CME

Food-induced Anaphylaxis: Who, What, Why, and Where?

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Food allergies affect up to 6% to 8% of children.[1] Food-induced anaphylaxis (severe allergic reaction) is the leading cause of anaphylaxis seen and treated in emergency departments in the United States.[2] Despite measures to help prevent accidental exposure, such as food labeling laws and food allergy education provided by healthcare providers to family members and caregivers, many children will experience accidental exposure. In fact, one study reported that 58% of children who were diagnosed with peanut allergy experienced an accidental peanut exposure within 5 years of their diagnosis.[3] Food allergen avoidance is difficult. Parents, children, and caretakers must maintain constant awareness of the foods that these children ingest.

This article discusses the epidemiology of food-induced anaphylaxis, implicated foods, characteristics of patients and other risk factors for food-induced anaphylaxis. Risk factors for fatal food-induced anaphylaxis are also reviewed.

EPIDEMIOLOGY

Food-induced anaphylaxis is the leading cause of anaphylaxis seen and

CME EDUCATIONAL OBJECTIVES

1. Review the epidemiology of food-induced anaphylaxis and identify the most commonly implicated foods.
2. Discuss patient-related factors that place individuals with food allergy at higher risk for food-induced anaphylaxis.
3. Identify factors that place individuals at higher risk for fatal food-induced anaphylaxis.

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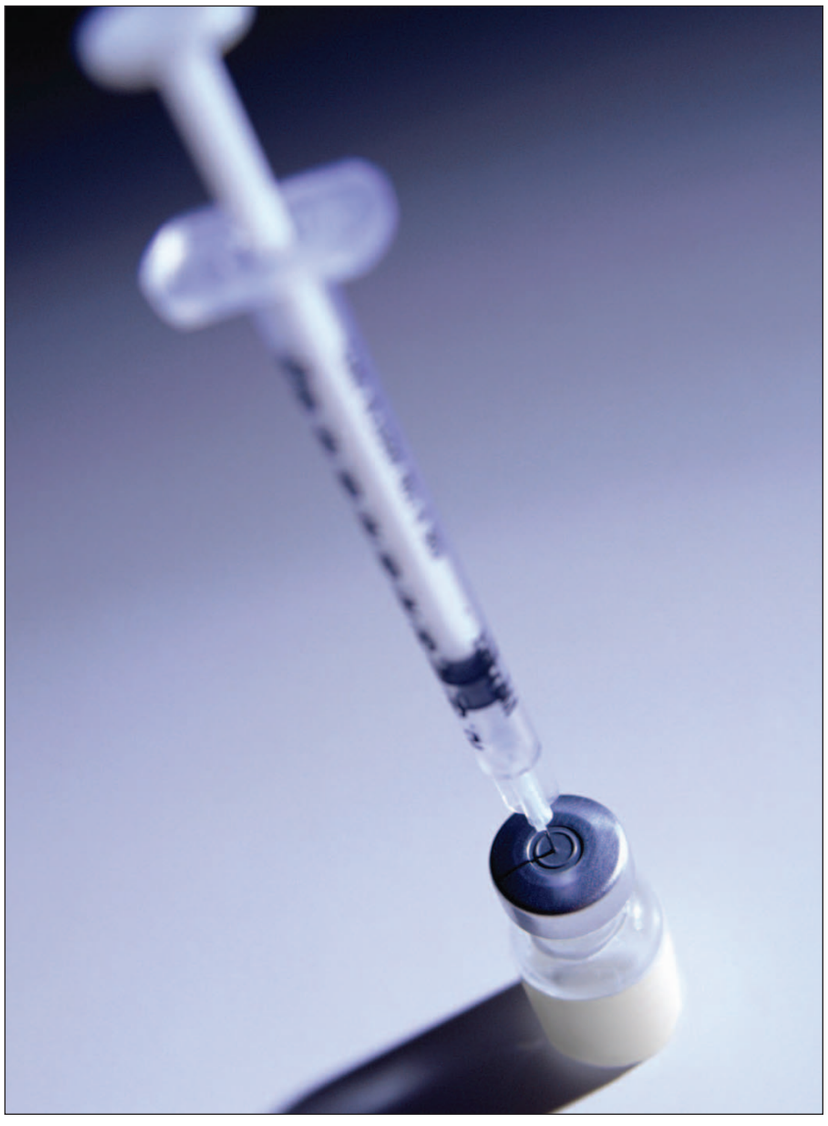
treated in emergency departments.[4] The National Electronic Injury Surveillance System (NEISS) is a database that collects data from 98 hospital emergency departments throughout the United States. A recent analysis of food-induced allergic and anaphylactic events from the NEISS indicated that 173 food-induced allergic events occurred during the 2-month study period in 34 participating emergency departments.[4] This study estimated that a total of 20,821 emergency department visits due to food-induced allergic events occurred nationally during the 2-month study period. In addition, food-induced anaphylaxis admissions have increased over the past several decades. In the United Kingdom, admission rates for anaphylaxis increased from 5 per million of population in 1990 to 1991 to 36 per million in 2003 to 2004.[5] In particular, food allergy admissions increased from 5 per million to 26 per million, and this trend was most dramatic in the pediatric population. A study in Australia discovered that there was an 8.8% increase yearly in the rate of hospital admissions for anaphylaxis per year between 1993 to 1994 and 2004 to 2005.[6] In children younger than 4 years, hospitalizations for anaphylaxis increased from 4.1 to 19.7 per 100,000 population over the study period. Food-related anaphylaxis increased by an average of 13.2% per year over the 12-year study period.



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IMPLICATED FOODS

Any food can cause anaphylaxis; however, there are certain foods that tend to be more commonly implicated in anaphylactic reactions. In the United States, the majority of severe allergic reactions are caused by peanuts and tree nuts. Data from the NEISS demonstrated that in children between 13 months and 5 years, such events most often involved peanuts and tree nuts.[4] In particular, patients with tree nut allergy are more likely to experience severe pharyngeal edema than those with peanut allergy.[7] In addition, fish and shellfish are also implicated in severe allergic reactions in children 6 to 18 years and in adults.[4] However, severe allergic reactions can be the result of any food, as evidenced by numerous case reports in the literature.

RISK FACTORS

Any patient with IgE-mediated food allergy is at risk for food-induced anaphylaxis. There are several patient-related factors that place some individuals at greater risk than others (see Sidebar, page 538).

Patients with a history of asthma and food allergy tend to have more severe food-induced allergic reactions. In patients hospitalized for anaphylaxis, patients with more severe reactions have coexisting asthma.[8] Life-threatening bronchospasm during anaphylaxis is also more likely in patients with severe asthma than those with milder asthma.[7]

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SIDEBAR.

Risk Factors for Anyaphylaxis, Non–fatal/Fatal

Risk Factors for Non–fatal Food-induced Anaphylaxis

High-risk food allergens:

— Peanut

— Tree nut

— Fish

— Shellfish

Diagnosis of asthma

Exercise

Severe rhinitis

Moderate to severe atopic dermatitis

Risk Factors for Fatal Food-induced Anaphylaxis

Patient age:

— Adolescents and young adults

High-risk food allergens:

— Peanut

— Tree nut

Consumption of food prepared outside of home setting

Diagnosis of asthma

Delayed administration of epinephrine

Exercise has also been identified as an important co-factor in certain patients. In a pediatric and adult study by Mullins et al, exercise was involved in 78 out of 262 (30%) patients with food-induced anaphylaxis.[9] The foods implicated in these patients included fruits and vegetables, wheat, nuts/seeds, shellfish, meats, soy, egg, and gelatin. Fruits, vegetables, and wheat accounted for 67% of the reactions. Almost all of the reactions occurred during exercise and within 6 hours after the ingestion of the implicated food. Interestingly, 60% of the reactions occurred within 1 hour after ingestion of the implicated food. Food-induced allergic reaction occurring during or soon after exercise is a well-described clinical syndrome. Food-dependent exercise-induced anaphylaxis (FDEIA) is defined as anaphylaxis that occurs when a patient exercises soon after the ingestion of an implicated food.[10] In patients with FDEIA, the implicated food can generally be tolerated in the absence of exercise. The most common food allergen implicated in FDEIA is wheat.[11] The pathophysiology of FDEIA is not well-understood. Current hypotheses include increased gut permeability leading to increased food absorption during exercise and abnormalities in the autonomic nervous system.[11]

Recent research from the United Kingdom has focused on identifying clinical and laboratory parameters that best predict the likelihood of severe food-induced allergic reactions.[7] The study population primarily consisted of children between the ages of 1 month and 15 years with peanut and tree nut allergy. The investigators identified that patients with a history of severe rhinitis, defined as rhinitis not controlled with oral antihistamines or intranasal steroids, were more likely to experience severe pharyngeal edema as a component of their food-induced allergic reaction. They also observed that patients with a history of moderate to severe atopic dermatitis were more likely to have altered levels of consciousness during a food-induced allergic reaction. This group also identified that patients with baseline serum angiotensin-converting enzyme concentrations less than 37 mmol/L had a 9.6-fold risk of severe pharyngeal edema.

In patients with a convincing history of food-induced allergic reaction, food-specific IgE concentrations may be used to identify those patients with a greater than 95% likelihood of clinical reactivity. However, food-specific IgE does not predict the type or severity of the reaction.[12] Likewise, wheal diameter size obtained through skin prick testing can also provide predictive information for likelihood of clinical reactivity to cow milk, egg, and peanut, but it does not predict severity.[13]

FATAL FOOD-INDUCED ANAPHYLAXIS

It has been estimated that there are 100 to 200 deaths per year caused by food allergy in the United States.[14] Food anaphylaxis fatalities have been described in both children and adults. In a 2-year prospective study of children less than 16 years of age in the United Kingdom and Ireland, there were three fatal and six near-fatal cases of food-induced anaphylaxis.[15] A similar study from the United States between 2001 and 2006 reported 31 fatal food allergic reactions in children and adults.[16] A study by Pumphrey reported 202 cases of fatal anaphylaxis of which approximately 25% were confirmed to be caused by food and approximately 10% were likely caused by food.[17]

Fatal food-induced anaphylaxis may occur at any age, but adolescents and young adults are at the highest risk. In a review of 32 food-induced

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fatalities in the United States, more than two-thirds of fatalities occurred in individuals between the ages of 13 and 21.[18] Similar findings have been reported in the United Kingdom. In 48 cases of fatal food-induced anaphylaxis in the United Kingdom between 1999 and 2006, 54% of the cases occurred in individuals between 11 and 30 years of age.[19] Fatal food anaphylaxis to cow's milk occurs mostly in young children, while fatal food anaphylaxis to peanuts and tree nuts occurs mostly in adolescents and young adults.[17] It is unclear why adolescents and young adults are at higher risk for food anaphylaxis fatalities. However, risk-taking behaviors and less adult supervision at those ages may play a role. In a survey of 174 adolescents and young adults with food allergy, 54% reported purposefully eating a food that potentially contained their particular food allergen.[20] More than half (57%) of the participants stated that the food "looked good" and that they wanted to eat it. Approximately one-fourth (23%) of the participants stated that they ate the food because they were with their friends. In fact, 29 of the 174 adolescents and young adults were considered high risk as they reported that they did not always carry self-injectable epinephrine and ate foods that potentially contained their food allergen. This high-risk group had a larger number of food allergic reactions in the previous 2 years (71%) compared with the rest of the participants (51%). Compared with the non-high-risk group, the individuals in the high-risk group were significantly more likely to report that they felt different from individuals without food allergies.

The type of food implicated in food-induced anaphylaxis also plays a role in fatality risk. A large number of food anaphylaxis fatalities are caused by peanuts and tree nuts although other foods, even milk and egg, have been reported. In six children with fatal food anaphylaxis, five of the fatalities were caused by peanuts and tree nuts.[21] In a larger patient series from the United Kingdom, 25 of 39 (64%) food-induced fatalities were caused by peanuts and tree nuts.[22] Similarly, a recent study from the United States reported 31 fatalities due to food-induced anaphylaxis, of which 25 (81%) were caused by peanuts and tree nuts.[16] This study also reported an increase in cow's milk-induced anaphylaxis fatalities in children compared with children studied between 1994 and 1999. Most patients had a known history of allergy to a specific food, but they did not know that the food allergen was an ingredient in the meal that resulted in death. In another study of fatalities caused by food-induced anaphylaxis, all but one patient had a known history of food allergy and had previously reacted to the food that caused the fatal reaction.[18]

The severity of a reaction appears to be at least partly determined by the time and onset of symptoms.

Food prepared in commercial settings or in settings outside of the patient's home is a risk factor for both near-fatal and fatal food-induced anaphylaxis. Approximately one-third of fatalities related to peanuts and tree nuts are caused by consumption of desserts that are prepared outside of the home.[16] In 129 patients with an allergic reaction to peanuts or tree nuts at restaurants or other food establishments, a large number of reactions occurred at Asian restaurants and dessert shops.[23] Surprisingly, only approximately half of the patients informed the restaurant about their particular food allergy. Fatal reactions have also been reported at schools and other childcare establishments.[18]

The severity of a reaction appears to be at least partly determined by the time to onset of symptoms. Severe reactions tend to be more rapid in onset. In six pediatric cases of fatal food-induced anaphylaxis, the initial symptoms occurred within 3 to 30 minutes of eating, and the onset of severe symptoms occurred somewhat later, between 20 and 150 minutes.[21] In three of these patients, the reactions were biphasic and included a symptom-free period between the initial onset of symptoms and the onset of severe symptoms.

The initial symptoms in fatal food-induced anaphylaxis can include cutaneous, respiratory, cardiovascular, gastrointestinal, and neurologic symptoms. However, in patients with fatal food-induced anaphylaxis, cutaneous symptoms are often less common than in near-fatal food-induced anaphylaxis. In six children with fatal food-induced anaphylaxis, only one had cutaneous symptoms compared to all seven children with nonfatal reactions.[21]

In many cases of food-induced anaphylaxis, the patients have a history of

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prior reactions to the implicated food. However, the previous reactions were generally not severe and, therefore, the severity of previous reaction cannot predict the severity of subsequent reactions.[17] In 61 children who had an initial mild reaction to peanuts, approximately one-third had a subsequent severe life-threatening reaction.[3] In a study of fatalities caused by food-induced anaphylaxis, all but one patient had a known history of food allergy and had previously reacted to the food that caused the fatal reaction.[21] In food allergy fatalities in children and adults in the United Kingdom, 22% of the fatalities had had a previous severe reaction to the implicated food.[22]

Food allergies and asthma often co-exist. Up to 24% of asthmatics with food allergy experience bronchospasm after challenge with the implicated foods.[24] In a prospective study of food-induced anaphylaxis in the United Kingdom and Ireland, all of the patients with fatal food-induced anaphylaxis had co-existing asthma.[15] Similarly, a retrospective study in the United States found that among 25 patients who died from food-induced anaphylaxis and in whom the asthmatic status was known, all but one had a history of asthma.[18] Fatal reactions in asthmatic children are often commonly caused by severe bronchospasm and respiratory failure.[22] The symptoms of bronchospasm during an anaphylaxis event in a patient who has food allergy and asthma may lead to confusion regarding appropriate treatment. This confusion may delay the administration of epinephrine.

The timely administration of epinephrine is current standard of care for severe food-induced anaphylaxis. Delayed administration of epinephrine may be a factor in some fatal reactions. In 32 cases of fatal food-induced anaphylaxis, 12 patients did not receive any epinephrine and 10 patients received delayed administration of epinephrine.[18] Other published case series have demonstrated this to be a common problem. In a study of 13 children with near-fatal and fatal food-induced anaphylaxis, only one patient of six with fatal food-induced anaphylaxis had received epinephrine within thirty minutes of ingestion of the implicated food.[21] Six of the seven patients with near fatal anaphylaxis received epinephrine within 30 minutes of the food ingestion. Of note, in the group of six children with fatal food-induced anaphylaxis there was a significant delay between the initial onset of symptoms and the time of the epinephrine dose compared to the group of seven children with near-fatal reactions. In the six children with fatal food-induced anaphylaxis the time between ingestion of the food and administration of epinephrine ranged between 25 minutes and 180 minutes, with the majority between 60 and 90 minutes. In the seven children with near-fatal food-induced anaphylaxis, all but one received epinephrine 10 to 30 minutes after ingestion of the implicated food.

Up to 24% of asthmatics with food allergy experience bronchospasm after challenge with the implicated foods.

Laboratory markers for the prediction of individuals at risk for fatal food-induced anaphylaxis are sorely needed. Interestingly, Vadas et al reported that platelet-activating factor (PAF) acetylhydrolase activity is significantly lower in patients with fatal peanut-induced anaphylaxis at the time of the event compared to those patients with mild peanut allergy, non-fatal peanut induced anaphylaxis, and healthy controls.[25]

SUMMARY

Food-induced anaphylaxis is a leading cause of anaphylaxis treated in emergency departments and hospitals around the world. Peanuts, tree nuts, fish, and shellfish are the most commonly implicated foods. Food-induced anaphylaxis may occur in any age group and with any food. However, food-induced anaphylaxis fatalities disproportionately affect adolescents and young adults with peanut and tree nut allergy. Individuals who have both IgE-mediated food allergy and asthma are at a higher risk for food-induced anaphylaxis fatality. Delayed administration of epinephrine is also associated with fatal outcome. Often, in fatal reactions, the food allergen is unknowingly ingested away from home, in settings such as restaurants and schools. Although avoidance of food allergens is critical, timely administration of epinephrine is also of great importance in the treatment of food-induced anaphylaxis. Patients, families, and caregivers must be well educated regarding the signs, symptoms and risk factors for anaphylaxis. They must also be counseled on the

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importance of strict food avoidance of the implicated food allergens, compliance with having self-injectable epinephrine available at all times, and the importance of timely administration of epinephrine, even when cutaneous symptoms are lacking.

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