Food Allergy: An Overview

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Food allergy affects between 5% and 7.5% of children and between 1% and 2% of adults. The greater prevalence of food allergy in children reflects both the increased predisposition of children to develop food allergies and the development of immunologic tolerance to certain foods over time. Immunoglobulin (Ig) E-mediated food allergies can be classified as those that persist indefinitely and those that are predominantly transient. Although there is overlap between the two groups, certain foods are more likely than others to be tolerated in late childhood and adulthood. The diagnosis of food allergy rests with the detection of food-specific IgE in the context of a convincing history of type I hypersensitivity-mediated symptoms after ingestion of the suspected food or by eliciting IgE-mediated symptoms after controlled administration of the suspected food. Presently, the only available treatment of food allergies is dietary vigilance and administration of self-injectable epinephrine. *Key words:* epidemiology, food allergy, IgE-mediated hypersensitivity. *Environ Health Perspect* 111:223–225 (2003). [Online 21 January 2003] doi:10.1289/ehp.5702 available via *http://dx.doi.org/*

As many as 30% of American adults self-report food allergy and alter their eating habits accordingly (Sloan and Powers 1986). Similarly, nearly one-third of parents perceive adverse food reactions to be responsible for a multitude of symptoms in their children and modify their children's diets in response (Bock 1987). Although accurate and recent epidemiologic data are scarce, current estimates of the prevalence of food allergy suggest that approximately 5% of young children and 1–2% of adults have reproducible symptoms resulting from food allergy (Bock 1987; Niestijl et al. 1994). Despite greater awareness and recognition of food allergy by both physicians and patients, many allergists believe that the actual prevalence has risen substantially over the past decade, similar to the rise in prevalence of other atopic conditions such as asthma and allergic rhinitis (Ninan and Russell 1992; Peat et al. 1994; Sears 1996).

An adverse reaction to food refers to any abnormal reaction after the ingestion of food or food additives. Adverse reactions to foods may result from enzyme deficiencies such as lactose intolerance, exaggerated pharmacologic responses to natural or added chemical agents such as vasoactive amines in wines, or immunologic responses. Immunologic responses to foods can be further defined mechanistically as immunoglobulin (Ig) E mediated and non-IgE mediated. The best-characterized adverse reactions to food are those that are Type I hypersensitivity reactions, i.e., IgE mediated. The spectrum of food allergy ranges from cutaneous symptoms, such as atopic dermatitis, appearing several hours after the ingestion of the responsible food to potentially life-threatening symptoms occurring immediately upon ingestion. Additionally, some individuals experience allergic symptoms only if the food is eaten before specific physical stimuli (for example, vigorous exercise) or if the individual has concomitant seasonal allergies, whereby certain foods elicit oral symptoms, such as pruritis and local swelling upon ingestion. This article is limited to classic type I hypersensitivity allergic reactions to foods.

Diagnosis

The diagnosis of food allergy rests with the detection of food-specific IgE and a history compatible with IgE-mediated symptoms occurring within an acceptable time frame (usually < 1 hr) after the isolated ingestion of the food in question. Symptoms that result from IgE-mediated mast cell degranulation products include flushing, urticaria, stridor or wheeze, and gastrointestinal symptoms such as abdominal pain or vomiting. Detection of food-specific IgE can be measured either with a skin prick test or, *in vitro*, with food-specific IgE. Skin prick tests are inexpensive, simple tests and can be performed in individuals of all ages. Skin prick tests have excellent sensitivity and negative predictive value, but variable specificity and positive predictive values; therefore skin tests, particularly when performed with fresh foods, can reliably exclude food allergies when negative, but cannot confirm food allergy when positive (Bock et al. 1978; May 1976; Sampson 1988). When measured with the ImmunoCAP method (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden), a fluoroenzymatic immunoassay, quantitative measures of food-specific IgE can be determined, and these measurements can be useful in the diagnosis of food allergy. The positive and negative predictive values of a limited number of food-specific IgE determinations have been published that define cutoff values that reliably predict the likelihood of food allergy when compared with double-blind, placebo-controlled, food challenges (DBPCFC) (Sampson 2001). The DBPCFC is the "gold standard" of food allergy diagnosis and requires the administration of incremental quantities of the suspected food to the patient in a controlled, blinded, and supervised setting, where observation and documentation of objective allergic signs are noted. The procedure and safety of DBPCFC have been described elsewhere (Bock et al. 1988). Thus, the diagnosis of food allergy can be made when the history is convincing of an IgE-mediated reaction and confirmatory skin tests or specific IgE assays are positive. However, when the history elicited is not clearly typical of an IgE-mediated reaction, either by description of symptoms or in timing, or when the meal that produced the reaction contained several allergic possibilities, positive skin tests or specific IgE measurements must be confirmed with DBPCFC before an accurate diagnosis of food allergy is made. Clearly, when the history and lab tests are convincing of food allergy, the DBPCFC is not indicated.

Natural History of Food Allergy

Most food allergies have their onset in infancy or early childhood, depending on when the food is introduced into the diet. Theoretically, any food containing a protein could elicit an allergic reaction; however, eight common foods are responsible for > 90% of food allergies (Hefle et al. 1996). The natural history of food allergy varies with the individual food, but many of the foods that elicit allergic reactions in young children can be eventually reintroduced into the diet. Thus, most food allergies can be classified as "likely to resolve" or "likely to persist." Food allergies that usually resolve include milk, soy, egg, and wheat. These allergies typically present in infancy and usually resolve by school age. Food allergies that usually persist include peanut, tree nuts, fish, and shellfish. These, too, usually present in early childhood, shortly after the introduction of these foods into the usual diet. Although most individuals with

allergies to foods in this latter group tend to persist with these allergies indefinitely, some children will develop tolerance to these foods and will be able to reintroduce them safely into their diet.

Milk allergy almost always presents in the first year of life, soon after the introduction of cow's milk or cow's milk–based infant formula, and usually resolves by school age. Most infants with cow's milk allergy develop gastrointestinal symptoms, approximately 50–70% have cutaneous features, and about 20–30% will have respiratory symptoms (Host 1994). Milk allergy affects up to 2.5% of infants, with approximately 1% of all children developing IgE-mediated milk allergy and approximately 1.5% of children developing non-IgE-mediated milk allergy (Host and Halken 1990). In a prospective study by Host and Halken (1990), 39 infants in a birth cohort of 1,749 unselected newborns were diagnosed with cow's milk protein allergy/intolerance based on elimination diets and milk rechallenges. Of 39 infants diagnosed with milk allergy or milk intolerance, 21 infants had positive skin or serum IgE tests to milk and 18 had non-IgE-mediated cow's milk intolerance. Of the total group, 56% were able to tolerate milk by 1 year of age, 77% by 2 years, and 87% by 3 years. Of children with IgE-mediated cow's milk allergy, 14% had persistent milk allergy at the age of 5 and 10 years. All of the children with non-IgE-mediated cow's milk allergy and most children with IgE-mediated cow's milk allergy were able to reintroduce milk products by age 5; however, 3 of 21 of the IgE-mediated group remained allergic well into mid-childhood. Thus, in an unselected population, milk allergy usually resolves by school age, but among highly atopic children, milk allergy is more likely to persist (Bishop et al. 1990; Tikkanen et al. 2000).

Risk factors for persistence of milk allergy include early dermatitis presentation of milk allergy; development of other atopic conditions, including other food allergies, asthma, and allergic rhinitis; and persistence of elevated levels of milk-specific IgE (Sicherer and Sampson 1999; Zeiger et al. 1999). In general, as tolerance to IgE-mediated milk allergy is achieved, the size of the wheal and flare on the skin prick tests decreases; however, it may continue to remain positive beyond acquisition of clinical tolerance. Serum-specific IgE, measured by the ImmunoCAP system, appears to be a more sensitive measure for the prediction of food allergy resolution, especially in patients with atopic dermatitis (Sampson 2001).

Soy is considered a major food allergen and is a food introduced to infants in the form of infant formulas and cereals. Soy-based infant formulas are recommended for families following vegetarian dietary restrictions, for children with congenital or acquired lactose intolerance, and for infants with diagnosed IgE-mediated cow's milk allergy. Of children with IgE-mediated cow's milk allergy, fewer than 15% will develop a concomitant allergy to soy, but most infants will tolerate soy protein without difficulty (Zeiger et al. 1999). The prevalence of soy allergy/soy intolerance varies with the frequency with which soy is introduced into regional diets, but it appears to affect 1–6% of infants (Giampietro et al. 1997; Magnolfi et al. 1996). Symptoms associated with soy allergy include typical IgE-mediated features as well as non-IgE-mediated—gastrointestinal symptoms such as hematochezia and malabsorption. Both skin prick tests and food-specific IgE are used to detect the presence of IgE; however, both modalities have poor specificity and positive predictive values (Giampietro et al. 1997; Sampson 2001). The natural history of IgE-mediated soy allergy is similar to that of other "predominantly transient" allergies, and most children can tolerate soy products by school age.

The prevalence of egg allergy is estimated at 1.6–2.6% of the general pediatric population but is significantly higher among individuals with atopic dermatitis and other collateral atopic conditions (Danneus et al. 1977; Eggesbo et al. 2001). Most children developing allergic symptoms to ingestion of egg develop symptoms within 30 min. More than 85% of egg-allergic children develop cutaneous symptoms, 60% have gastrointestinal symptoms, and up to 40% will have associated respiratory symptoms (Eggesbo et al. 2001; Ford and Taylor 1982). In Ford and Taylor's (1982) description of the natural history of egg allergy, 44% of egg-allergic children were able to reintroduce egg products into their diet by school age, but the remaining 56% persisted with egg allergy. Children with persistent egg allergy had significantly more target organs affected at the time of the initial allergic reaction, were more likely to acquire additional atopic conditions, and continued to have positive prick skin tests to egg. Egg-specific IgE, measured by the ImmunoCAP method, is useful in predicting the likelihood of positive challenges, and cut-off values have been proposed for this effect (Sampson 2001).

Peanuts, nuts, fish, and seafood allergies generally persist indefinitely. Other foods, particularly seeds (e.g., sesame, poppy, mustard), might also be added to this list. Uncommonly, reports of tolerance developing to these foods have been published, but until very recently, the persistence of these food allergies has been expected.

Peanut allergy deserves particular attention because it almost always presents early in life, is often severe, generally persists indefinitely, and is the most common cause of fatal food-related anaphylaxis (Bock and Atkins 1989; Sampson et al. 1992). Additionally, because of peanut's relative ubiquity, accidental exposures occur frequently, despite vigilant attempts to avoid peanut-containing foods (Bock and Atkins 1989; Vander Leek et al. 2000). The prevalence of peanut allergy is approximately 0.6%, and there is some evidence that this has increased (Grundy et al. 2002; Sampson 1996; Sicherer et al. 1999; Tariq et al. 1996). Tariq et al. (1996) described the prevalence of peanut allergy and peanut sensitization in a birth cohort of children born between 1989 and 1990. The prevalence of sensitization to peanut was 1.1% and the prevalence of confirmed peanut allergy was 0.5%. In 2001, a similar birth cohort, born between 1994 and 1996, was prospectively followed for evidence of peanut sensitization and allergy. The sensitization prevalence had increased to 3.2%, and the peanut allergy prevalence rose to 1.5% (Grundy et al. 2002).

Approximately 80% of peanut-allergic children develop allergic symptoms at the time of their first known exposure to peanut, > 90% develop symptoms within 30 min of ingestion, 90% have cutaneous features, 40% have respiratory symptoms, and 50% develop allergic manifestations to contact alone (Hourihane et al. 1997; Sicherer et al. 1998). After diagnosis and despite avoidance measures, most peanut-allergic children have accidental exposures to peanut resulting in allergic symptoms, and > 40% of subsequent allergic reactions may be more severe than the initial reaction (Bock and Atkins 1989; Vander Leek et al. 2000). However, in a subset of peanut-allergic children, up to 20% will become tolerant to peanut and will be able to reintroduce peanut into their diets (Hourihane et al. 1998; Skolnick et al. 2001; Spergel et al. 2000). Factors that appear to predict resolution of peanut allergy include mild cutaneous allergic features at onset, fewer associated atopic features, loss or diminution of skin prick test reactions to peanut, and low levels of peanut-specific IgE.

Studies on the natural history of allergies to other foods considered to be "lifelong" are scant. Although it does appear that most adults with shellfish allergy remain allergic to crustaceans, reports of individuals becoming tolerant to shrimp have been published (Daul et al. 1990). Likewise, it is possible that tolerance to other "persistent" food allergies may develop in some individuals, but publications provide little guidance in determining which patients may resume eating these foods. In the interim, patients with allergies to nuts, seeds, fish, and crustaceans are advised to avoid ingesting these foods indefinitely, unless oral challenge tests demonstrate acquisition of tolerance.

Treatment

The treatment of food allergy is limited to encouraging strict dietary vigilance and the ability to self-treat an allergic reaction if it were to occur. Maintaining dietary vigilance is difficult and stressful but can reduce the likelihood of experiencing an accidental ingestion of the allergic food (Bock and Atkins 1989; Ewan and Clark 2001; Primeau et al. 2000; Vander Leek et al. 2000). Currently, the only available therapy for food allergy is avoidance and self-treatment with auto-injectable epinephrine. Early administration of epinephrine is life-saving, and proper technique should be taught to all food-allergic individuals (Sampson et al. 1992). Promising immunotherapy interventions are being developed to diminish the severity of life-threatening food allergies but are not yet commercially available.

Conclusion

Food allergies affect between 5% and 8% of the pediatric population and between 1% and 2% of the adult population and appear to be rising. Many food allergies are "outgrown" during childhood, but some individuals never develop tolerance to some of the more commonly seen "transient" food allergens and remain symptomatic indefinitely. Factors associated with the persistence of "transient" food allergies include early onset, greater severity of allergy expression, collateral atopic conditions, persistence of skin prick test reactions, and elevated food-specific IgE. Conversely, a minority of individuals with allergy to foods traditionally believed to persist indefinitely have demonstrated loss of the allergy and clinical tolerance. Further research into the risk factors and associated clinical and laboratory tests that may predict persistence or resolution of food allergy may help to characterize this dichotomy.

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