

Pitfalls in anaphylaxis diagnosis and management at a university emergency department

Amy Castilano, M.D.,¹ Britni Sternard, M.D.,² Earl D. Cummings, M.D.,² Runhua Shi, M.D., Ph.D.,³ Thomas Arnold, M.D.,² and Sami L. Bahna, M.D., Dr.P.H.¹

ABSTRACT

Background: Some previous reports revealed suboptimal management of anaphylaxis (ANX) in the emergency department (ED).

Objective: To evaluate the recorded diagnosis and management of patients who presented with ANX at our university hospital ED and to assess how the management correlated with the severity of the case and the training level of the ED staff.

Methods: A descriptive study that involved reviewing the electronic medical records of patients who presented with ANX at the ED during a period of 4 years.

Results: When reviewing 1341 charts of potential cases, 60 met the criteria for ANX, but only 23% were correctly coded. Inaccurate coding was noted in 77%, mainly as an "allergic reaction." Systemic corticosteroids were administered in the ED to 85% of the patients and H₁-antihistamines to 73%; only 20% received epinephrine. Ten patients required hospital admission, and, on discharge, only four patients (40%) were given epinephrine autoinjector prescriptions. Of the 50 who were discharged home, 48% were given epinephrine autoinjector prescriptions and 16% were given a referral for allergy evaluation.

Conclusion: The observed low rates of appropriate diagnostic coding of ANX, of epinephrine administration, epinephrine autoinjector prescribing at discharge, and referral for allergy evaluation call for more education on these issues. Some of these pitfalls can be partly attributed to the setting in a university ED where health providers are usually busy in rendering urgent care.

(Allergy Asthma Proc 39:316–321, 2018; doi: 10.2500/aap.2018.39.4144)

Anaphylaxis (ANX) is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after exposure to an allergen. Patients may present to the emergency department (ED) at various stages of the reaction, with symptoms that range from urticarial rash to life-threatening cardiorespiratory compromise. Despite published diagnostic criteria,^{1–3} misdiagnosis or inaccurate coding of ANX is common. Underrecognition of ANX can lead to suboptimal management, including the underuse or late administration of epinephrine as a first-line treatment.^{4–7} The objective of this study was to evaluate the diagnosis and management of patients who presented with ANX at a university hospital ED in the United States. We further assessed how the management correlated to the severity of the case and the training level of the ED staff.

METHODS

This retrospective, descriptive study involved reviewing the electronic medical records of patients who presented to a university ED during a 4-year period between January 1, 2012, and December 31, 2015, with symptoms consistent with ANX. The study was approved by the institutional review board of Louisiana State University Health Sciences Center in Shreveport. During this 4-year study period, our ED had a total number of annual patient visits between 64,200 and 64,920. Our emergency medicine department operates an accredited training program for 34 residents, with 20 faculty members and 8 physician extenders.

Cases were obtained from the electronic medical records by using the *International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9 CM)* and the *International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10 CM)* that cover the period of the study.^{8,9} Codes of ANX included ICD-9 CM: 995.0, 999.4, 999.6, 989.5; and ICD-10 CM: T78, T80, T63. To identify potentially missed cases, we also reviewed all cases coded as "allergic reaction" (ICD-9 CM: 995, 989, 477, 909, 693; and ICD-10 CM: T78, Z88, T63, T65, J30, T36) and were given an Emergency Severity Index of ≥ 3 , as designated by hospital protocol.¹⁰

There were 1341 total records of potential cases reviewed by us to identify true ANX cases. Subjects included were of any age who fulfilled generally ac-

From the ¹Allergy/Immunology Section, Louisiana State University Health Sciences Center, Shreveport, Louisiana, ²Emergency Medicine Department, Louisiana State University Health Sciences Center, Shreveport, Louisiana, and ³Medicine Department, Louisiana State University Health Sciences Center, Shreveport, Louisiana. Presented in part at joint AAAAI/WAO Congress in Orlando, Florida, March 1–5, 2018.

No external funding sources reported

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

Address correspondence to Sami L. Bahna, MD, Allergy and Immunology Section, Louisiana State University Health Sciences Center, 1501 Kings Highway, Shreveport, Louisiana 71130-3932

E-mail address: sbahna@lsuhsc.edu

Copyright © 2018, OceanSide Publications, Inc., U.S.A.

Table 1 Baseline demographics of 60 subjects with anaphylaxis who presented to the emergency department

Patient Characteristics	Study Population, no. (%)
Age (range 1–81 y)	
1–17 y	15 (25.0)
18–49 y	30 (50.0)
≥50 y	15 (25.0)
Sex	
Male	27 (45.0)
Female	33 (55.0)
Race	
White	14 (23.0)
African American	36 (60.0)
Unknown	10 (17.0)
Pertinent comorbidities	
Asthma	17 (28.3)
Cardiovascular disease	2 (3.3)
Concomitant medications	
Angiotensin-converting-enzyme inhibitor	2 (3.3)
β -adrenergic blocker	5 (8.3)

cepted National Institute of Allergy and Infectious Diseases/ Food Allergy and Anaphylaxis Network criteria of ANX,¹ briefly, as an acute severe systemic allergic reaction that involved at least two body systems. The initial review of the medical records was by a senior allergy/immunology fellow (AC), and every case with a possible diagnosis of ANX was reviewed with an ED attending staff (BS); an agreement between both of them settled the diagnosis. Rare instances required a consultation with the chief of the allergy/immunology section (SLB).

Statistical Analysis

In this descriptive study, the data were presented as frequencies, percentages, ranges; averages were presented as means or medians.

RESULTS

Demographics

We identified 60 cases that met the criteria for ANX. The patients' ages ranged from 1 to 81 years, with a median of 35.5 years and a mean $\pm$ standard deviation of 34 $\pm$ 19.7 years. There was a slight female predominance (55%), the majority of the patients were African American (60%), and 28.3% had a history of asthma (Table 1). On the occurrence of ANX, two patients were already receiving angiotensin-converting-enzyme inhibitors and five were on β -adrenergic blocking medications.

Treatment Before Arrival to the ED

Initiation of treatment began before arrival to the ED in 27 patients (45%). Of the 60 patients, H₁-antihistamines were taken by 20 (33.3%), and 9 (15%) received epinephrine (4 by self-administration and 5 by emergency medical service [EMS] personnel). Intravenous (IV) fluids were given to five patients, inhaled bronchodilators to four, corticosteroids to three, antiemetics to two, and H₂-antihistamines to one.

Causative Agent

The reported suspected causative agent was food in 17 (28.3%), insect sting in 14 (23.3%), a drug in 11 (18.3%), others in 5 (8.3%), and unknown in 15 patients (25.0%). Two agents were suspected in each of two patients.

Severity

The severity of ANX in our patients was graded as 1–5 according to the World Allergy Organization Systemic Reaction grading system (Table 2).¹¹ Grade 1 is for a single organ dysfunction and, therefore, by definition, did not meet our criteria for ANX. The majority of our patients (40 [67%]) had grade 2, 8 (13%) had grade 3, and 12 (20%) had grade 4 ANX. None of the patients in these cases was grade 5 (fatal ANX). Epinephrine was administered to a total of 21 patients (35.0%); 9 of whom (42.9%) received treatment before arrival to the ED and 12 (57.1%) in the ED. Of those who received epinephrine, the frequency was 32.5% for grade 2 and 40.0% for grades 3 and 4 combined.

ED Management

Only 14 of the 60 patients (23%) were correctly diagnosed as having had ANX, 32 (52.3%) were recorded as "allergic reaction," and 4 (6.7%) as "allergic reaction to insect sting." Epinephrine was administered to 12 patients (20.0%); intramuscularly in 8, subcutaneously in 3, and IV in 1 patient. The time from arrival to the ED until epinephrine was administered ranged from 4 to 69 minutes, with a median of 25 minutes and a mean $\pm$ standard deviation of 31 $\pm$ 20.7 minutes. In the 12 patients who received epinephrine, the prescribers were 10 senior-level residents (83%) at postgraduate years (PGY) 3, 4, and 5; and 2 (17%) were residents at PGY-1 or PGY-2 or were physician extenders. Systemic corticosteroids were administered to 85% and H₁-antihistamines to 73%.

Disposition and Follow-up

Disposition and follow-up information are presented in Fig. 1. Fifty patients were discharged from the ED with prescriptions for oral corticosteroids in 32 (64%), H₁-antihistamines in 28 (56%), and an epinephrine autoinjector in 24 (48%). Three additional patients already

Table 2 Epinephrine administration before arrival to the ED and during ED management according to anaphylaxis severity

Grade	Criteria Summarized*	Subjects, no. (%) (N = 60)	Epi before arrival to ED, no. (n = 9)	Epi in the ED, no. (n = 12)
1	Symptoms/signs of 1 organ system present	0	N/A	N/A
2	Mild symptoms in >1 organ system	40 (66.7)	5	8
3	Major respiratory compromise	8 (13.3)	1	4
4	Major cardiopulmonary compromise	12 (20.0)	3	0
5	Death	0	N/A	N/A

ED = Emergency department; Epi = epinephrine; N/A = not applicable.

*Abbreviated from Ref. 9.

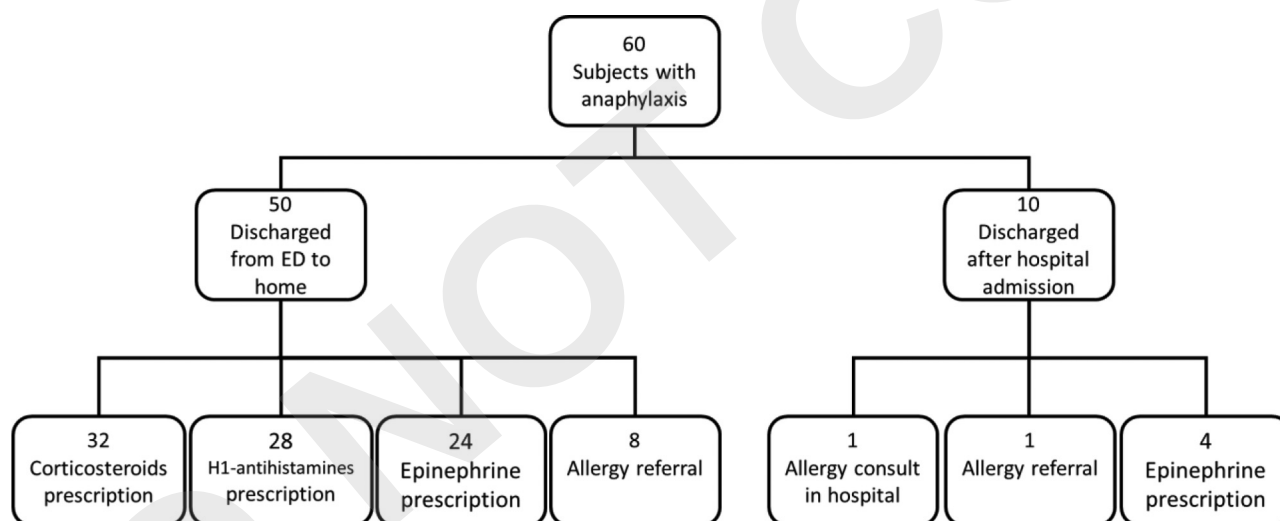


Figure 1. Disposition of 60 patients who presented with ANX to a university hospital emergency department.

had the autoinjector at home. Referral for outpatient allergy/immunology evaluation was recommended for eight patients (16%). Both an epinephrine prescription and referral for allergy/immunology were recommended for 6 (12%). Ten patients (17%) were admitted to the hospital for further observation and management; seven had ANX grade 4; only three had received epinephrine (one before arrival and two in the ED) (Table 3). One patient was on a β -adrenergic blocking medication. The allergy/immunology service was consulted on one patient during hospitalization, and a referral was recommended for another patient at discharge. At discharge, 4 of the 10 admitted patients received a prescription for an epinephrine autoinjector.

DISCUSSION

In reviewing 1341 records with a potential ANX diagnosis, 60 fulfilled the criteria. We would have liked

to increase our case numbers but the electronic medical records system at our institution was not available for a longer period. In similar studies the number of patients was 40 to 211, gathered over durations that ranged from 1 to 10 years, and some were from multiple centers.^{12–15} Our study revealed multiple important findings relevant to the diagnosis and management of ANX at a tertiary care center ED. Only approximately one-fourth of all the subjects who met the criteria of ANX were correctly diagnosed. Inaccurate coding was noted in 77%, mainly as an “allergic reaction” (52.3%), which, although not completely inaccurate, is not specific enough for the reaction’s phenotype.

Analysis of data from the U.S. National Electronic Injury Surveillance System revealed that 57% of the “likely anaphylactic events” to food allergy did not have an ED diagnosis of ANX.¹⁶ Another retrospective study, from Rochester, Minnesota, revealed that 25% of

Table 3 Characteristics of 10 subjects with anaphylaxis admitted to the hospital from the ED

Grade	Age, y	Sex	On β -blocker	Epi Given	Suspected Agent	Allergy Consulted in Hospital	Epi Prescribed at D/C	Allergy Referral at D/C
2	21	F	No	No	Insect sting	No	Yes	Yes
2	55	F	No	Yes (in ED)	Radiopaque contrast media	No	No	No
3	25	M	No	No	Insect sting	No	Yes	No
4	12	M	No	No	Chemotherapy	Yes	No	No
4	39	F	No	No	Iron (IV)	No	No	No
4	49	M	No	Yes (BA)	Insect sting	No	Yes	No
4	59	F	No	Yes (BA)	Unknown	No	No	No
4	60	F	Yes	No	Neomycin, polymyxin B, bacitracin	No	Yes	No
4	78	M	No	No	Chemotherapy	No	No	No
4	81	F	No	No	Chemotherapy	No	No	No

ED = Emergency department; Epi = epinephrine; D/C = discharge from hospital; BA = before arrival to ED.

211 ANX cases were given less-specific allergy codes.¹⁰ This observation may be attributed to either improvement in symptoms by the time of arrival to the ED or to a reluctance of the ED staff to correctly diagnose mild-to-moderate cases of ANX. Underdiagnosis may lead to suboptimal management, including the nonadministration of epinephrine.

Before arrival to our ED, epinephrine was administered to a total of nine patients (15%); four by the patient and five by the EMS personnel. Such a low figure is similar to the reported 15% administered by EMS in a series of 103 subjects.¹⁷ A review of medical records of young patients (<26 years old) who presented with ANX to the ED or the urgent care center revealed that only 36.3% received epinephrine before arrival.¹⁸ The low rate of epinephrine administration, despite its being recommended worldwide as the first-line treatment,^{3,19,20} reflects the judgment by patients and/or parents or EMS staff. In the ED, epinephrine was administered to 12 subjects, which brought the total number of patients who received epinephrine to 21 (35%).

This is similar to previously reported figures: 27% of 64 patients in one study¹³ and 32.5% of 40 patients in another series.¹⁵ The prescribers of epinephrine were senior-level residents (PGY-3 to PGY-5) or faculty members in 83% of the cases, whereas 17% were PGY-1, PGY-2, or physician extenders. Low epinephrine administration rates may be partly attributed to some providers' concern about the potential risk of the drug, particularly in adults. Such concern should be alleviated by the findings published in the literature and reviewed by Wood *et al.*,²¹ who noted that intramuscular epinephrine is safe for ANX in children and adults. Adverse reactions were due to dosing errors or a cardiovascular disease, or when using the IV route.

The timing from arrival to our ED ranged from 4 to 69 minutes, with a median of 25 minutes and a mean of 31 minutes. Although none in our series had a fatal outcome, rapid administration of epinephrine within minutes of onset of symptoms has been shown to be the major factor for improved outcome.^{3,20,22,23} We did not find reliable data in our records on the timing of epinephrine administration from the onset of ANX symptoms. In a series of six patients with fatal ANX to food despite epinephrine administration, the earliest injection was 25 minutes or later after allergen ingestion.²⁴ Several factors may influence the timing of epinephrine administration, including the immediate availability of the drug or the severity of the reaction, or when seeking medical help of the EMS or ED staff. In our series, although epinephrine was administered in the ED to only 20% of the subjects, systemic corticosteroids were administered to 85% and H₁-antihistamines to 73%. Even higher figures were reported in another study; corticosteroids were administered to 95% and antihistamines to 86%.¹⁶ The occurrence of biphasic ANX was reported to be related to the severity on the initial reaction and not to a lack of corticosteroids administration.^{25,26}

The administration of epinephrine was intramuscular in the majority of our patients (75%). In recent years, there has been a shift in the preferred administration route from subcutaneous to intramuscular. The latter route has been associated with a much earlier and higher epinephrine plasma concentration.²⁷ At discharge from the ED, epinephrine autoinjector prescriptions were given to only half of the patients and allergy evaluation was recommended to only one of six patients. Even lower figures were reported by other studies. A retrospective review of records obtained from an ED in Spain revealed that only 6.7% of children treated

for ANX were given a prescription for epinephrine autoinjectors.¹³ A questionnaire completed by ED physicians in Belgium revealed that only 8.7% of patients with ANX received a prescription for an epinephrine autoinjector at discharge.¹⁴

Such figures are far below expectation when considering the widely publicized guidelines for management of ANX^{1,3,23,28} and point to the great need for further education on this issue, not only for health care providers but also for patients. It is not clear whether the low rate of prescribing epinephrine autoinjectors is being influenced by the cost. In the United States, the cost for a twin pack of autoinjectors was constantly increasing and reached close to \$700, with a high out-of-pocket payment. The cost was recently reduced after the issue was vigorously addressed in the media and prompted intervention by legislators as well as development of formulations by other manufacturers.

A telephone interview of 41 of the subjects who reported allergic reactions after exposure to peanuts in commercial flights revealed that, although, self-injectable epinephrine was prescribed to 32 (80%), only 20 (63%) stated that they carried it regularly, and 12 (29%) had it on the flight.²⁹ Such a finding should emphasize the importance of patient education on filling the prescription and keeping the autoinjector available for immediate use. A recent study in Canada reported that, of 1212 epinephrine autoinjector prescriptions, 69.9% were filled within 90 days.³⁰

A retrospective review of 2622 cases of severe ANX revealed that filling a prescription for an epinephrine autoinjector and allergy evaluation by an allergist lowered the risk of subsequent severe episodes.³¹ Self-injectable epinephrine should be particularly emphasized in patients with a concomitant history of asthma, a major risk factor for fatal ANX.^{3,23} In our series, we noted that 17 (28.3%) of the patients had asthma, 8 of whom received epinephrine: 3 before arrival to the ED and 5 in the ED. In our series, the records did not contain specific information on instructing patients who received prescriptions for epinephrine autoinjectors on when and how to use it. The instruction may have been provided to some patients but not recorded. We also did not have information on the rate of filling the prescriptions.

CONCLUSION

Our study supported the findings of previous studies in revealing multiple pitfalls in the diagnosis and management of ANX in the ED. There is a great need for education on the correct diagnosis and coding, and on appropriate management regarding epinephrine administration, on prescribing and instructing on epinephrine autoinjectors, and referral for allergy evaluation. Actually, the findings prompted us to incorporate

the topic of ANX in our emergency medicine residents' teaching core conferences. We recommend the same for other hospitals, although some of these pitfalls may not be totally avoidable in EDs where health providers can be busy in rendering urgent care.

ACKNOWLEDGMENTS

The authors thank Kim Hutchinson and Bret Crenshaw for their valuable assistance in the preparation of the study's documents and data extraction.

REFERENCES

1. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report—second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *Ann Emerg Med.* 2006; 47:373–380.
2. Simons FE, Arduoso LR, Bilò MB, et al. World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis. *World Allergy Organ J.* 2011; 4:13–37.
3. Simons FE, Ebisawa M, Sanchez-Borges M, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J* 2015; 8:32.
4. Patel BM, Bansal PJ, and Tobin MC. Management of anaphylaxis in child care centers: evaluation 6 and 12 months after an intervention program. *Ann Allergy Asthma Immunol.* 2006; 97:813–815.
5. Gaeta TJ, Clark S, Pelletier AJ, and Camargo CA. National study of US emergency department visits for acute allergic reactions, 1993 to 2004. *Ann Allergy Asthma Immunol.* 2007; 98:360–365.
6. Wheeler DW, Carter JJ, Murray LJ, et al. The effect of drug concentration expression on epinephrine dosing errors: a randomized trial. *Ann Intern Med.* 2008; 148:11–14.
7. Kanwar M, Irvin CB, Frank JJ, Weber K, and Rosman H. Confusion about epinephrine dosing leading to iatrogenic overdose: a life-threatening problem with a potential solution. *Ann Emerg Med.* 2010; 55:341–344.
8. International Classification of Diseases, Ninth Revision, (ICD-9-CM), Geneva, World Health Organization, 1977. Clinical Modification (ICD-9-M). <https://www.cdc.gov/nchs/icd/icd9cm.htm>.
9. International Statistical Classification of Diseases and Related Health Problems (ICD-10). 10th Revision, Fifth edition, Geneva, World Health Organization, 2016. Clinical Modification (ICD-10-M). <https://www.cdc.gov/nchs/icd/icd10cm.htm>.
10. Wuerz RC, Milne LW, Eitel DR, Travers D, and Gilboy N. Reliability and validity of a new five-level triage instrument. *Acad Emerg Med.* 2000; 7:236–242.
11. Cox L, Larenas-Linnemann D, Lockey RF, and Passalacqua G. Speaking the same language: The World Allergy Organization subcutaneous immunotherapy systemic reaction grading system. *J Allergy Clin Immunol.* 2010; 125:569–574, 574.e1–574.e7.
12. Decker WW, Campbell RL, Manivannan V, et al. The etiology and incidence of anaphylaxis in Rochester, Minnesota: a report from the Rochester Epidemiology Project. *J Allergy Clin Immunol.* 2008; 122:1161–1165.
13. Arroabarren E, Lasa EM, Olaciregui I, Sarasqueta C, Muñoz JA, and Pérez-Yarza EG. Improving anaphylaxis management in a pediatric emergency department. *Pediatr Allergy Immunol.* 2011; 22:708–714.
14. Mostmans Y, Grosber M, Blykers M, Mols P, Naeije N, and Gutermuth J. Adrenaline in anaphylaxis treatment and self-administration: experience from an inner city emergency department. *Allergy.* 2017; 72:492–497.
15. Wright CD, Longjohn M, Lieberman PL, and Lieberman JA. An analysis of anaphylaxis cases at a single pediatric emergency

- department during a 1-year period. *Ann Allergy Asthma Immunol.* 2017; 118:461–464.
16. Ross MP, Ferguson M, Street D, Klontz K, Schroeder T, and Luccioli S. Analysis of food-allergic and anaphylactic events in the National Electronic Injury Surveillance System. *J Allergy Clin Immunol.* 2008; 121:166–171.
 17. Manivannan V, Hyde RJ, Hankins DG, et al. Epinephrine use and outcomes in anaphylaxis patients transported by emergency medical services. *Am J Emerg Med.* 2014; 32:1097–1102.
 18. Robinson M, Greenhawt M, Stukus DR. Factors associated with epinephrine administration for anaphylaxis in children before arrival to the emergency department. *Ann Allergy Asthma Immunol.* 2017; 119:164–169.
 19. Muraro A, Roberts G, Worm M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy.* 2014; 69:1026–1045.
 20. Sicherer SH, Simons FE, and AAP Section on Allergy and Immunology. Epinephrine for first-aid management of anaphylaxis. *Pediatrics.* 2017; 139:e20164006.
 21. Wood JP, Traub SJ, and Lipinski C. Safety of epinephrine for anaphylaxis in the emergency setting. *World J Emerg Med.* 2013; 4:245–251.
 22. Fleming JT, Clark S, Camargo CA Jr, and Rudders SA. Early treatment of food-induced anaphylaxis with epinephrine is associated with a lower risk of hospitalization. *J Allergy Clin Immunol Pract.* 2015; 3:57–62.
 23. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis—a practice parameter update 2015. *Ann Allergy Asthma Immunol.* 2015; 115:341–384.
 24. Sampson HA, Mendelson L, and Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med.* 1992; 327:380–384.
 25. Alqurashi W, Stiell I, Chan K, Neto G, Alsadoon A, and Wells G. Epidemiology and clinical predictors of biphasic reactions in children with anaphylaxis. *Ann Allergy Asthma Immunol.* 2015; 115:217–223.e2.
 26. Alqurashi W, and Ellis AK. Do corticosteroids prevent basic anaphylaxis? *J Allergy Clin Immunol Pract.* 2017; 5:1194–1205.
 27. Simons FE, Roberts JR, Gu X, and Simons KJ. Epinephrine absorption in children with a history of anaphylaxis. *J Allergy Clin Immunol.* 1998; 101:33–37.
 28. Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy.* 2014; 69:1008–1025.
 29. Comstock SS, DeMera R, Vega LC, et al. Allergic reactions to peanuts, tree nuts, and seeds aboard commercial airliners. *Ann Allergy Asthma Immunol.* 2008; 101:51–56.
 30. Abrams EM, Singer AG, Lix L, Katz A, Yogendran M, and Simons FER. Adherence with epinephrine autoinjector prescriptions in primary care. *Allergy Asthma Clin Immunol.* 2017; 13:46.
 31. Clark S, Wei W, Rudders SA, and Camargo CA. Risk factors for severe anaphylaxis in patients receiving anaphylaxis treatment in US emergency departments and hospitals. *J Allergy Clin Immunol.* 2014; 134:1125–1130. □

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.