

Clinical diagnosis and management of anaphylaxis in infancy

Emine Dibek Misirlioglu, M.D.,¹ Emine Vezir, M.D.,¹ Müge Toyran, M.D.,¹ Murat Capanoglu, M.D.,¹ Hakan Guvenir, M.D.,¹ Ersoy Civelek, M.D.,¹ and Can Naci Kocabas, M.D.²

ABSTRACT

Background: Anaphylaxis is increasingly reported in infancy. Diagnosis and management of anaphylaxis is difficult, and data are limited in infants. The aim of the present study was to determine the clinical course and management strategies used for anaphylaxis in infancy.

Methods: Patients attending to our clinic and who had anaphylaxis under 2 years old were evaluated. Sixty-three patients were enrolled for the study. The mean $\pm$ standard deviation age was 10.6 ± 6.1 months (median, 11 months).

Results: Anaphylaxis occurred at home in 48 infants (76.2%). Food was the most common causative agent ($n = 52$ [82.5%]), with cow's milk ($n = 21$ [40.4%]) and egg white ($n = 13$ [25%]) being the most frequent. Medication was the other causative agent ($n = 9$ [14.3%]), with antibiotics being the most frequent ($n = 6$ [66.7%]). The clinical manifestations were cutaneous (95.2%) and respiratory symptoms (79.4%). The median time lapse between contact and onset of symptoms was 10 minutes (5–15 minutes) (median, interquartile range [IQR] 25–75%). The total duration of symptoms was 2 hours (0.5–3 hours) (median, IQR 25–75%). Six patients had mild (9.5%), 40 moderate (63.5%), and 17 severe (27%) symptoms. A biphasic course was noticed in two infants (3.2%), with a symptom-free interval between a minimum of 30 minutes and a maximum of 4 hours. Forty-three (68.3%) received H_1 antihistamines, 31 received corticosteroids (49.2%), and 23 received adrenaline (36.5%). Only one patient needed intensive care.

Conclusion: This study provided detailed clinical information in the diagnosis of anaphylaxis in infants. Diagnosing and managing anaphylaxis are difficult in infancy. Arrangements for definition of symptoms should be made in the new anaphylaxis guidelines.

(Allergy Asthma Proc 38:38–43, 2017; doi: 10.2500/aap.2017.38.4009)

Anaphylaxis is a serious generalized hypersensitivity reaction and is increasingly reported in infancy. There are few reports that provide information about the characteristics and course of anaphylaxis that occur in this special age group.¹ Anaphylaxis in infants can be triggered by a variety of agents, of which foods are the most common triggers. The most common responsible foods are cow's milk, egg, and peanut, but any food can be implicated, including tree nuts, soy and other legumes, fish, vegetables, fruits, and grains. Medications are other potential triggers: antibiotics, ibuprofen, and neuromuscular blockers are the most common susceptible agents. Latex and vaccinations can also cause anaphylaxis in infants.¹ Diagnosing and treating anaphylaxis in infancy have some special is-

ssues that should be taken into account during management.

Diagnosing anaphylaxis is difficult in infants. Most of the time infants cannot describe their symptoms, such as pruritus, throat tightness, and lightheadedness. Furthermore, some of the symptoms of anaphylaxis, such as behavioral changes, irritability, and incontinence of urine and stool, may also occur in healthy infants. Data are limited about the course of anaphylaxis in infants. The clinical course is usually reported to involve the skin, respiratory tract, and/or gastrointestinal tract. Cardiovascular symptoms are seldomly reported, and blood pressure is rarely documented because it is hard to measure in infants.¹

Adrenaline is the main treatment of anaphylaxis. However, other medications, such as antihistamines and corticosteroids, are more frequently used in emergency departments. Although helpful in the course of treatment, these medications cannot reverse anaphylaxis. After treatment of an anaphylactic episode at the emergency department, follow up by a pediatric allergist is important for confirmation of triggers, prevention of recurrences, and prescription of an adrenaline autoinjector (EAI).¹ For infants there are few options for optimal EAI dose for first-aid treatment. The EAI

From the ¹Department of Pediatric Allergy and Immunology, Ankara Children's Hematology Oncology Training and Research Hospital, Ankara, Turkey, and ²Department of Pediatric Allergy and Immunology, Muğla Sıtkı Kocman University, Muğla, Turkey

No external funding sources reported

The authors have no conflicts of interest to declare pertaining to this article

Address correspondence to Can Naci Kocabas, M.D., Department of Pediatric Allergy and Immunology, Faculty of Medicine, Muğla Sıtkı Kocman University, Muğla, Turkey

E-mail address: cankocabas@yahoo.com

Copyright © 2017, OceanSide Publications, Inc., U.S.A.

available with the lowest dose contains 0.15 mg of adrenaline; however, most of the infants need doses lower than this, and there is not a suitable alternative.² When ampule and syringes are given to parents, this may lead to inaccurate dosing and delays in administration. The aim of the present study was to determine the clinical course and management strategies used for anaphylaxis in infancy.

METHODS

Definition of Anaphylaxis and Severity Grading

The diagnosis of anaphylaxis was defined and classified according to the criteria indicated in the European Academy of Allergology and Clinical Immunology Taskforce on the management of anaphylaxis in childhood position paper (Table 1).³ The ethical committee of our hospital, Ankara Children's Hematology Oncology Training and Research Hospital, approved the study, all the parents of the participants provided written informed consent.

Collection of Data

From January 1, 2010, through July 30, 2015, we prospectively collected data on all consecutive patients who were admitted to our outpatient clinic for investigation and who had anaphylaxis when <2 years old. All the patients were evaluated by a pediatric allergist (E.V., M.C., H.G.). A detailed history was taken by using standardized questions, including (1) demographic data; (2) the symptoms of anaphylaxis; (3) the trigger of anaphylaxis and investigations used to confirm the implication of the trigger; (4) the course of anaphylaxis and the time lapse between contact with the trigger and onset of subsequent symptoms, total duration of symptoms, biphasic course or not; (5) the treatment of anaphylaxis and time lapse between the onset of symptoms and administration of medication; (6) exposure to the same agent before and a previous reaction; and (7) coexistence of allergic disease.

Description of the Symptoms

The symptoms were determined with separate questions for dermatologic, respiratory, gastrointestinal, and neurologic symptoms. Any rash, urticaria, or angioedema was labeled as dermatologic; wheezing, stridor, cough, and dyspnea were labeled as respiratory; and vomiting was labeled as gastrointestinal symptoms. We defined the symptom as neurologic if the infant had persistent crying, restlessness, decrease in activity level, and/or convulsions. Crying with a low-pitched or different voice was labeled as hoarseness. Increased salivation (drooling) was labeled as dysphagy. As indicated in the European Academy of Allergology and Clinical Immunology Taskforce position paper,³ hoarseness and dysphagy were labeled as respiratory symptoms. Hy-

Table 1 Grading the severity of anaphylactic reactions

Grade	Skin	GIS	Respiratory	CVS	Neurologic
Mild	Sudden itching of eyes and nose, generalized pruritus, flushing, urticaria, angioedema	Oral pruritus, oral itching, mild lip swelling, nausea or emesis, mild abdominal pain	Nasal congestion and/or sneezing, rhinorrhea, throat pruritus, throat tightness, mild wheezing,	Tachycardia	Change in activity level plus anxiety
Moderate	Any of the symptoms given above	Any of the above, crampy abdominal pain, diarrhea, recurrent vomiting	Any of the above, hoarseness, barky cough, difficulty swallowing, stridor, dyspnea, moderate wheezing	As above	Light headedness, impending feeling of doom
Severe	Any of the above	Any of the above, loss of bowel control	Any of the above, cyanosis, oxygen saturation <92%, respiratory arrest	Hypotension and/or collapse, dysrhythmia, bradycardia, and/or cardiac arrest	Confusion, loss of consciousness

GIS = Gastrointestinal system; CVS = cardiovascular system.

potonia and faintness may be symptoms of both cardiovascular and neurologic systems. We noted both cardiovascular and neurologic systems for these symptoms.

Identification of the Trigger

Skin-prick tests (SPT) and/or specific immunoglobulin E (sIgE) for the suspected etiologic agent were performed. When at least one of these tests was positive and the history was compatible, the agent was defined as susceptible for the anaphylactic reaction. The patients who had a clear history of medication anaphylaxis were diagnosed as having anaphylaxis due to that medication and without receiving any tests.

SPT

Depending on each individual case, SPTs were performed at least 4 to 6 weeks after the reaction with one or more of the following: (1) a commercial extract of suspected food and also of standard inhalant allergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Alternaria*, *Cladosporidium*, *Aspergillus*, cockroach, and cat and dog dander) (Stallargenes SA, Antony, France) and (2) a fresh sample of suspected food by means of prick-to-prick testing.

Allergen sIgE

Allergen sIgE levels were measured by using the CAP system (Phadia, Uppsala, Sweden). The sIgE test results were defined as positive if the results were above the detection limit (≥ 0.35 kU/L).

Statistics

All statistical analyses were performed with the SPSS 18.0 program (SPSS Inc., Chicago, IL). We expressed categorical variables as percentages. The values are presented as means and standard deviations for data that demonstrate a normal distribution, and as medians and interquartile ranges for data that do not demonstrate a normal distribution. A χ^2 test was performed to compare the nonparametric data, a Mann-Whitney test was used for non-normally distributed data, and an independent *t*-test was used for normally distributed continuous data. A *p* value of <0.05 was considered statistically significant.

RESULTS

During the study period, 248 patients with anaphylaxis were admitted to our clinic, and 63 of the patients (25.4%) had anaphylaxis when <2 years old.

Demographic Data and Place of Occurrence

Sixty-three patients who had anaphylaxis under 2 years old were enrolled for the study. Forty-two of the patients (66.7%) were boys. The mean (standard deviation)

age was 10.6 ± 6.1 months (median, 11 months). Anaphylaxis occurred at home in 48 patients (76.2%) and at the hospital in 12 patients (19.4%).

Triggers of Anaphylaxis

The anaphylactic triggers were identified in all the patients. Food was the most common causative agent ($n = 52$ [82.5%]) and medication was the other causative agent in this age group ($n = 9$ [14.3%]). Foods implicated most frequently were cow's milk ($n = 21$ [40.4%]), egg white ($n = 13$ [25%]), tree nuts (13 [25%]: 7 for nut, 3 for walnut, 1 for pistachio, 2 for almond), lentil ($n = 2$), 1 green pea ($n = 1$), fish ($n = 1$), and honey ($n = 1$). All of our patients, except one, had a reaction after direct ingestion of the offending food. All of the patients who had a history of food anaphylaxis had a positive SPT result and/or positive sIgE result. Nine children who had a history of medication anaphylaxis had not received any test and were diagnosed based on a history highly compatible with anaphylaxis due to drug intake. The medications implicated most frequently were antibiotics ($n = 6$ [66.7%]), 1 chemotherapeutic medication ($n = 1$), 1 antiepileptic medication ($n = 1$), and 1 ferroglycine sulfate ($n = 1$). The route of exposure to the medications was intravenous in 55.5% ($n = 5$), oral in 22.2% ($n = 2$), and intramuscular in 22.2% ($n = 2$) of the patients. Two patients had venom allergy.

Symptoms of Anaphylaxis

The clinical manifestations during anaphylaxis in order of frequency were cutaneous (95.2%), followed by the respiratory system (79.4%) (Table 2). Seventeen patients' families (27%) described their infant as crying with a hoarse voice (hoarseness) and 5 (7.9%) described drooling; and these symptoms were included in the respiratory system. Nine patients' families (14.3%) described hypotonia and faintness, 3 (4.8%) described only hypotonia. These symptoms were included in both neurologic and cardiovascular symptom groups. Six families (9.5%) described continuous crying and restlessness in their infants, and these symptoms were included in the neurologic symptom group.

Recurrence of Anaphylaxis

Thirty patients (47.6%) had a previous exposure to the same agent (25 to food, 5 to medication) and 27.9% of these patients ($n = 17$) had anaphylaxis (16 to food, 1 to medication) during previous exposure, two patients had experienced urticaria with the same food before the last reaction. Six patients had adrenaline, and two of them had an autoinjector, but none of them had used EAI during the reaction.

Table 2 Characteristic of the patients

Characteristics	Patients, no. (%) (<i>n</i> = 63)
Boys	42 (66.7)
Trigger	
Food	52 (82.5)
Medication	9 (14.3)
Venom	2 (3.2)
Route of allergen	
Enteral	54 (85.7)
Location of exposure	
Home	48 (76.2)
Hospital	12 (19)
Outdoors	3 (4.8)
Organ system involvement	
Skin	60 (95.2)
Respiratory tract	50 (79.4)
Gastrointestinal tract	30 (47.6)
Cardiovascular	14 (22.2)
Neurologic	15 (23.8)
Signs and symptoms	
Hoarseness	17 (27)
Persistent vomiting	9 (14.3)
Drooling	5 (7.9)
Hypotonia and faintness	9 (14.3)
Hypotonia	2 (4.8)
Crying	6 (9.5)
Time lapse between exposure and symptoms	
0-5 min	29 (46)
5-30 min	29 (46)
>30 min	5 (7.9)
Severity of anaphylaxis	
Mild	6 (9.5)
Moderate	40 (63.5)
Severe	17 (27)
Acute management of anaphylaxis	
Adrenaline	23 (36.5)
Steroid	31 (49.2)
H ₁ antihistamines	43 (68.3)
No treatment	15 (23.8)
Coexisting allergic diseases	44 (69.8)
Atopic dermatitis	26 (41.3)
Asthma	21 (33.3)

Course of Anaphylaxis

The median time lapse between contact with the trigger and onset of symptoms was 10 minutes (5-15 minutes) (median interquartile range [IQR] 25-75%). The total duration between the onset of symptoms and complete recovery was 2 hours (0.5-3 hours) (median IQR 25-75%). A biphasic course was noticed in two patients (3.2%), with a symptom-free interval between

a minimum of 30 minutes and a maximum of 4 hours. Two of the patients were girls. The etiologic agent was food in one and medication in the other patient. One patient was at home, the other patient was at the hospital during the reaction. One of the patients, who had food anaphylaxis, had had two episodes of anaphylaxis; the other patient, who had medication anaphylaxis, had only one episode of anaphylaxis until the last reaction. One of the patients who had severe anaphylaxis presented with respiratory and cardiovascular systems involvement, and the other patient who had moderate anaphylaxis presented with mucocutaneous and respiratory systems involvement. Concurrent allergic disease (recurrent wheezing and atopic dermatitis) was present in one patient with biphasic anaphylaxis.

Severity of Anaphylaxis

Six of the patients with anaphylaxis (9.5%) were classified as mild, 40 (63.5%) as moderate, and 17 (27%) as severe. These severity groups were separated as mild-moderate and as severe for better statistical analysis. There was no difference between the severity groups according to sex ($p = 0.422$), the place where anaphylaxis occurred ($p = 0.101$), and the coexistence of atopic disease ($p = 0.247$). Cardiovascular and neurologic manifestations were more common in the severe group ($p < 0.001$). Severe anaphylaxis was more frequent among patients with drug anaphylaxis and among patients who received the etiologic agent through the parenteral route ($p = 0.038$ and $p = 0.003$, respectively). The frequency of exposure to the same agent before and a history of anaphylaxis were not different among the severity groups ($p = 0.607$ and $p = 1.00$, respectively). The frequency of receiving adrenaline, corticosteroid, H₁ antihistamines, H₂ antihistamines, and fluid replacement at presentation was not different between the mild-moderate and severe anaphylaxis groups. There were no fatalities in our patients.

Treatment of Anaphylaxis

Forty-three patients (68.3%) received H₁ antihistamines, 31 (49.2%) received corticosteroids, 23 (36.5%) received adrenaline, 19 (30.2%) received fluid replacement therapy, 12 (19%) received β -2 mimetics, and 3 (4.8%) received H₂ antihistamines. Only one patient needed intensive care. Fifteen patients (23.8%) had no medications for treatment; all of them had had the reaction at home. The time lapse between the onset of symptoms and the first administration of medication was recorded in 45 of 63 patients, which ranged from 1 to 120 minutes (mean, 24 minutes; median, 15 minutes). In cases with severe anaphylaxis, this time lapse

ranged from 1 to 60 minutes (mean, 19 minutes; median, 12 minutes).

Atopic Status

Thirty-eight children (60.3%) had a personal history of atopic disease. Twenty-four of the patients (38.1%) had a family history of allergic disease. None of the families of the patients had a history of anaphylaxis. The number of anaphylactic episodes was not different between patients with or those without concurrent allergic disease (median, 1; $p = 0.343$).

DISCUSSION

Anaphylaxis is increasingly reported in infancy. Accordingly, in this study, it was determined that approximately a fourth (25.4%) of the patients with anaphylaxis admitted to our clinic had their first anaphylactic reaction during infancy. A wide range of frequencies were given in previous reports. Huang *et al.*⁴ reported that 3.1% of their cases with anaphylaxis (6/192) were infants; Silva *et al.*⁵ gave this frequency as 18%; and one study, conducted in our country, reported a frequency of 22.1%, close to our study results.⁶ The ambiguity of symptoms makes the diagnosis of anaphylaxis difficult, and this may have resulted in differences of frequency among the studies. Although reported as a wide range in different studies, it was noteworthy that an important part of anaphylaxis is seen during infancy.

A high index of suspicion is needed to diagnose anaphylaxis during infancy because symptoms may not be easily recognized. Early recognition of anaphylaxis and the use of adrenaline is very important. Clinical criteria for diagnosis in infants cannot be clearly defined.¹ Infants cannot describe some symptoms (*e.g.*, pruritus, throat tightness, lightheadedness), and some of the signs of anaphylaxis may be seen in a healthy infant (*e.g.*, irritability, regurgitation, urine incontinence). Furthermore, vital signs may be hard to measure but must be taken and should be interpreted according to age-adjusted reference ranges. Unfortunately we did not have information about the blood pressure measurement of our patients, and the absence of this information was a limitation of our study. However, patients had other criteria and symptoms of anaphylaxis, and the difficulty of blood pressure measurement and definition of anaphylaxis in infancy is reported in previous articles on the subject.¹

In our study, 17 patients' families (27%) described patients crying with a hoarse voice (hoarseness) and 5 (7.9%) described drooling, and these symptoms were defined as symptoms of the respiratory system. Nine patients' families (14.3%) described hypotonia and faintness, 3 (4.8%) described only hypotonia, and these symptoms were included in both neurologic and car-

diovascular symptoms. Six patients (9.5%) described continuous crying and restlessness, and these symptoms were defined as symptoms of neurologic system. Nonspecific symptoms, as mentioned above, are indicated in previous reports, and they are remarkable in this age group.^{6,7}

Clinical signs usually involve the skin, the respiratory tract, and/or the gastrointestinal tract during infancy. Rudders *et al.*⁷ reported that 98% of the patients with food-induced anaphylaxis during infancy presented with skin, 59% with respiratory, and 56% with gastrointestinal symptoms.⁷ In a report from our country, 78% of patients were reported to have presented with skin and respiratory involvement; 26% with skin and gastrointestinal involvement; and 4.3% with skin, gastrointestinal, and respiratory involvement.⁶ In our study, clinical manifestations in order of frequency were cutaneous (97.7%), respiratory system (79%), gastrointestinal tract (44%), cardiovascular (11%), and neurologic (9%). Cutaneous manifestations were the most common signs in all the patients. Six of the anaphylaxis cases (9.5%) were classified as mild, 40 (63.5%) as moderate, and 17 (27%) as severe. Similar results have been reported in the literature.⁶ Biphase anaphylaxis is also reported in infants.⁸ The previous reports noted that delayed administration of adrenaline and the need of adrenaline more than once are related to biphase reactions. Two of our patients had a biphase reaction. One had a food allergy and the other had medication allergy. Biphase reactions must be kept in mind when managing anaphylaxis during infancy, as in reactions in older children.

Food is the most common cause of anaphylaxis in children. Cow's milk is the most common trigger.⁹ As in a previous study,⁶ in our study, 82.5% of the cases were triggered by food, and cow's milk (40.4%), egg (25%), and tree nuts (25%) were the most common causative agents. Food-induced anaphylaxis can occur after direct ingestion or indirect ingestion through breast milk.¹ All but one of our patients had a reaction after direct ingestion of the offending food. Most reactions usually occur at home because food is the most common cause. This situation causes delay in the diagnosis and early intervention. In our study, 76.2% of the patients experienced anaphylaxis at home. The rate was lower when compared with the other study (76.2 versus 91.3%).⁶

Adrenaline is the main medication and should be administered as the first medication for anaphylaxis treatment. Fatal anaphylaxis is related to delayed use of adrenaline. Antihistamines and glucocorticoids are commonly given and are often used as the first medication, but none of these medications has been shown to reverse anaphylaxis.² It is important not to use these medications as initial treatment or as monotherapy.¹ In our study, 43 patients (68.3%) received H₁ antihista-

mines, 31 (49.2%) received corticosteroids, and 23 (36.5%) received adrenaline. In accordance with our results, it was reported that 100% of children <1 year old who had anaphylaxis received antihistamines and 95% received corticosteroids, whereas only 30% received adrenaline for treatment.⁶ The importance of adrenaline use as the initial treatment for anaphylaxis in infancy must be emphasized for better treatment of anaphylaxis. In our study, adrenaline was the third treatment that applied. One possible cause may be the difficulty of diagnosis in this age group.

Long-term management plans for anaphylaxis may be effective in reducing the risk of recurrence and the severity of subsequent reactions. EAI may be life saving for these patients, but, unfortunately, EAI is underprescribed and underused in the treatment of anaphylaxis.¹⁰ Fleischer *et al.*¹¹ reported that only 29.9% of infants with severe anaphylaxis received adrenaline injections. In our study, 23.8% of the patients ($n = 10$) had anaphylaxis before the last reaction. Six of these patients had adrenaline and two of them had an EAI, but none of them used their EAI at the time of reaction. Caregivers should be educated and encouraged to use EAI. Use of EAI is further problematic during infancy because available EAI contain higher adrenaline doses than an infant usually needs. It is hard for caregivers without a medical background to prepare the dose by using adrenaline vials and injection syringe, and it can take several minutes.¹ EAI that contain lower adrenaline would be used in infancy.^{2,12}

The main limitation of this study was that we did not have the chance to examine the patients at the time of anaphylaxis. Some of our patients were treated for anaphylaxis at other clinics, and we evaluated them when they were sent to our pediatric allergy clinic for consultation. All data we could gather from hospital reports and from caregivers were carefully recorded onto standard forms, but, unfortunately, some important data, *e.g.*, blood pressure, were not available for most of the patients. A prospective study, including examination during anaphylaxis, may help with a better definition. Another limitation was the low number of patients. When data on larger groups are collected, better information on infant anaphylaxis will be available.

CONCLUSION

This report provided detailed clinical information about anaphylaxis during infancy. Symptoms such as "hypotonia," "continuous crying," "restlessness," "drooling," and "crying with hoarse voice" can be incorporated into the symptoms of anaphylaxis for infants. Arrangements for definition of symptoms should be made in the new anaphylaxis guidelines.

REFERENCES

1. Simons FE, and Sampson HA. Anaphylaxis: Unique aspects of clinical diagnosis and management in infants (birth to age 2 years). *J Allergy Clin Immunol* 135:1125–1131, 2015.
2. Halbrich M, Mack DP, Carr S, et al. CSACI position statement: Adrenaline auto-injectors and children < 15 kg. *Allergy Asthma Clin Immunol* 11:20, 2015.
3. Muraro A, Roberts G, Clark A, et al. The management of anaphylaxis in childhood: Position paper of the European Academy of Allergology and Clinical Immunology. *Allergy* 62:857–871, 2007.
4. Huang F, Chawla K, Jarvinen KM, and Nowak-Wegrzyn A. Anaphylaxis in a New York City pediatric emergency department: Triggers, treatments, and outcomes. *J Allergy Clin Immunol* 129:162–168.e1–3, 2012.
5. Silva R, Gomes E, Cunha L, and Falcao H. Anaphylaxis in children: A nine years retrospective study (2001–2009). *Allergol Immunopathol (Madr)* 40:31–36, 2012.
6. Topal E, Bakirtas A, Yilmaz O, et al. Anaphylaxis in infancy compared with older children. *Allergy Asthma Proc* 34:233–238, 2013.
7. Rudders SA, Banerji A, Clark S, and Camargo CA Jr. Age-related differences in the clinical presentation of food-induced anaphylaxis. *J Pediatr* 158:326–328, 2011.
8. Mehr S, Liew WK, Tey D, and Tang ML. Clinical predictors for biphasic reactions in children presenting with anaphylaxis. *Clin Exp Allergy* 39:1390–1396, 2009.
9. Macdougall CF, Cant AJ, and Colver AF. How dangerous is food allergy in childhood? The incidence of severe and fatal allergic reactions across the UK and Ireland. *Arch Dis Child* 86:236–239, 2002.
10. White MV, Hogue SL, Bennett ME, et al. EpiPen4Schools pilot survey: Occurrence of anaphylaxis, triggers, and epinephrine administration in a U.S. school setting. *Allergy Asthma Proc* 36:306–312, 2015.
11. Fleischer DM, Perry TT, Atkins D, et al. Allergic reactions to foods in preschool-aged children in a prospective observational food allergy study. *Pediatrics* 130:e25–e32, 2012.
12. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis: A practice parameter update 2015. *Ann Allergy Asthma Immunol* 5:341–384, 2015. □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.