Food Allergy and Food Intolerance

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\textbf{Key Words}

Food allergy · Food intolerance · IgE · Dietary restriction · Nutritional deficiency

\textbf{Key Messages}

- Adverse reactions to food can be classified as either immune mediated (e.g. food allergy, FA) or non-immune mediated (e.g. food intolerance, FI). Non-immune-mediated reactions are the most prevalent.
- Eight foods (milk, eggs, peanuts, tree nuts, soy, wheat, fish, and shellfish) account for 90\% of all IgE-mediated food allergies.
- Celiac disease is a classical example of a non-IgE-mediated adverse food reaction that affects 1\% of the population. Examples of other immune-mediated adverse food reactions are food protein-induced enterocolitis syndrome, eosinophilic esophagitis, and eosinophilic gastrointestinal disorders.
- FI is much more common than FA. Examples of FI include food poisoning, lactose intolerance, as well as toxic, pharmacological, and functional adverse reactions to foods. Quite often, these reactions mimic reactions due to FA.

- Appropriate diagnosis is important in order to avoid the unnecessary elimination of a particular food item from the diet.
- When a restricted diet is clinically indicated for long-term management, it should be undertaken under close supervision from an experienced nutritionist and expert physician to reduce the risk of nutritional deficiencies.

\textbf{Introduction}

Food allergy (FA) is defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food. FA is a growing public health concern and its prevalence seems to be on the rise. It is estimated that 9 million, or 4\%, of adults have FA in the United States. Up to 20\% of the population, however, frequently confuses food intolerance (FI) with FA, leading to unnecessary dietary restriction and potential nutritional deficiency. In
In general, any adverse reaction to food can be classified into either immune mediated (e.g. FA) or nonimmune mediated (FI), with the latter being the most prevalent (fig. 1). The fundamental difference between FA and FI is that the former is immune mediated, while the latter is not [1]. In clinical practice, it is of paramount importance to distinguish the two, because their clinical implication and nutritional needs are distinctly different. For instance, while consumption of milk in a patient with lactose intolerance causes self-limited symptoms such as diarrhea, bloating and abdominal discomfort, ingestion of even a trace amount of milk by a patient with cow milk allergy (CMA) can trigger potentially life-threatening anaphylactic shock.

**Food Allergy**

To understand FA, we first need to understand the nomenclature. ‘Allergy’ has conventionally been associated with IgE-mediated processes. It is therefore not surprising that FA is often equated to IgE-mediated FA, though there are other food allergies that are not IgE mediated. For our discussion, we will use the term ‘IgE-mediated food allergy’ to specifically refer to FA that are mediated by IgE. Another term you may encounter in the literature is food hypersensitivity. It is often used to describe FA, although some have used this term more broadly to include FI. For this reason, we will avoid using the term food hypersensitivity in our discussion.

Eight foods account for 90% of all IgE-mediated food allergies: milk, eggs, peanuts, tree nuts, soy, wheat, fish and shellfish [1]. The onset of symptoms is rapid and even minute amounts of the allergen can trigger severe reactions. The reactions can range from self-limited localized hives to life-threatening generalized anaphylaxis. Common symptoms include hives, pruritus, ery-
thema, angioedema, nasal congestion, cough, chest tightness, vomiting, nausea, diarrhea, dizziness, wheezing and rhinoconjunctivitis. Patients with suspected IgE-mediated FA should be referred to an allergist for evaluation and management.

Shellfish, peanut, tree nuts and fish are responsible for most of the FA in adults. Although these foods contain valuable nutrients, they do not usually account for a large percentage of daily dietary intake in a Western diet. Many other foods can supply the nutrients found in these specific foods, and substitution can easily be made. Although significant nutritional deficiency secondary to a single FA is rare among adults in the US, CMA, wheat allergy and multiple food allergies (MFA) remain a significant challenge for nutritionists and clinicians. Adults with CMA are at risk of vitamin D and calcium deficiency because it is difficult to meet calcium needs through nondairy sources without careful substitution. Therefore, calcium supplements should always be considered in patients with CMA to reduce the risk of osteoporosis and fracture [2].

Wheat is present in many processed foods such as crackers, cookies, cakes, pasta, bread and cereal. Moreover, wheat is also a minor ingredient in condiments, marinades, cold cuts, soy sauce, hard candies, low-fat products, etc. The major product of wheat, wheat flour, is a great source of carbohydrates, iron, thiamine, riboflavin, niacin, folic acid, vitamin B₆, magnesium and fiber. Fortunately, there are a wide variety of wheat-free products made from alternative flours (rice, corn, oat, barley, buckwheat, rye, amaranth, millet and quinoa). The availability of gluten-free foods can also benefit those with wheat allergy. It is important to note that up to 20% of the individuals with an allergy to one grain will have allergies to other grains. Use of these alternative grain products should be individualized and based upon tolerance as determined by an allergy specialist.

### Non-IgE-Mediated Adverse Reactions to Food

Celiac disease is a classical example of non-IgE-mediated adverse food reaction found in adults. It is caused by an abnormal immune reaction to gluten and affects 1% of the population [3]. Life-long elimination of gluten is the only treatment. Since gluten is present in a variety of food items, the diagnosis should be confirmed by a specialist before committing patients to a life-long gluten-free diet. Gluten-free diets are often low in vitamin B, calcium, vitamin D, iron, zinc, magnesium and fiber. Until fairly recently, few gluten-free products were enriched or fortified, adding to the risk of nutritional deficiency. Food protein-induced enteropathy is another non-IgE-mediated adverse reaction to food, and is most commonly seen in young infants.

### Other Immune-Mediated Adverse Reactions to Food

Examples of other immune-mediated adverse food reactions are food-induced allergic contact dermatitis, eosinophilic gastrointestinal disorders and eosinophilic esophagitis (EoE). EoE deserves special attention because a subset of patients respond very well to elimination diets, which pose significant nutritional risks. EoE is a chronic immune-/antigen-mediated disorder characterized by eosinophilic infiltration of the esophagus [4]. Adults with EoE often present with refractory reflux, epigastric or chest pain, dysphagia and food impaction. The majority of affected adults are men in their 20s or 30s. Over the past few years, the treatment modality for adults has shifted from primarily medical (swallowed topical corticosteroids) to dietary approach (elimination diet) [5]. The three primary dietary treatment options are testing-directed elimination (foods are eliminated based on allergy testing results), empirical elimination (milk, soy, egg, wheat, peanut/tree nuts, and fish/shellfish are
eliminated) and elemental diet (amino-acid based formula that eliminates all potential food allergens). If a dietary approach is employed, patients should be closely followed by a registered dietitian to avoid nutritional deficiency.

### Food Intolerance

FI is much more common than FA. Examples of FI include food poisoning, lactose intolerance, as well as toxic, pharmacological, and functional adverse reactions to foods. Quite often, these reactions mimic reactions due to FA. It is therefore important to keep in mind the differential diagnosis when evaluating patients with suspected FA.

Food poisoning typically manifests as nausea, vomiting, fever, abdominal pain and diarrhea. A good history and physical examination is usually sufficient to distinguish such reactions from FA. GI infections can also result in transient lactose intolerance. Since most food poisoning episodes are self-limited, they do not pose a significant risk for malnutrition.

Lactose intolerance is the most common adverse reaction to a specific food, with most cases resulting from a genetically regulated reduction of intestinal lactase activity later in adult life [6]. The lactose intolerance breath test provides a simple, accurate and noninvasive way to confirm the diagnosis. It is important to confirm the diagnosis so patients will not unnecessarily avoid milk consumption, which is one of the most bioavailable sources of ingested calcium and vitamin D. Naturally low-lactose dairy products such as yogurt, hard cheeses and kefir are typically well tolerated in patients with lactose intolerance. Commercially available lactase enzymes can be added to lactose-containing food or ingested with meals containing lactose to reduce symptoms. Moreover, lactose-free milk products are readily available in grocery stores. Since patients with lactose intolerance often have significantly lower calcium intake, calcium supplementation should be considered to reduce the risk for osteoporosis and fracture [7].

Scombroid fish poisoning is the most common seafood-associated disease in the US. Shortly after ingesting contaminated fish, patients experience acute onset of flushing, a sensation of warmth, an erythematous rash, palpations and tachycardia [8]. The symptoms resemble an IgE-mediated allergic reaction and are often misdiagnosed as FA, leading to unnecessary diet restriction and nutritional compromise.

Pharmacological reactions to food or food additives represent a relatively common type of FI. Ingestion of foods with high histamine content such as well-ripened cheese, pickled cabbage, red wine and tuna fish can cause a wide range of allergic-like symptoms in susceptible individuals with a genetic defect in the metabolism of exogenous histamine [9]. In some instances, FI can result from drug-food interactions. A classic example is hypertensive crisis observed in individuals taking monoamine oxidase inhibitors and ingesting tyramine-rich food (e.g. wine and cheese). Adverse reactions to food additives such as artificial colors (FD&C yellow No. 5) and various preservatives (for example, sulfites) are other examples of FI. Avoidance is the only treatment. Management of the nutritional needs for these FI is similar to that of food allergies, but they are typically not a concern given a less restricted list of foods to be avoided in such disorders. Functional FI no doubt exists and appears to be more prevalent in patients with irritable bowel syndrome and other functional GI disorders with or without underlying psychiatric disorders [10]. Patients often report adverse reactions to multiple foods. They often self-eliminate multiple food classes from their diet and are at particular high risk for nutritional deficiency. Since some patients may be willing to reintroduce foods into their diet if diagnostic tests fail to confirm a food-related reaction, targeted skin testing, specific IgE serology and/or food challenges may be helpful in liberalizing
their diet and minimizing nutritional risk. On the other hand, this same group of patients is also more likely to supplement their diet with suprapharmacologic amounts of ‘health food’ preparations and nutritional supplements. The dangers of oversupplementation are well described.

Symptoms triggered by physiological reactions to food are frequently encountered in clinical practice. Fatty foods, chocolate, peppermint, colas, red wine, orange juice and excessive alcohol are known to reduce lower esophageal sphincter pressure and worsen symptoms of gastroesophageal reflux disease. Legumes, onions, cabbage, bran fiber, and grains serve as a substrate for gas production by colonic flora and can aggravate bloating symptoms. These physiological reactions to foods are typically noted by patients with functional GI disease, many of whom appear to exhibit heightened sensory responses to normal digestive events. As long as a balanced diet is maintained, avoidance of the specific food items described herein has virtually no impact on nutritional status.

Special Nutritional Issues of Multiple Food Allergies

In the previous sections, we discussed the nutritional management of patients with a particular FA. Patients with MFA present a unique diagnostic and nutritional challenge. They are at high risk for malnutrition. Although MFA is more commonly seen in pediatric patients, it is infrequently seen in adults. One example is adult patients undergoing multiple food elimination diet for the treatment of EoE. Close monitoring of nutritional status is warranted, and supplements should be considered in appropriate settings. The same applies to patients with specific immune-mediated food-induced conditions who are on a restricted diet for other reasons (e.g. a strict vegetarian with celiac disease). Clinicians should be sensitive to a patient’s dietary preference and understand that changing one’s diet might not be acceptable to the individual for cultural, religious or other reasons. Some useful resources for patients suffering from FA are listed in table 1.

Table 1. Useful resources for patients suffering from FA

| General information | http://www.foodallergy.org/  
|                     | http://www.niaid.nih.gov/topics/foodallergy/Pages/default.aspx  
|                     | http://www.acaai.org/allergist/allergies/Types/food-allergies/Pages/default.aspx  
|                     | http://community.kidswithfoodallergies.org/about  

| Food allergy recipes | http://www.realfoodallergyfree.com/allergy-free-recipe-index/  
|                     | http://www.foodallergykitchen.com/pages/recipes.php  

Conclusions

- Dietary limitation due to adverse reactions to food can have a significant impact on nutritional intake.
- It is therefore important to identify individuals in whom restricted diets are truly justified.
- When a restricted diet is clinically indicated for long-term management, it should be undertaken under close supervision from an experienced nutritionist and expert physician to reduce the risk of nutritional deficiencies.
References


