

Anaphylaxis in the Young Adult Population

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ABSTRACT

It is critical that clinicians treating young adults understand the presentation and management of anaphylaxis. The most common trigger for anaphylaxis in this population is food. The prevalence of food allergy is growing, with 8% of US children and adolescents affected. All patients at risk for anaphylaxis should be prescribed epinephrine autoinjectors, as epinephrine is the only life-saving medication for a severe anaphylactic reaction. The presentation of anaphylaxis can involve multiple organ systems (eg, mucocutaneous, respiratory, cardiovascular, gastrointestinal) and, as such, patient education is needed to assist in prompt recognition. Appropriate training of patients and caregivers about how to identify anaphylaxis and what to do in an emergency is critical. Training of school and college staff also is essential, as 1 in 4 first-time reactions occurs outside the home. Additional counseling for adolescents at risk for anaphylactic reactions should address increased risk-taking behavior, decreased adult supervision, dating, and the transition of disease management from an adult to the patient.

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This article reviews several aspects of anaphylaxis in young adults. Although food allergy is the most common trigger of anaphylaxis in children and adolescents,^{1,2} other triggers include drugs, chemicals, insect venom, and exercise.^{3,4} Clinical manifestations most often involve the mucocutaneous, respiratory, cardiovascular, and gastrointestinal systems.^{5,6} Key aspects of management include a consistent history, appropriate diagnostic tests, medications,

counseling about identifying reactions and management, and referral to an allergist.⁷ The first-line medication for a patient experiencing an anaphylactic reaction is epinephrine, and patients should carry 2 epinephrine autoinjectors with them at all times.^{5,6,8} Management of anaphylaxis in young adults also involves training school and college personnel and developing management protocols in these settings.^{9,10}

EPIDEMIOLOGY AND IMPACT

Anaphylaxis is defined as “a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance.”¹¹ Several studies have shown increases in the incidence of anaphylaxis in the population at large.^{3,12-16} Common triggers include foods, drugs, chemicals, insect venom, and exercise. The top 8 food allergens associated with anaphylaxis are peanuts, cow's milk, shellfish, tree nuts, eggs, fin fish, wheat, and soy.¹⁷ Common medications associated with anaphylaxis include penicillins, nonsteroidal anti-inflammatory drugs, and biologic response modifiers.⁶

Food Allergy

Food allergy impacts up to 8% of children and adolescents in the US,¹⁸ corresponding to nearly 6 million nationwide.¹⁷ The National Center for Health Statistics of the Centers for

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Disease Control and Prevention reported an 18% increase from 1997 through 2007 in the national incidence of food allergy among individuals <18 years old.¹⁹ Food allergy is the most common trigger for anaphylaxis treated in the outpatient setting.^{1,2}

There is significant age-related variation in the prevalence of specific food allergens (**Figure 1**).¹⁷ Milk and egg allergies are seen more commonly in younger children, while allergies to shellfish and fin fish are more frequent in teens. Peanut allergy has a high incidence and is consistent across all ages. Tolerance seems to develop more frequently to milk, egg, wheat, and soy, compared with peanuts, shellfish, tree nuts, and fin fish.¹⁷

Drug Allergy

Anaphylaxis in young adults also may occur due to drug allergens, including medications, vaccines, natural rubber latex, radiocontrast media, and other chemicals. Skin tests and medication challenges can identify specific triggers. Once triggers have been identified, drug allergies can be managed using immunotherapy and desensitization.⁶ The actual incidence of drug allergies remains unclear. Studies have several limitations, such as inconsistent definitions, a focus on subpopulations or dermatologic reactions alone, or a failure to distinguish between immunologic and non-immunologic reactions.²⁰

Allergic reactions to vaccines may be due either to packaging (eg, latex stoppers) or the product itself.²¹ Anaphylactic reactions occur in approximately 1 per million doses. If a patient experiences anaphylaxis, later doses of the same vaccine are contraindicated. However, if

a patient experiences only minor symptoms (eg, skin reaction alone), risk of reaction with subsequent doses is generally less than the benefits of full vaccination. Full guidelines regarding the use of vaccines in patients with allergy have been disseminated by the American Academy of Allergy, Asthma and Immunology (AAAAI); the American College of Allergy, Asthma and Immunology; and the Joint Council of Allergy, Asthma and Immunology.²²

Insect Venom Allergy

The third most common allergy trigger is insect venom. As with drugs, the true incidence of allergy to insect venom is unknown, due to many of the same limitations, and varies substantially by location. However, it is known that allergy to insect venom is less common among children and adolescents than adults, who have a far greater likelihood of holding outdoor jobs with consequent exposure to insects.^{3,23}

Anaphylactic reactions in children and adolescents have been estimated to occur in 0.4%-0.8% of insect stings, with an estimated 40 fatalities annually in the US, although fatalities are likely significantly underestimated.²⁴ Venom-induced large local reactions have been reported in 2.4%-10.2% of all patients.²³ By definition, these reactions exhibit edema, pruritus, and erythema, have a diameter >10 cm, and peak at 1-2 days.²³

Costs of Anaphylaxis

The economic impact of anaphylaxis on society is not fully appreciated. Previous research has estimated the cost of food-induced allergic reactions in a combined pediatric and

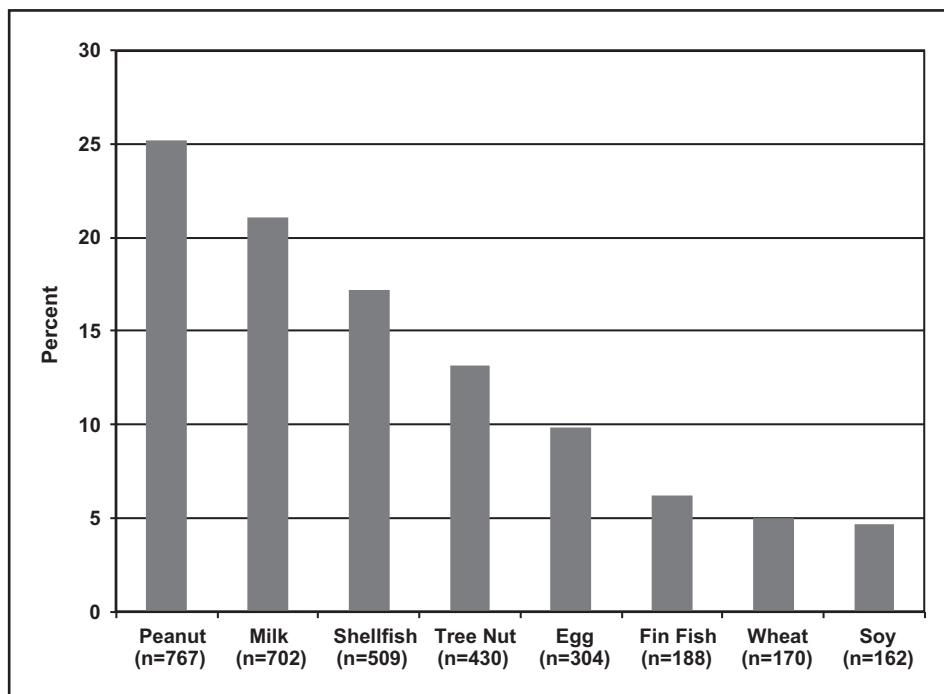


Figure 1 Prevalence of food allergens among children with food allergy.¹⁷

adult population to be \$500 million annually.²⁵ However, this study was limited, as it neglected resource use associated with the prevention of severe reactions and underestimated childhood food allergy.

A more recent study estimated the economic impact of food allergy specifically in children and adolescents.²⁶ Total annual direct and indirect costs were \$24.8 billion, or \$4184 per patient. An additional analysis by Sclar et al²⁷ of the economic costs of anaphylaxis in both adult and pediatric populations is presented in detail in another article in this supplement.²⁸

SIGNS AND SYMPTOMS

Signs and symptoms of anaphylaxis primarily involve the mucocutaneous, respiratory, cardiovascular, and gastrointestinal systems (**Figure 2**).^{9,29-31} The National Institute of Allergy and Infectious Diseases (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) have developed diagnostic criteria for food-induced anaphylaxis,¹¹ as discussed in more detail in the earlier article in this supplement by Dr Phillip Lieberman.³² (Note: As of November 12, 2012, FAAN merged with the Food Allergy Initiative under the name Food Allergy Research & Education [FARE].) Application of these criteria for children and adolescents has been summarized elsewhere.⁸

Presentation of anaphylaxis differs among patients and may vary within a single patient exposed to the same allergen on different occasions.⁶ It may be difficult to predict progression of any single reaction (eg, what starts as a mild attack may rapidly develop into a life-threatening reaction). Caregivers are encouraged to respond quickly to suspected anaphylaxis and monitor the patient based on symptoms exhibited. In addition, a biphasic reaction, in which clinical manifestations initially resolve but are followed several hours later by recurrent symptoms, occurs in 6%-11% of children and up to 23% of adults.^{6,8,33} A protracted reaction, in which symptoms may last for an extended time despite aggressive treatment, also may occur.²²

MANAGEMENT

The management strategy discussed earlier in this supplement³² and general treatment guidelines are often not easily

translated into clinical practice in young adults. A recent chart review conducted at 3 clinics in the Chicago area revealed a stark difference between developing and disseminating guidelines and actually implementing guidelines into clinical practice. For example, only 55% of charts documented prescription of an epinephrine autoinjector, 33% of charts documented patient education and counseling, and 77% of charts documented referral to an allergist for suspected food allergy.³⁴

In response to varied practices among these clinics, we developed a management protocol for food allergy for physicians that streamlines the NIAID guidelines into 5 categories to ensure optimal management in the primary care setting (**Table 1**).⁷ Basic management by a primary care provider is critical, as patients have been estimated to wait 4 months after being referred to an allergist for their first consultation.³⁴

There are 2 key medications used in response to allergic reactions: epinephrine (ie, EpiPen, EpiPen Jr, [Mylan Specialty L.P., Basking Ridge, NJ]; Auvi-Q [sanofi-aventis U.S. LLC, Bridgewater, NJ]; Adrenaclick [Amedra Pharmaceuticals LLC, Horsham, PA]; and an authorized generic of Adrenaclick) and antihistamines (eg, diphenhydramine). The branded epinephrine autoinjectors are unique and not interchangeable other than the generic for Adrenaclick, which can be substituted for Adrenaclick only. During a severe allergic reaction or anaphylaxis, the first-line choice for treatment is intramuscular epinephrine. Use of antihistamines alone is inappropriate for anaphylaxis.

Epinephrine Use and Training

Administration of epinephrine should be intramuscular in the mid-thigh using 0.01 mg/kg of the 1:1000 solution, to a maximum of 0.3 mg in children and 0.5 mg in adolescents and adults.^{5,6} Current epinephrine autoinjectors in the US (ie, EpiPen, EpiPen Jr, Auvi-Q, Adrenaclick, and an authorized generic for Adrenaclick) are available in pre-measured doses of 0.15 mg, indicated for weights of 15-30 kg, and 0.3 mg for weights ≥ 30 kg.³⁵⁻³⁸ A common issue when pediatricians prescribe an epinephrine autoinjector is selecting the appropriate dosage for patients.³⁹

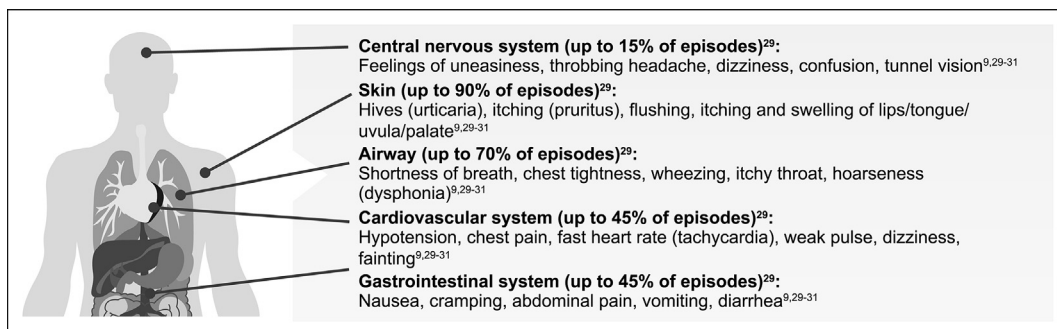


Figure 2 Signs and symptoms of anaphylaxis.^{9,29-31}

Table 1 Protocol for Assessment and Management of the Patient with Suspected Food Allergy⁷

Step	Category	Comments
1	Clinical history	Severe symptoms • Lung: shortness of breath, wheeze, repetitive cough • Heart: pale, blue, fainting, weak pulse, dizzy, confused • Throat: tight, hoarse, trouble breathing/swallowing • Mouth: obstructive swelling of throat/lips • Combination of symptoms from different sites: ○ Skin: hives, itchy rash, swelling ○ Gut: vomiting, diarrhea, crampy pain Mild symptoms • Mouth: itchy mouth • Skin: a few hives around mouth/face, mild itch • Gut: mild nausea/discomfort
2	Diagnostic testing	Gold standard: double-blind placebo-controlled food challenge With consistent clinical history: • Allergen-specific serum IgE • Skin prick • Oral food challenge
3	Medications	Epinephrine as first-line therapy
4	Counseling and education	Antihistamine and other medications can be added as judged appropriate Allergen avoidance Early recognition of signs/symptoms of anaphylaxis Emergency action plan Appropriate epinephrine autoinjector administration Wearing medical identification jewelry or carrying anaphylaxis wallet card
5	Referral	To an allergist

IgE = immunoglobulin E.

A precise dose may be desired for children <15 kg,⁶ but must be drawn up individually from an epinephrine ampule. If ampules are to be used, patients/caregivers should receive training on the proper method for drawing up each dose. The relative pros and cons of epinephrine autoinjectors versus ampules are discussed in the supplement article by Drs. Richard Nowak and Charles Macias.⁴⁰

Epinephrine autoinjectors must be replaced after the expiration date (typically 1 year from the date of issue),⁵ which should be checked on a regular basis and prior to use. The color of the fluid, normally clear, also should be verified before use. Clinics may ask patients to bring their devices to each visit in order to verify expiration dates. In addition, parents may receive reminder calls or e-mails from the prescriber, pharmacy, or autoinjector manufacturer. Devices should be stored at room temperature (eg, NOT in a car glove box) and protected from light to remain potent until the expiration date. To guard against a protracted or biphasic reaction, 2 autoinjectors should be prescribed and readily available to patients.⁵

Verbal training of each caregiver/patient is critical to ensure proper use.⁵ This should be accompanied by a pamphlet, DVD, or other tangible aid to reinforce training and educate other caregivers. (For example, brochures can be purchased from AAAAI at <https://aaaai.execinc.com/store/Default.asp> or downloaded for free from FARE at <http://www.foodallergy.org/resources/healthcare-providers>.)

Each autoinjector device has unique steps for use, so training must be specific to the product used. Previous research suggests that autoinjector training is often deficient among caregivers and physicians alike.⁴¹ All patients and their families should be trained on when and how to use an epinephrine autoinjector, and this may be done by the physician, nurse, or other delegated clinic personnel. A checklist to summarize the proper use and storage of epinephrine autoinjectors is shown in **Table 2**.^{5,6,35,36}

Counseling Adolescents

Unique issues related to adolescents must be considered when counseling about anaphylaxis management (**Table 3**). Adolescents have cited social isolation as the most difficult aspect of living with food allergy.⁴² Fatalities due to food-induced anaphylaxis may be seen in any age group, but the greatest risk is observed in adolescents and young adults, particularly reactions to peanuts and tree nuts.⁴³ Risk steadily increases with age in pediatric patients. For example, one survey found a >2-fold increase in risk among adolescents aged 14-17 years compared with children aged 0-2 years.¹⁷ The cause of the increased severity is unclear, but may be due to increased risk-taking and decreased supervision by adults.

Adolescents have many factors that may contribute to nonuse of an epinephrine autoinjector in an emergency

Table 2 Epinephrine Autoinjector Checklist^{5,6,35,36}

• Dosage	■ 0.01 mg/kg of 1:1000 solution — Premeasured epinephrine autoinjector 0.15 mg for weights 15-30 kg — Premeasured epinephrine autoinjector 0.3 mg for weights ≥ 30 kg ■ Maximum dose — 0.3 mg per dose in children — 0.5 mg per dose in adolescents and adults
• Administration	■ Intramuscularly ■ Lateral mid-thigh ■ Hold in place for 5-10 seconds ■ May inject through clothing ■ Never see the needle with autoinjectors
• Refills	■ Refill each year ■ Check expiration date and color of fluid (should be clear) prior to use
• Storage	■ Room temperature ■ Protect from light ■ Do NOT store in locations subject to temperature extremes (eg, car glove box)

(eg, lack of availability, poor training of patient/caregiver, risk-taking behavior). Noimark et al⁴⁴ surveyed children and adolescents in the UK and reported that 83% of patients experiencing anaphylaxis over a 1-year period did not use an epinephrine autoinjector (Table 4). Proper training, including practice giving injections with a trainer autoinjector and role-playing, both simulating emergency scenarios, can help to alleviate uncertainty and fear. Patients also should be educated that, after using an autoinjector, 911 should be called and further medical care is needed.

In a survey of adolescents and young adults aged 13-21 years, only 36% reported that their most recent reaction was “anaphylactic,” but this rate nearly doubled to 71% when asked about individual symptoms.⁴² Of these patients, 37% did not receive epinephrine. In practice, there seems to be a disconnect between commonly accepted diagnostic criteria and patient recognition of anaphylaxis. When patients are taught to use epinephrine for “anaphylaxis” rather than for specific symptoms, this misperception can pose a significant problem. Patients reported carrying an epinephrine

Table 3 Management Challenges in the Adolescent Population

- Increasing independence, resulting in more meals outside the home
- Peer pressure
 - Greater risk-taking
 - Reluctance to carry epinephrine autoinjector
- Administration of vaccines in the allergic patient
- Transitioning care from a parent or other caregiver to the patient
- Increasing activities outside of the home (eg, school/college, camps, sporting events)

Table 4 Reasons Among 245 Children and Adolescents for Nonuse of an Epinephrine Autoinjector during Anaphylactic Emergencies⁴⁴

Reason Cited for Nonuse	%
Thought autoinjector was not needed	54.4
Unsure whether autoinjector was needed	19.1
Had already called an ambulance	7.8
Autoinjector was not available	5.4
Was afraid to use autoinjector	2.5
Not trained to use autoinjector	2.5
Went to emergency department	1.5
Autoinjector had expired	1.0

autoinjector at all times in 61% of cases, but this varied widely according to location, activity, and extenuating circumstances (Figure 3).⁴² The authors advocate teaching parents to remind teens to carry an autoinjector to all social events, even when perceived risk is low.

Adolescents and young adults should be encouraged to discuss their allergy with significant others, including when to administer epinephrine and how to use an epinephrine autoinjector. Significant others may benefit from education and training by a health care professional. Food allergens may remain present in saliva for several hours after consumption. At a minimum, toothbrushing or waiting before kissing is suggested if the allergen isn't avoided entirely on days a couple will see each other.⁴⁵ Physicians should take the initiative to bring up such sensitive subjects as they may be uncomfortable for patients to discuss.

Another challenge is when to transition responsibility in management from an adult to the adolescent patient. In a survey of members of the American Academy of Pediatrics Section on Allergy and Immunology, most respondents expected patients aged 12-14 years to assume

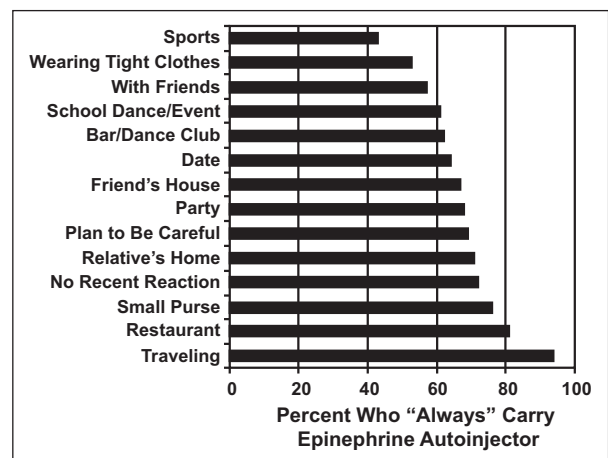


Figure 3 Percent of adolescents and young adults who “always” carry an epinephrine autoinjector on their person, reported by location, activity, and extenuating circumstances. (Reprinted with permission from *J Allergy Clin Immunol* © 2006 Elsevier.⁴²)

some responsibility for anaphylaxis management and use of an epinephrine autoinjector (**Table 5**).⁴⁶ **Table 5** also shows factors cited by >75% of respondents when assessing individual readiness to share responsibilities for management. Whenever transitioning care, thorough education and training of patients is critical.

Food Allergy Management in Schools

One in 13 children, or 2 students per classroom, have food allergy.¹⁷ Severe reactions were reported in 39% of subjects in this study. It is well established that the majority of food allergy reactions and deaths occur away from home.⁴⁷ In fact, approximately 25% of first-time anaphylactic reactions among children and adolescents occur at school.^{9,48} Although anaphylaxis in schools remains relatively rare, school fatalities due to anaphylaxis have been reported at an increasing frequency in recent years.⁹

Legislation has been passed and/or introduced to address this subject in schools.⁴⁹ The Food Allergy and Anaphylaxis Management Act was signed by President Barack Obama in January 2011. This law requires the Secretary of Health and Human Services to develop and disseminate voluntary guidelines to manage food allergy in schools. As of 2012, 19 states had school-based food allergy guidelines. Furthermore, emergency protocols for anaphylaxis in schools were required by 39 states.

The District of Columbia and all states but New York allow students with a prescription and proper consent to self-carry epinephrine autoinjectors.⁴⁹ The School Access to Emergency Epinephrine Act, introduced in Congress in

Table 5 Cumulative Portion of Pediatric Allergists Who Begin to Transfer Responsibilities for Anaphylaxis Management and Use of an Epinephrine Autoinjector to Patients Aged 12-14 Years, and Readiness Factors Assessed as "Very Important" by >75% of Respondents⁴⁶

	%
Skill/technique	
Describe some anaphylaxis symptoms	95.4
Demonstrate use of an epinephrine autoinjector trainer	93.1
Begin carrying an epinephrine autoinjector	88.2
Recognize need for epinephrine	88.1
Take responsibility for learning to self-inject epinephrine	84.5
Use an epinephrine autoinjector	78.6
Use a live autoinjector on an orange	38.3
Readiness factors assessed as "very important" by >75% of respondents	
Can demonstrate epinephrine autoinjector technique with trainer	96.4
Can describe reasons to inject epinephrine	92.9
Developmental level of patient	92.9
History of severe life-threatening anaphylaxis	89.3
History of >1 anaphylactic episode	79.8
Patient request	78.6
Cognitive or psychiatric comorbidity	75.0

late 2011, was signed into law on November 13, 2013. The bill encourages states to require schools to stock undesignated epinephrine autoinjectors and to ensure that school personnel are properly trained to use them in emergency situations. The bill was widely supported among professional organizations. Through 2012, Georgia, Illinois, Kansas, Maryland, and Virginia already had laws requiring or allowing undesignated epinephrine autoinjectors in schools. More information about these policies and programs to supply autoinjectors to schools can be found at <http://www.foodallergy.org>.

When selecting a college, its food-allergy policies should be considered (**Table 6**).⁵⁰ FARE maintains a database that can be used as a resource (<http://www.foodallergy.org/resources/college-students>).⁵⁰ College students are likely to

Table 6 Factors to Consider When Choosing and Attending a College, Camp, or Restaurant

Colleges⁵⁰

- Tour dining facilities and ask how meal ingredients can be verified
- Investigate housing options to ensure an allergen-free environment
- Distribute emergency action plan to roommates, residence advisor, boyfriend/girlfriend, etc., with all having ready access to an epinephrine autoinjector
- Consider the impact of alcohol on the individual and others
- Camps
 - Food allergy policies in place
 - Adequate health care staff and a designated emergency response team
 - Including appropriate coverage for any field trips
 - More complete health care services accessible within an acceptable distance
 - Emergency action plan provided to camp personnel

Restaurants^{51,52}

- Investigate restaurants online before dining out, including menus if available
- Restaurants should be able to provide customers with a list of meal ingredients, if requested
- Restaurant staff should be familiar with the principles of cross-contact
- When traveling, chain restaurants are likely to use the same ingredients at each site
- Particular caution with:
 - Fried foods (high risk of cross-contact)
 - Buffets and bakeries (high risk of cross-contact)
 - Pre-made foods
 - Restaurants with a large number of dishes prepared with allergens (eg, ice cream parlors, Asian restaurants, seafood restaurants)
 - Desserts (hidden allergens)
- Customers are encouraged to carry "chef cards," which can be given to staff to inform them of allergens (available at <http://www.foodallergy.org/document.doc?id=140>)
- Ask about allergy-friendly meals at catered events

consume alcohol themselves or be around others who do. Alcohol can increase the rate at which a food allergen is absorbed and impair judgment and muscle coordination, in addition to impairing judgment in others, who intentionally may give an allergen as a “prank.”

Food Allergy Management in Other Public Places

In addition to schools, management plans should be in place at restaurants, athletic events, camps, church activities, airports, workplaces, and any other settings where young people regularly gather (Table 6).^{51,52} A “fire extinguisher mentality” should be considered for epinephrine autoinjectors, similar to that increasingly adopted for automated external defibrillators, as they should be readily available to all people in high-risk public settings (eg, food courts).

Tips are available from FARE for patients to use when dining out (Table 6).^{51,52} However, despite thorough precautions by patients, restaurant staff members have been shown to have many misunderstandings about food allergy;⁵³ ultimately, individuals should be prepared for unintentional ingestion (eg, carrying an epinephrine autoinjector, wearing medical identification jewelry).

CONCLUSIONS

The rate of anaphylaxis is increasing in adolescents and young adults. Proper diagnosis and management are critical, as is counseling and education for this special population. All adolescents should be educated about signs and symptoms of anaphylaxis and how and when to use an epinephrine autoinjector. Increased risk-taking behaviors, dating, and transitioning care from adults to patients, among other factors, must be addressed. Management strategies also must be followed in public places where young adults regularly gather.

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