>[37][38][39]</sup>
- Blood testing is another way to test for allergies; however, it poses the same disadvantage and only detects IgE allergens and does not work for every possible allergen. Radioallergosorbent testing (RAST) is used to detect IgE antibodies present to a certain allergen. The score taken from the RAST is compared to predictive values, taken from a specific type of RAST. If the score is higher than the predictive values, a great chance the allergy is present in the person exists. One advantage of this test is that it can test many allergens at one time.<sup>[40]</sup>



Degranulation process in allergy.

- antigen
- IgE antibody
- FcεRI receptor
- preformed mediators (histamine, proteases, chemokines, heparin)
- granules
- mast cell
- newly formed mediators (prostaglandins, leukotrienes, thromboxanes, PAF)



Skin testing on the arm is a common way for detecting an allergy, but it is not as effective as other tests.



Patch test

A CAP-RAST has greater specificity than RAST; it can show the amount of IgE present to each allergen.<sup>[41]</sup> Researchers have been able to determine "predictive values" for certain foods, which can be compared to the RAST results. If a person's RAST score is higher than the predictive value for that food, over a 95% chance exists that patients will have an allergic reaction (limited to rash and anaphylaxis reactions) if they ingest that food. Currently, predictive values are available for milk, egg, peanut, fish, soy, and wheat.<sup>[42][43][44]</sup> Blood tests allow for hundreds of allergens to be screened from a single sample, and cover food allergies as well as inhalants. However, non-IgE-mediated allergies cannot be detected by this method. Other widely promoted tests such as the antigen leukocyte cellular antibody test and the food allergy profile are considered unproven methods, the use of which is not advised.<sup>[45]</sup>

- Food challenges test for allergens other than those caused by IgE allergens. The allergen is given to the person in the form of a pill, so the person can ingest the allergen directly. The person is watched for signs and symptoms. The problem with food challenges is that they must be performed in the hospital under careful watch, due to the possibility of anaphylaxis.<sup>[46]</sup>

Food challenges, especially double-blind, placebo-controlled food challenges, are the gold standard for diagnosis of food allergies, including most non-IgE-mediated reactions. Blind food challenges involve packaging the suspected allergen into a capsule, giving it to the patient, and observing the patient for signs or symptoms of an allergic reaction.

The best method for diagnosing food allergy is to be assessed by an allergist. The allergist will review the patient's history and the symptoms or reactions that have been noted after food ingestion. If the allergist feels the symptoms or reactions are consistent with food allergy, he/she will perform allergy tests. Additional diagnostic tools for evaluation of eosinophilic or non-IgE mediated reactions include endoscopy, colonoscopy, and biopsy.

## Differential diagnosis

Important differential diagnoses are:

- Lactose intolerance generally develops later in life, but can present in young patients in severe cases. It is due to an enzyme deficiency (lactase) and not allergy, and occurs in many non-Western people.
- Celiac disease is an autoimmune disorder triggered by gluten proteins such as gliadin (present in wheat, rye, and barley). It is a non-IgE-mediated food allergy by definition.
- Irritable bowel syndrome
- C1 Esterase inhibitor deficiency (hereditary angioedema), a rare disease, generally causes attacks of angioedema, but can present solely with abdominal pain and occasional diarrhea.

## Prevention

Breastfeeding for more than four months may prevent atopic dermatitis, cow's milk allergy, and wheezing in early childhood.<sup>[47]</sup> Early exposure to potential allergens may be protective.<sup>[2]</sup> Specifically, early exposure to eggs and peanuts reduces the risk of allergies to these.<sup>[4]</sup>

To avoid an allergic reaction, a strict diet can be followed. It is difficult to determine the amount of allergenic food required to elicit a reaction, so complete avoidance should be attempted. In some cases, hypersensitive reactions can be triggered by exposures to allergens through skin contact, inhalation, kissing, participation in sports, blood transfusions, cosmetics, and alcohol.<sup>[48]</sup>

## Treatment

The mainstay of treatment for food allergy is total avoidance of the foods identified as allergens. An allergen can enter the body by consuming a food containing the allergen, and can also be ingested by touching any surfaces that may have come into contact with the allergen, then touching the eyes or nose. For people who are extremely sensitive, avoidance includes avoiding touching or inhaling the problematic food.

If the food is accidentally ingested and a systemic reaction (anaphylaxis) occurs, then epinephrine should be used. A second dose of epinephrine may be required for severe reactions. The person should then be transported to the emergency room, where additional treatment can be given. Other treatments include antihistamines and steroids.<sup>[49]</sup>

## Epinephrine

Epinephrine is another name for the hormone adrenaline, which is produced naturally in the body. An epinephrine injection is the first-line treatment for severe allergic reactions (anaphylaxis). If administered in a timely manner, epinephrine can reverse its effects.

Epinephrine relieves airway swelling and obstruction, and improves blood circulation; blood vessels are tightened and heart rate is increased, improving circulation to body organs. Epinephrine is available by prescription in an autoinjector.<sup>[50]</sup>

## Antihistamines

Antihistamines can alleviate some of the milder symptoms of an allergic reaction, but do not treat all symptoms of anaphylaxis.<sup>[51]</sup> Antihistamines block the action of histamine, which causes blood vessels to dilate and become leaky to plasma proteins. Histamine also causes itchiness by acting on sensory nerve terminals. The most common antihistamine given for food allergies is diphenhydramine.

## Steroids

Glucocorticoid steroids are used to calm down the immune system cells that are attacked by the chemicals released during an allergic reaction. This treatment in the form of a nasal spray should not be used to treat anaphylaxis, for it only relieves symptoms in the area in which the steroid is in contact. Another reason steroids should not be used is the delay in reducing inflammation. Steroids can also be taken orally or through injection, by which every part of the body can be reached and treated, but a long time is usually needed for these to take effect.<sup>[52]</sup>

## Desensitization

The benefits of allergen immunotherapy for food allergies is unclear, thus is not recommended as of 2015.<sup>[5]</sup> A number of desensitization techniques are being studied, though.<sup>[53]</sup>

## Epidemiology

The most common food allergens account for about 90% of all allergic reactions;<sup>[54]</sup> in adults they include shellfish, peanuts, tree nuts, fish, and egg.<sup>[55]</sup> In children, they include milk, eggs, peanuts, and tree nuts.<sup>[55]</sup> Six to 8% of children under the age of three have food allergies and nearly 4% of adults have food allergies.<sup>[55]</sup>

For reasons not entirely understood, the diagnosis of food allergies has apparently become more common in Western nations recently.<sup>[56]</sup> In the United States, food allergy affects as many as 5% of infants less than three years of age<sup>[57]</sup> and 3% to 4% of adults.<sup>[58]</sup> A similar prevalence is found in Canada.<sup>[59]</sup>

About 75% of children who have allergies to milk protein are able to tolerate baked-in milk products, i.e., muffins, cookies, cake, and hydrolyzed formulas.<sup>[60]</sup>

About 50% of children with allergies to milk, egg, soy, peanuts, tree nuts, and wheat will outgrow their allergy by the age of 6. Those who are still allergic by the age of 12 or so have less than an 8% chance of outgrowing the allergy.<sup>[61]</sup>

Peanut and tree nut allergies are less likely to be outgrown, although evidence now shows<sup>[62]</sup> that about 20% of those with peanut allergies and 9% of those with tree nut allergies will outgrow them.<sup>[63]</sup>

In Central Europe, celery allergy is more common. In Japan, allergy to buckwheat flour, used for soba noodles, is more common.

Meat allergy is extremely rare in the general population, but a geographic cluster of people allergic to meat has been observed in Sydney, Australia.<sup>[64]</sup> There appears to be a possible association between localised reaction to tick bite and the development of meat allergy.

Corn allergy may also be prevalent in many populations, although it may be difficult to recognize in areas such as the United States and Canada where corn derivatives are common in the food supply.<sup>[65]</sup> <sup>[66]</sup>

## United States

In the United States, an estimated 12 million people have food allergies.<sup>[67]</sup> Food allergies cause roughly 30,000 emergency room visits and 100 to 200 deaths per year<sup>[68]</sup> and the prevalence is rising.<sup>[56]</sup> Food allergy affects as many as 5% of infants less than three years of age<sup>[57]</sup> and 3% to 4% of adults.<sup>[58]</sup>

## Society and culture



Epinephrine autoinjectors are portable single-dose epinephrine-dispensing devices used to treat anaphylaxis.

In response to the risk that certain foods pose to those with food allergies, some countries have responded by instituting labeling laws that require food products to clearly inform consumers if their products contain major allergens or byproducts of major allergens. Some countries also require companies to warn customers when food has been prepared around certain allergens that have been known to cause severe reactions.

From 13 December 2014, new legislation – the EU Food Information for Consumers Regulation 1169/2011 – requires food businesses to provide allergy information on food sold unpackaged, for example, in catering outlets, deli counters, bakeries and sandwich bars.<sup>[69]</sup>

## Law

Under the Food Allergen Labeling and Consumer Protection Act of 2004 (Public Law 108-282), companies are required to disclose on the label whether the product contains a major food allergen in clear, plain language. The allergens have to clearly be called out in the ingredient statement. Most companies list allergens in a statement separate from the ingredient statement.<sup>[70]</sup>

In 2009, Governor Deval Patrick signed into Massachusetts law the Act Relative to Food Allergy Awareness in Restaurants. The allergy awareness act requires food protection managers to view a video about food allergens, a poster identifying the eight most common food allergens, and information about identifying and responding to food allergies posted for food service staff, and customers must be notified of their obligation to inform staff about any food allergies.<sup>[71]</sup>

On 4 January 2011, President Barack Obama signed into federal law the Food Safety and Modernization Act of 2010 (S510/HR2751, 111th Congress). Section 112 of this Act establishes voluntary food allergy and anaphylaxis management guidelines for public kindergartens and elementary and secondary schools.

## Research

Areas of research include anti-IgE antibody (omalizumab) and specific oral tolerance induction (SOTI), which have shown some promise for treatment of certain food allergies.

## See also

- List of food allergies
- SEICAP

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## External links

- Food Allergy  
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*Merck Manual*
- "Food Allergies and Intolerances Resource List for Consumers" (PDF). Food and Nutrition Information Center, National Agricultural Library. December 2010. – a collection of resources on the topic of food allergies and intolerances

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