True food allergies are common in children and somewhat less in adults. However, they are not quite as common as many people believe. Vague and non-specific symptoms are often mistakenly attributed to allergies to foods or food additives, whereas the actual spectrum of adverse reactions to foods is well-defined and based on specific immunologic mechanisms.

How are food reactions classified?

Foods may cause adverse reactions by a number of different mechanisms. Broadly speaking, these adverse reactions may be thought of as either immunologic or non-immunologic. Non-immunologic reactions are further subclassified as either toxic/pharmacologic or non-toxic/intolerance.

The case of John

John, 42, described two systemic reactions associated with restaurant meals. The first began five to 10 minutes after a main course of pasta with pesto sauce and the second reaction occurred while eating a dessert of cheesecake. Both reactions were characterized by itching of the palms, soles, and groin, and progressed to generalized hives, periorbital edema, dysphagia with hoarse voice, and shortness of breath. On the second occasion, he felt faint and presyncopal. The paramedics were called and documented a blood pressure of 88/54 mmHg.

Following the initial consultation, during which he was advised to carry an epinephrine auto-injector, he was asked to return to the restaurants to obtain a detailed list of the ingredients of the pasta sauce and cheesecake. A review of the ingredients showed that pine nuts were present in both dishes. A prick skin test to pine nut was strongly positive and a radioallergosorbent (RAST) test for pine nut-specific immunoglobulin (Ig) E was extremely high. The life-threatening nature of his food allergy was reinforced.

He was strongly advised to avoid dishes containing pine nuts, to carry epinephrine at all times, and to wear a Medic Alert® bracelet stating this allergy.

In this article:

1. How are food allergies classified and what characterizes them?
2. How are they diagnosed?
3. What are the treatment options?
Many foods exert pharmacologic effects which are predictable and reproducible based on the chemical constituents of the foods. For example, alcohol causes intoxication because of its ability to penetrate phospholipid membranes, altering the phospholipid packing density. Caffeine in chocolate, coffee, and tea has dose-dependent predictable effects on the cardiovascular and central nervous systems.

Examples of food-induced toxicity include bacterial food poisoning (e.g., salmonella, staphylococcal exotoxins, botulism), heavy metal poisoning (mercury in fish), scombroid fish poisoning, and tetrodotoxin in blowfish. In contrast, nontoxic/intolerance-type reactions to foods are exemplified by lactase deficiency resulting in lactose intolerance, gustatory rhinitis, and gallbladder disease.

Foods may give rise to specific manifestations by way of immunologic reactions. These reactions may be immunoglobulin (Ig) E-mediated immediate hypersensitivity reactions. They may range from mild manifestations (such as oral allergy syndrome to fresh fruits or vegetables and hives due to foods) through to life-threatening anaphylaxis. In contrast, non-IgE mediated reactions to foods tend to be delayed, require higher levels of exposure, and typically do not progress on to life-threatening manifestations. Non-IgE mediated immunologic mechanisms have been implicated in milk-induced enterocolitis, protein-induced enteropathy, celiac disease, and dermatitis herpetiformis. Some conditions, such as atopic dermatitis, are characterized by mixed immunologic mechanisms.

There is little evidence to implicate immunologic reactions to foods or food additives in the pathogenesis of migraine headaches, behavioural disorders, arthritis, multiple sclerosis, inflammatory bowel disease, and seizures.

What characterizes a food allergen?

Food allergies are typically induced by protein constituents, rather than carbohydrate or fat moieties. Typically, allergenic proteins are glycosylated and, thus, resistant to degradation by gastric acid and digestive enzymes. Glycosylation also makes food allergens high-
Food Allergies

Table 1: Foods on priority allergen list (Canada)

- Cow’s milk
- Hen’s egg
- Soy
- Wheat
- Peanut
- Tree nuts
- Fish
- Shellfish

Table 2: Risk factors for fatal anaphylaxis to foods

- History of previous severe reactions to that food
- Co-existent asthma (especially poorly controlled asthma)
- Delayed administration of epinephrine during an acute reaction
- A tendency to minimize or deny the potential severity of food allergy (especially problematic among teenagers)

ly resistant to degradation or processing. Most food allergens are highly stable proteins of moderate molecular weight, ranging from 10 kDa to 70 kDa. Because of the relative stability of most food allergens, allergenic epitopes remain intact despite processing, storage, cooking, and digestion. Intact IgE-binding epitopes are capable of triggering allergic reactions after passage into the bloodstream. The notable exceptions to the above mechanism are fresh fruits and vegetables, which contain heat labile allergens rapidly degraded by microwaving or cooking. For this reason, fresh fruits and raw vegetables will tend to trigger more severe reactions than their cooked counterparts, although there are notable exceptions to this rule.

Eight foods, responsible for most of the food-related allergic reactions, have been assigned to a priority allergen list in Canada (Table 1). All of these food allergies are typically acquired in childhood, but most will subside over time. However, in most individuals, allergies to peanut, tree nut, fish, and shellfish persist into adulthood. The vast majority of food-allergic individuals react to only a single food, whereas only a small proportion 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 most anaphylactic fatalities in North America.

The major risk factors for fatal anaphylaxis to foods are listed in Table 2.

What is the prevalence of food allergies?

True food allergies, confirmed by double-blind, placebo-controlled oral challenge, are present in 4% to 8% of children and 1% to 2% of adults. However, the self-reported prevalence of food allergy ranges from 20% to 25% in North America. More than 200 foods have been reported to cause allergic reactions and virtually any food is capable of inducing a reaction. However, the actual prevalence rate of allergy to any given food depends in large part on the dietary habits of the population. Cow’s milk allergy is present in about 2.5% of
infants and allergy to peanut and tree nut is present in approximately 1.1% of the North American population. Allergy to sesame seed is becoming increasingly commonplace and will likely assume a place among the top 10 food allergens in the future.

Allergic reactions to foods are responsible for 30% to 50% of all anaphylactic reactions. Specific foods, such as soy, milk, wheat, fish, peanut, and tree nut, may contribute to flares in atopic dermatitis in 30% to 50% of children. However, foods rarely contribute to worsening of atopic dermatitis in adults. Food allergies have been implicated in about 20% of cases of acute, self-limited urticaria, whereas foods rarely contribute to long-lasting hives.

How are food allergies diagnosed?

**History and physical examination**
Immediate hypersensitivity reactions to foods typically occur within one to two hours of ingestion and are seldom delayed. Non-IgE-mediated immunologic reactions to foods may be delayed by hours or days. The severity of manifestations will be related to the dose of the food ingested and manifestations are reproducible on repeated challenge. However, given the vast array of foods consumed by the average individual, patients often fail to identify a specific food responsible for their reactions. The cause can often be ascertained on the basis of a detailed dietary history, especially if a symptom diary is kept in conjunction with details of ingested foods. However, hidden ingredients as a cause of allergic or immunologic reactions may not be evident from a food diary.

Other atopic disorders, such as asthma, allergic rhinitis, and atopic dermatitis, are known to contribute to the severity of allergic reactions to foods. These will easily be identified on history and physical examination. Some clinical conditions can mimic anaphylaxis, such as systemic mastocytosis. The typical physical findings of systemic mastocytosis will often be evident on physical examination.

**Laboratory investigations**
Prick skin testing to suspect foods will usually give a positive skin test when done in conjunction with appropriate controls. Alternatively, in vitro testing for food-specific IgE (using radioallergosorbent [RAST] tests) may be performed instead of prick skin testing. RAST testing is also useful to confirm skin test results and yields additional information on the risk of systemic reactions. In those patients in whom the history is more compatible with a non-IgE mechanism, biopsy of the skin or gut may provide valuable information.

Neither prick skin tests, nor in vitro tests alone will establish a diagnosis of food allergy. The positive skin test or blood test must be

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interpreted in the context of the clinical reactions, as false positive tests are frequently encountered with foods. In contrast, negative prick skin tests and negative RAST tests for food-specific IgE are very accurate at ruling out food allergies.

Patients sometimes seek alternative forms of testing which are generally unvalidated. These include Vega testing, IgG4 subclass analysis, applied kinesiology, hair analysis, provocation/neutralization testing, and cytotoxic testing. None of these methods has withstood rigorous scientific analysis and some have been shown to be potentially harmful.

Food challenges
Where history, physical examination, and diagnostic testing point to a specific food as a cause of allergic reactions, elimination of that food from the diet should bring about resolution of symptoms. In some cases, the cause is unclear and definitive testing is required. Double blind, placebo-controlled food challenges are the gold standard in establishing the role of a food in allergic reactions. Oral challenges with suspect foods should be undertaken in a supervised medical setting with resuscitation facilities immediately at hand.

How can food allergies be treated?

There are no safe means by which to “desensitize” food-allergic individuals. Currently, the only effective approach to treatment of food allergy is to eliminate the causative food allergen from the diet. This often requires a great deal of education of the patient, family members, and caregivers. In spite of best efforts, accidental exposures are distressingly common and have been associated with life-threatening and fatal reactions. Part of the problem resides in food allergens hidden in packaged or prepared foods in the absence of adequate labelling. Another problem is the absence of readily recognizable terminology on labels. For example, milk protein may be denoted as casein, lactalbumin, nougat, pudding, whey, or artificial butter flavour. A milk-allergic individual may not appreciate that all of these ingredients represent milk protein.

Certain ingredients, such as peanut, may be hidden in prepared foods. Fatal anaphylaxis has been reported to peanut butter which had been used to “glue” the ends of egg rolls and to thicken chili and pasta sauces. Cross-contamination of foods in manufacturing facilities, in bulk retail outlets, and in restaurants may pose a hazard to the allergic individual. Oriental restaurants are also hazardous for individuals with peanut or shellfish allergies. Certain confectionery products, such as chocolates imported from Eastern Europe,
Take-home message

**Diagnosis**
- The cause of an allergy can often be ascertained from a detailed dietary history.
- Prick skin testing to suspect food will usually give a positive skin test when done in conjunction with appropriate controls.
- RAST tests may be performed in place of prick skin testing and will yield additional information on the risk of systemic reactions.
- Food challenges are the gold standard in establishing the role of a food in an allergic reaction.

**Treatment**
- Currently, the only effective approach to allergy treatment is to eliminate the causative food allergen.

frequently contain high levels of undeclared peanut protein, which may trigger reactions in unsuspecting individuals. These foods are subject to recalls initiated by the Canadian Food Inspection Agency.

Suggested Readings
7. Vadas P, Perelman B: Presence of undeclared peanut protein in chocolate bars imported from Europe. Journal of
Food Allergies

Food Protection (In Press).