Food Allergies:
A GP's Guide

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Langdon's Problem

- 15-month-old Langdon is brought to your office by his parents.
- Four hours after eating a new baby food he developed severe vomiting, pain and lethargy.
- He is pale, lethargic and dehydrated.
- Langdon is admitted to the hospital and he passes a small amount of blood with a loose stool.
- The next morning after re-hydration, Langdon appears well.

Could this be a food allergy? How should you proceed?

For the answers to these questions, go to page 82.

Table 1

Adverse reaction to food

Non-immune adverse reaction to food

- Chemical/pharmacologic agents (*e.g.,* caffeine, monosodium glutamate)
- Physiologic factors (*e.g.,* lactose intolerance, irritable bowel)
- Psychogenic aversion (*e.g.,* eating disorder)

Immune adverse reaction to food

- IgE mediated food allergy
- Non-IgE mediated food allergy
- Celiac disease (gluten sensitive enteropathy)

Food allergies are most common in infancy and early childhood, affecting up to six per cent to eight per cent of children. An allergy to cow's milk is the most common, with a prevalence of three per cent to five percent. Food allergies are increasing in prevalence and severity, with the number of peanut allergies having doubled in the past 15 years. Furthermore, it is estimated that food allergies now affect two per cent of adults. Celiac disease now affects one per cent of the population. Food allergies present a diagnostic challenge (Table 1) because they cause wide-ranging symptoms that mimic other diseases (*e.g.,* food poisoning, anatomic abnormality, inflammatory bowel disease) and non-allergic food intolerance (*e.g.,* lactose intolerance).

IgE food allergies

An IgE immediate food allergy (Table 2) is caused by the release of mast cell mediators after two food specific IgE antibodies are cross- linked. Symptoms include:

- urticaria,
- respiratory difficulties,
- anaphylaxis and if ingested,
- mostly upper gastrointestinal (GI) symptoms (pain and vomiting).

Studies indicate that young children with severe atopic dermatitis often have co-existing food allergies that exacerbates the skin condition and leads to GI symptoms.

Because reactions occur early after ingestion (usually within minutes), diagnosis is often straightforward. However, reactions that occur after the ingestion of a variety of foods, cross-contaminated foods during preparation, or foods that have been unusually exposed, may be more difficult to diagnose.

A good history, with supporting evidence of IgE to the offending food (*i.e.,* skin-prick or serum IgE test which correlate well with one another) is diagnostic. However, in the absence of a history of reaction, skin prick tests are only 50% predictive, that is, any person exhibiting a positive skin-prick test will have a 50% chance of reacting to the food.

Table 2

Spectrum of IgE immediate hypersensitivity reactions to food

- Symptoms occur within two hours of ingestion, usually ≤ 15 minutes

Non-GI	GI
- Oral itching	- Vomiting
- Urticaria	- Diarrhea
- Atopic dermatitis	- GI bleeding
- Brochospasm	- Abdominal pain
- Angioedema	
- Anaphylaxis	

- **Foods:**
  - Children: peanut, milk, soy, egg
  - Adults: peanut, tree nut, shellfish

GI: Gastrointestinal

In some cases, open or blinded food challenges may be needed to prove or disprove food sensitivity. Treatment includes:

- advice on avoiding the offending food,
- the use of epinephrine when respiratory or anaphylaxis symptoms begin and
- emergency room consultation.

Table 3

Spectrum of non-IgE mediated food allergies

- Celiac disease (gluten-induced enteropathy)
- Non-IgE food allergy (milk and soy are most common)
  - Eosinophilic esophagitis
  - Eosinophilic gastritis
  - Eosinophilic gastroenteropathy
  - Eosinophilic colitis
  - Food-protein induced enterocolitis syndrome

Furthermore, future monoclonal anti-IgE therapy may be useful to prevent severe reaction to inadvertent exposure. Factors associated with death include:

- delay in administration of epinephrine,
- co-existing asthma and
- failure to recognize the possibility of a second (biphasic) reaction.

Non-IgE food hypersensitivity

Non-IgE food hypersensitivity (Table 3) may present with a variety of symptoms and signs including:

- growth delay,
- diarrhea,
- vomiting,
- protein-losing enteropathy,
- rectal bleeding or a
- enterocolitis syndrome

These are cell-mediated (largely T-lymphocyte) immune disorders leading to GI inflammation. Signs, symptoms and inflammation will improve when the offending food is removed and will return upon re-introduction of the food. This may take days or weeks. While milk is the most common offending food, soy, egg, wheat, other grains and any other food, may

cause similar symptoms and signs. Symptoms often parallel the site of involvement. The following distinct syndromes can all be caused by a food allergy:

- Allergic colitis: is the most common manifestation of a protein allergy in infants, frequently secondary to cow milk, soy protein from formula, or an antigen from breast milk. It presents as loose stool with streaks of blood and mucous and a negative stool culture. It resolves within four weeks after removal of the offending antigen.
- Small bowel enteropathy: a food allergy (especially to milk) can cause chronic inflammation with villous atrophy which can lead to diarrhea, failure to thrive, protein-losing enteropathy with hypoalbuminemia, eosinophilia and anemia.
- Allergic gastritis: presents with pain, reflux symptoms or vomiting. Gastric outlet obstruction may mimic hypertrophic pyloric stenosis.
- Allergic eosinophilic esophagitis: is an emerging entity, predominantly in atopic males, which presents with dysphagia, food impaction and occasional symptoms of gastroesophageal reflux, pain, vomiting and feeding aversion. Marked esophageal eosinophilia is found by endoscopy. It is associated with milk/soy allergy in infants, but in older individuals, its relation to food is uncertain.
- Food protein-induced enterocolitis syndrome: shows a severe reaction four to six hours after ingestion of the offending food and is characterized by vomiting, diarrhea, lethargy and a shock-like picture with occasional hematochezia. This non-IgE reaction may mimic sepsis and intussusception, but it resolves quickly with intravenous fluids.

Back to Langdon

- Langdon was investigated for sepsis, metabolic disease, intussusception and other surgical pathology. His prompt response to intravenous re-hydration and history of a new food suggests food-protein induced enterocolitis syndrome.
- Skin-prick tests to the foods were negative. The only new food introduced contained soy protein.
- You explain to Langdon's parents that this severe and unusual food allergy (in this case to soy) is usually outgrown after two to three years.
- Langdon's parents need to consult with a dietitian so that Langdon can avoid accidentally ingesting soy.

Table 4

Celiac disease

- Enteropathy secondary to cell mediated reaction to gluten
- Classic presentation (malabsorption)
  - Chronic diarrhea
  - Failure to thrive
  - Distension
- Atypical presentation
  - Short stature/linear growth delay
  - Iron deficiency anemia
  - Osteopenia/Osteoporosis
  - Dermatitis herpetiformis
- Diagnosis
  - Elevated tissue transglutaminase IgA antibody (TTG)
  - Small bowel biopsy
- Treatment: nutrition counseling on a strict gluten-free diet

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FAQ

A school-aged child experienced acute anaphylaxis to peanut at 15 months. Her allergy was confirmed, at the time, with a large skin prick test. Can we predict if she has outgrown the allergy, or is there any other treatment?

Approximately 20% to 25% of children may outgrow their peanut allergy with time; however, challenging the patient would put the child at risk for a severe reaction. The new IgE CAPRAST test measures a specific food antibody from the patient's serum. Ranges have been determined for peanut and other common food allergens to help predict the risk of anaphylaxis. For example, for peanut, levels below 0.35 kU/L predict that 85% of patients will have a negative challenge. On the other hand, levels above 15 kU/L predict an 95% chance of anaphylaxis. By following levels over time, we can determine when it is safe to challenge a patient. Food challenges are done in a hospital setting with an IV of medications in place to treat a reaction. For those patients with persistent hypersensitivity and anaphylaxis risk, there is a new therapy on the horizon. Anti-IgE therapy has been shown to be effective for a peanut allergy, but presumably would work for any IgE mediated allergy. Monthly infusions of a monoclonal anti-IgE antibody greatly reduces the risk of anaphylaxis if small quantities of the antigen are consumed inadvertantly.

Celiac disease

Celiac disease (Table 4) is a defined food allergy distinct from other non-IgE mediated diseases, with a well defined pathophysiology and natural history. Ingestion of gluten in genetically predisposed individuals (HLA-DQ2 and HLA-DQ8) leads to inflammation and villous atrophy. The classic presentation (malabsorption, chronic diarrhea, weight loss, failure to thrive) is becoming less common. Patients are now being identified through diabetes screening, Down's syndrome screening, through relatives of celiac patients and through any unusual manifestations, such as early onset osteoporosis or isolated iron deficiency anemia. Population studies indicate that celiac disease affects approximately one per cent of the population. Treatment is a life-long gluten-free diet. Consultation with an experienced dietitian is essential to eliminate all gluten exposure.

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Take-home message

1. Food allergies are on the increase.
2. We need to recognize the existence of both IgE and non-IgE mediated food allergies.
3. Celiac disease now has a prevalence approaching one per cent of the population with atypical presentations predominating.

FAQ

Can infants develop allergic enteropathy while being breast-fed or taking hydrolyzed infant formulas?

Yes, the full spectrum of food allergy disorders that have been described can be seen in infants who are exclusively breast-fed or who are exclusively fed with hydrolyzed formula. Infants may become sensitized to protein antigens from their mother's diet (often milk protein) that is transmitted into breast milk. Protein hydrolysates made from cow's milk contain protein fragments large enough to be antigenic in sensitive individuals.

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