

Accidental versus new food allergy reactions in a pediatric emergency department

Peter Capucilli, MD^{a,b}, Katie Kennedy, MD^{a,b},
Juhee Lee, MD^{a,b}, Robert W. Grundmeier, MD^{b,c}, and
Jonathan M. Spergel, MD, PhD^{a,b}



Clinical Implications

- Although the rate of emergency department visits due to food allergy and anaphylaxis appears to be increasing, this study in a pediatric population provides evidence that unexpected or accidental reactions to established food allergens requiring emergency department evaluation are rare.

TO THE EDITOR:

Food allergy (FA) remains a growing problem and is the leading cause of anaphylaxis in children.¹ Strict adherence to avoidance diets remains the best option in preventing food reactions, although food desensitization trials are ongoing. Patients and families are regularly educated about the possibility of unexpected or accidental FA reactions (AFARs); however, the exact frequency with which these occur is not definitively known. Systematic reviews have addressed this, but acknowledge the limits of comparability across studies due to heterogeneity in methodology and study populations.^{2,3} In review of 34 studies, Umasunthar et al³ reported that the incidence of anaphylaxis in patients with known FA was low. Other reports, including a prospective study by Fleischer et al,⁴ found rates of AFARs to be more striking, with roughly 87% of reactions in their study being secondary to accidental exposures (as compared with new food reactions in study participants). Data have also clearly shown an increase in emergency department (ED) visits secondary to FA, both by hospital billing code and case history assessments.^{5,6} However, the frequency of AFARs requiring ED level care in children with established FA remains in question. The objective of our study was to estimate the incidence of AFARs in children requiring ED evaluation in a select population.

We identified all children presenting to the Children's Hospital of Philadelphia (CHOP) ED between January 1, 2014, and December 31, 2017, with food-related allergic reactions or anaphylaxis using International Classification of Disease ninth/tenth revision (ICD-9/10) diagnostic codes, including ICD-9 (995.60-9, 995.7, 995.0), ICD-10 (T78.40XA, T78.40XD, T78.00XA, T78.01XA, T78.1XXA, T78.05XA, T78.02XA, T78.07XA, T78.08XA). We limited our review to children with current home address within 6 contiguous zip codes previously identified for which >90% of children <18 years of age would preferentially be referred to our hospital's ED services,⁷ and estimated FA prevalence based on previously defined rates within the CHOP care network.⁸

A structured chart review of ED documentation was performed to characterize patient demographics, atopic history,

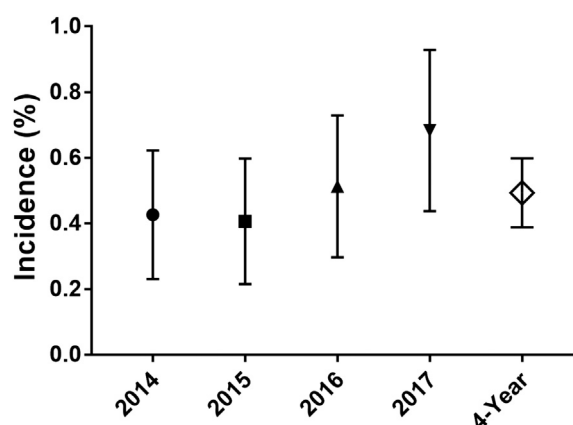


FIGURE 1. Yearly and 4-year incidence of accidental food allergy reactions.

ED presentation, treatment, and follow-up. We defined AFARs as reactions consistent with an IgE-mediated process, in which onset of reaction was immediate and triggered by a previously identified food allergen. Reactions to nonfood triggers were excluded. Histories deemed consistent with IgE-mediated food reactions were then differentiated as either new FA reactions (NFARs) (reaction to a food without previously identified allergy) or as an AFAR. The incidence of AFARs from 2014 to 2017 was determined cumulatively and for each individual year. Percentage of food culprits and reaction classification were also defined. Charts were reviewed by 2 pediatric allergy fellow physicians, with discrepancies determined by an attending allergist. Initial inter-rater agreement for qualitative parameters was measured using Cohen's kappa coefficient. Data were analyzed using GraphPad v.7 (Prism Software, San Diego, Calif) and STATA v.15 (StataCorp LP, College Station, Texas). The study was approved by the CHOP Institutional Review Board.

A total of 316 charts were reviewed, of which 53 were excluded for allergic reactions secondary to nonfood triggers (n = 31), or cases with no documented concern for allergic reaction (n = 22), despite the presence of a billing code diagnosis for allergic reaction. A remaining 263 visits suggested a food-induced reaction. On review, 95 cases were deemed inconsistent with IgE-mediated FA, with the following reasons implicated: inconsistent time course; acute/chronic idiopathic or viral urticaria/angioedema more likely; vomiting, wheezing consistent with infection; environmental allergic rhinoconjunctivitis and/or asthma exacerbation. We found 168 cases to be consistent with an IgE-mediated food reaction, of which 77 (46%) were considered NFARs and 91 (54%) AFARs. Initial inter-rater reliability showed 89% agreement for reactions considered to be AFARs and 90% for those considered NFARs ($\kappa = 0.79$ and 0.82, respectively).

The 4-year incidence of AFARs was 0.5% (95% confidence interval, 0.4% to 0.6%), with individual yearly incidence rates depicted in Figure 1 and enumerated in Table 1 with patient demographics. Most AFARs (83%) involved multisystem anaphylaxis, and roughly 40% were secondary to peanut or tree

TABLE 1. Classification of accidental and new food allergy reactions

	4-year AFAR rates N = 91	4-year NFAR rates N = 77
Total N (%) [*] reactions	91 (54)	77 (46)
N reactions [incidence rate %; 95% CI]		
Cumulative 4 y	91 [0.5; 0.4-0.6]	NC
2014	19 [0.4; 0.2-0.6]	NC
2015	18 [0.4; 0.2-0.6]	NC
2016	23 [0.5; 0.3-0.7]	NC
2017	31 [0.7; 0.5-0.9]	NC
Patient characteristics, N (%)		
Mean age, range (y)	8 (0.5-19)	6.2 (0.4-18)
Female gender	43 (47)	41 (53)
Known CHOP patient	49 (54)	16 (21)
Atopic history, N (%)		
Hx SAR	59 (65)	23 (30)
Hx atopic dermatitis	47 (52)	34 (44)
Hx asthma	66 (73)	36 (47)
Hx urticaria	5 (6)	4 (5)
Hx multiple FA	73 (80)	21 (27) [†]
Food triggering reaction, N (%)		
Peanut	20 (22)	12 (16)
Tree nut	17 (19)	25 (33)
Shellfish	11 (12)	16 (21)
Egg	9 (10)	3 (4)
Milk	8 (9)	4 (5)
Fish	5 (6)	12 (16)
Seed	4 (4)	1 (1)
Soy	1 (1)	1 (1)
Wheat	1 (1)	0 (0)
Fruit	0 (0)	1 (1)
Multiple potential allergens	15 (17)	2 (3)
Reaction classification, N (%) [‡]		
Anaphylaxis	75 (83)	66 (86)
Cutaneous only	11 (12)	10 (13)
Respiratory only	3 (3)	1 (1)
GI only	1 (1)	0 (0)
Treatment, N (%)		
Epinephrine before ED	36 (40)	17 (22)
Epinephrine (pre-ED or ED)	80 (88)	62 (81)
>1 epinephrine necessary	6 (7)	8 (10)
Admission to hospital, N (%)		
Short stay or general hospital unit	15 (17)	26 (34)
ICU	2 (2)	1 (1)

AFAR, Accidental food allergy reaction; CHOP, Children's Hospital of Philadelphia; CI, confidence interval; ED, emergency department; FA, food allergy; GI, gastro-intestinal; ICU, intensive care unit; N, number; NC, noncalculable; NFAR, new food allergy reaction; SAR, seasonal allergic rhinoconjunctivitis.

^{*}Percent of total food-related reactions, n = 168.

[†]Established specific FA distinct from food triggering NFAR.

[‡]Total n = 90 for AFARs, 1 patient exposed to allergen without reaction symptoms.

nut exposure. Epinephrine was administered in the majority of cases (88%) and 19% requiring hospital admission. NFARs similarly manifested primarily with anaphylaxis (86%), with nearly half (48%) due to peanut or tree nut exposure. Total epinephrine use reached a similar proportion in NFARs

compared with AFARs (81%) and approximately one-third required inpatient admission.

Using a previously defined FA prevalence rate (6.7%)⁸ in a pre-established patient population,⁷ we determined that AFARs in children requiring ED evaluation are rare (0.4% to 0.6% yearly incidence). These data are similarly low compared with the overall incidence of food-induced anaphylaxis in food-allergic individuals previously reported by Umasunthar et al³ to be 0.11 to 0.21 per 100 person-years. Of note, in contrast to this study, our data also encompassed all food-related allergic reactions, including but not limited to anaphylaxis. Furthermore, we present the first pediatric population incidence estimate of AFARs requiring ED level care. Consistent with other reports,⁵ reactions presenting to the ED were most frequently secondary to peanut or tree nut exposure, demonstrated in our study for both NFARs and AFARs. Use of epinephrine in our population was higher compared with similar studies,⁶ which may represent changing awareness of prompt epinephrine administration after improvement in our hospital's ED anaphylaxis guidelines,⁹ differences in reaction severity, or both.

Importantly, our study highlights limitations in using ED billing codes to characterize rates of FA. We specifically note 22 cases billed for but without clinical history of allergic reaction and 95 cases suspected as FA reactions, secondarily deemed inconsistent by allergist review. This discrepancy may be due to low treatment thresholds for suspected anaphylaxis, but also proposes a potential role for allergists to assist in diagnostic accuracy during acute ED visits for suspected reactions.

Our study's estimated incidence proportion was limited by our inability to calculate the exact FA prevalence within the study population and may not be generalizable to other regions. A direct review of case histories, however, likely decreased misclassification bias. We acknowledge the possibility that incidence may be underestimated if patients from the selected zip codes experienced AFARs in far proximity from our hospital and sought care elsewhere. Conversely, accuracy may well be intact considering reports showing that AFARs most commonly occur at home² and with foods provided by parents,⁴ and so we would have captured >90% of cases requiring ED evaluation.

In summary, within a single pediatric population, the incidence of AFARs requiring ED evaluation was low. Although future studies are needed to replicate this work, these data are important to consider in patient and caregiver education, particularly as new treatments for FA with potential associated adverse effects become available.

Acknowledgments

We wish to acknowledge Jesse Dudley, MS, and Rachel S. Rogers, MS, for their assistance in electronic data acquisition and statistical analysis.

^aDivision of Allergy and Immunology, Children's Hospital of Philadelphia, Philadelphia, Pa

^bPerelman School of Medicine, University of Pennsylvania, Philadelphia, Pa

^cDepartment of Biomedical and Health Informatics, Children's Hospital of Philadelphia, Philadelphia, Pa

This study received Children's Hospital of Philadelphia Food Allergy fund.

Conflicts of interest: J. M. Spergel reports no conflicts of interest related to this article. He reports unrelated funding from DBV Technology, Aimmune Therapeutics, Danone, National Institutes of Health, Food Allergy Research and

Education, Medscape, and UpToDate. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication August 29, 2018; revised October 29, 2018; accepted for publication November 16, 2018.

Available online November 27, 2018.

Corresponding author: Peter Capucilli, MD, Division of Allergy and Immunology, Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA 19104. E-mail: capucilli@email.chop.edu.

2213-2198

© 2018 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2018.11.021>

REFERENCES

1. Parlaman JP, Oron AP, Uspal NG, DeJong KN, Tieder JS. Emergency and hospital care for food-related anaphylaxis in children. *Hosp Pediatr* 2016;6:269-74.
2. Versluis A, Knulst AC, Kruizinga AG, Michelsen A, Houben GF, Baumert JL, et al. Frequency, severity and causes of unexpected allergic reactions to food: a systematic literature review. *Clin Exp Allergy* 2015;45:347-67.
3. Umasunthar T, Leonardi-Bee J, Turner PJ, Hodes M, Gore C, Warner JO, et al. Incidence of food anaphylaxis in people with food allergy: a systematic review and meta-analysis. *Clin Exp Allergy* 2015;45:1621-36.
4. Fleischer DM, Perry TT, Atkins D, Wood RA, Burks AW, Jones SM, et al. Allergic reactions to foods in preschool-aged children in a prospective observational food allergy study. *Pediatrics* 2012;130:e25-32.
5. Dyer AA, Lau CH, Smith TL, Smith BM, Gupta RS. Pediatric emergency department visits and hospitalizations due to food-induced anaphylaxis in Illinois. *Ann Allergy Asthma Immunol* 2015;115:56-62.
6. Rudders SA, Banerji A, Vassallo MF, Clark S, Camargo CA Jr. Trends in pediatric emergency department visits for food-induced anaphylaxis. *J Allergy Clin Immunol* 2010;126:385-8.
7. Coffin SE, Zaoutis TE, Rosenquist AB, Heydon K, Herrera G, Bridges CB, et al. Incidence, complications, and risk factors for prolonged stay in children hospitalized with community-acquired influenza. *Pediatrics* 2007;119:740-8.
8. Hill DA, Grundmeier RW, Ram G, Spergel JM. The epidemiologic characteristics of healthcare provider-diagnosed eczema, asthma, allergic rhinitis, and food allergy in children: a retrospective cohort study. *BMC Pediatrics* 2016;16:133.
9. Lee J, Rodio B, Lavelle J, Lewis MO, English R, Hadley S, et al. Improving anaphylaxis care: the impact of a clinical pathway. *Pediatrics* 2018;141:e20171616.

Reproduced with permission of copyright owner. Further reproduction
prohibited without permission.