

Epidemiology of anaphylaxis among children and adolescents enrolled in a health maintenance organization

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Background: There is little information about the incidence of anaphylaxis from all causes.

Objective: The objects of this study were (1) to estimate the incidence of anaphylaxis; (2) to explore the range of diagnoses attributed to an anaphylactic episode; and (3) to describe the clinical features of anaphylaxis.

Methods: The study population consisted of children and adolescents enrolled at a health maintenance organization. We identified potential episodes of anaphylaxis occurring between 1991 and 1997 from automated databases and reviewed the medical record to confirm the diagnosis. We reviewed all diagnoses specific for anaphylaxis (eg, ICD-9 995.0, anaphylactic shock) and sampled from among other related diagnoses (eg, ICD-9 995.3, allergy unspecified). Estimation of the incidence of provider-diagnosed anaphylaxis was based on cases confirmed from among the specific diagnosis codes. Description of the clinical features of anaphylaxis involved all confirmed cases regardless of diagnosis.

Results: We identified 67 episodes of anaphylaxis among children with diagnosis codes specific for anaphylaxis (10.5 episodes per 100,000 person-years). There was no increase in incidence over time. Review of samples of diagnoses not specific for anaphylaxis yielded an additional 18 episodes. Among all identified episodes (n = 85), mucocutaneous and respiratory manifestations were the most common. Seventy-one percent of episodes were treated in the emergency department. Nine episodes (11%) resulted in hospitalization.

Conclusions: The incidence of anaphylaxis did not increase during these years. A majority of episodes were treated in the emergency department. Anaphylaxis in this population was frequently diagnosed as another related condition, and the basis and implications of diagnostic practices in this disorder warrant further exploration. (*J Allergy Clin Immunol* 2004;113:536-42.)

Key words: Anaphylaxis, children, adolescents, epidemiology

Anaphylaxis is a life-threatening, IgE-mediated hypersensitivity reaction that can involve the cutaneous, respiratory, cardiovascular, and/or gastrointestinal organ systems. Anaphylactoid reactions are clinically similar to anaphylaxis but are not IgE-mediated.¹ Despite the serious nature of these reactions, there are few population-based estimates of their incidence. Two prior population-based studies include a description of the underlying cause of anaphylaxis in Olmsted County, Minnesota, from 1983 through 1987² and a school-based study of anaphylaxis and allergy in Australia.³ Most other studies of anaphylaxis in children have focused on episodes associated with a specific exposure⁴ or have been limited to the hospital or emergency department setting⁵ or allergy practices.⁶

In the current study, we describe the epidemiology of anaphylaxis in a population of children and adolescents enrolled at one of the health maintenance organizations participating in the Centers for Disease Control and Prevention's Vaccine Safety Datalink (VSD) project.^{7,8} A previous study from the VSD quantified the risk of anaphylaxis after vaccination.⁹ In the current study, our objectives were (1) to estimate the incidence of anaphylaxis from all causes; (2) to explore the range of diagnoses that may be attributed to an anaphylactic episode; and (3) to describe the clinical features of anaphylaxis.

METHODS

Study population

The study was based at Group Health Cooperative, a health maintenance organization (HMO) based in western Washington State. The study population consisted of the 229,422 children and adolescents under the age of 18 years enrolled at Group Health Cooperative for any duration between March 1, 1991, and December 31, 1997.

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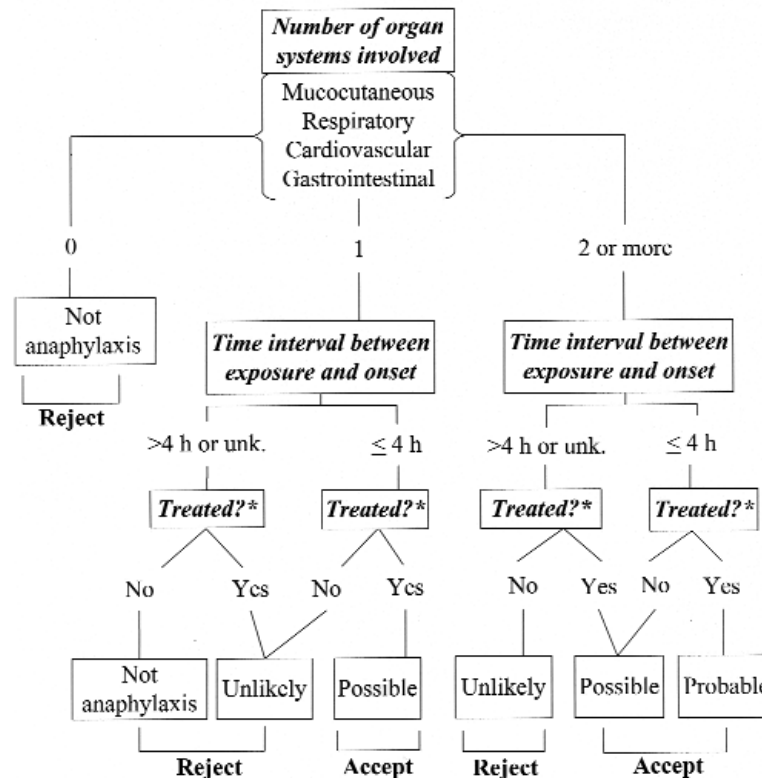
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* With any of the following:
Epinephrine, parenterally administered antihistamines, parenterally administered corticosteroids, intravenous fluids, bronchodilators

FIG 1. Algorithm for assessing anaphylaxis (reproduced by permission of Pediatrics⁹).

Abbreviations used

HMO: Health maintenance organization
PPV: Positive predictive value
VSD: Vaccine Safety Datalink

Definition of anaphylaxis

Our algorithm for assessing anaphylaxis (Fig 1) has been described previously.⁹ The decision to incorporate treatment was based on the observation that prompt treatment of an anaphylactic episode can stop progression to more than one organ system. We did not distinguish between anaphylactic and anaphylactoid reactions in this study.

Identification of cases

We searched the automated hospital, emergency department, and outpatient clinic records for all occurrences of ICD-9 codes indicative of anaphylaxis (995.0, anaphylactic shock; 995.6, anaphylactic shock caused by adverse food reaction; 999.4, anaphylactic shock caused by serum; and 995.4, shock caused by anesthesia). ICD-9 995.6 was introduced during the study period (effective October 1993). Confirmed cases (those classified as “probable” or “possible” anaphylaxis) with these diagnoses formed the basis of the incidence calculations.

In addition, we randomly sampled from less specific but related codes to estimate the frequency with which anaphylaxis was found among these other diagnoses. Previous studies have indicated that anaphylaxis may be found among those with other diagnoses.^{10,11}

For ICD-9 codes 708.0 (allergic urticaria), 708.9 (urticaria, unspecified), 995.1 (angioneurotic edema), 995.3 (allergy, unspecified), and 695.1 (erythema multiform), our sample size estimates were based on the assumption that 1% of the diagnoses would be classified by chart review as anaphylaxis. We then selected a sample size such that the maximum difference between the sample proportion and the population proportion would be no more than 2.2%, with 95% probability (Table 1). For ICD-9 code 989.5 (toxic effect of venom), pilot data suggested that a higher proportion of diagnoses may be classified as anaphylaxis, and we selected a larger sample size.

If a particular episode received more than one of the diagnosis codes of interest (eg, 999.4 and 995.6), the episode was assigned to the most appropriate code, based on information collected by chart review. In addition, since a child could have had visits in more than one setting on a single day, we coded setting (outpatient clinic, emergency department/urgent care, or hospital) as the highest level of care that the child received.

Medical record review

Details of our chart abstraction methods have been published previously.⁹ For each potential case, we reviewed the medical record to collect information about date of onset, signs and symptoms, cause posited by the treating physician, time interval between exposure and onset of signs and symptoms, treatment, and history of atopy. A child was classified as potentially atopic if he or she had a medically recorded history of asthma, hay fever, eczema, allergic bronchitis, reactive airway disease or bronchiolitis, other allergies, or use of albuterol or another inhaler.

TABLE I. ICD-9 codes used to identify potential cases of anaphylaxis

ICD-9 code	No. of diagnoses in automated data	No. of diagnoses selected for chart review
Codes specific for anaphylaxis*		
995.0 (anaphylactic shock)	106	All
995.6 (anaphylactic shock caused by adverse food reaction)	103	All
999.4 (anaphylactic shock caused by serum)	12	All
995.4 (shock caused by anesthesia)	1	All
Codes not specific for anaphylaxis†		
989.5 (toxic effect of venom)	1714	220
708.0 (allergic urticaria)	331	64
708.9 (urticaria unspecified)	6210	78
995.1 (angioneurotic edema)	193	56
995.3 (allergy, unspecified)	20,055	78
695.1 (erythema multiforme)	310	63

*The codes specific for anaphylaxis formed the basis of the primary incidence rate calculations.

†The nonspecific codes were sampled to estimate the frequency with which anaphylaxis is coded as another related condition.

TABLE II. Distribution of reviewed cases by diagnosis code and likelihood of anaphylaxis

ICD-9 code	Classification of likelihood of anaphylaxis			
	Probable	Possible	Unlikely	Not
Codes specific for anaphylaxis				
995.0 (anaphylactic shock)	25 (24.3)	32 (31.1)	10 (9.7)	36 (35.0)
995.6 (anaphylactic shock caused by adverse food reaction)	6 (5.9)	4 (3.9)	3 (2.9)	89 (87.3)
999.4 (anaphylactic shock caused by serum)	0 (0.0)	0 (0.0)	0 (0.0)	10 (100.0)
995.4 (shock caused by anesthesia)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
Codes not specific for anaphylaxis				
989.5 (toxic effect of venom)	6 (2.8)	4 (1.9)	7 (3.2)	199 (92.1)
708.0 (allergic urticaria)	2 (3.7)	1 (1.9)	4 (7.4)	47 (87.0)
708.9 (urticaria unspecified)	0 (0.0)	0 (0.0)	4 (5.2)	73 (94.8)
995.1 (angioneurotic edema)	0 (0.0)	4 (7.4)	13 (24.1)	37 (68.5)
995.3 (allergy, unspecified)	0 (0.0)	1 (1.3)	3 (3.9)	73 (94.8)
695.1 (erythema multiform)	0 (0.0)	0 (0.0)	2 (4.4)	57 (96.6)

Analysis

We estimated the incidence of provider-diagnosed anaphylaxis (defined as provider assignment of a diagnosis code specific for anaphylaxis) on the basis of cases drawn from the most specific diagnosis codes and classified by chart review as “probable” or “possible” anaphylaxis. Person-time was calculated for each member of the cohort as the time enrolled in the HMO during the study period. We estimated age-, sex-, and year-specific incidence rates.

We also conducted a secondary incidence analysis, in which we estimated the total number of cases of anaphylaxis in the population, regardless of assigned diagnosis code. Although the sampling of the nonspecific diagnosis codes introduced a great deal of uncertainty into this estimate, the discrepancy between the incidence estimate based on the most specific codes and the incidence estimate based on all codes provides information about the possible sensitivity of the most specific codes. In this analysis, we estimated the total number of cases in the population by multiplying the number of automated diagnoses with a particular ICD-9 code by the positive predictive value of that ICD-9 code as determined by chart review. We then summed over ICD-9 codes and used a Poisson distribution to generate confidence intervals.

RESULTS

Of 781 diagnoses selected for chart review, 25 were excluded because of missing chart information. In addition, 3 duplicate diagnoses were excluded (the episode

received more than one diagnosis of interest and appeared more than once in Table I). This left 753 diagnoses for review.

The code with the highest positive predictive value (PPV) for anaphylaxis was 995.0 (anaphylactic shock); approximately 55% of these visits were confirmed as “probable” or “possible” anaphylaxis (Table II). The code with the second-highest PPV was 995.6 (anaphylactic shock caused by adverse food reaction), although only 10 of 102 visits (10%) with this code were accepted as anaphylaxis. The majority (87 of 92) of the rejected diagnoses of ICD-9 995.6 were follow-up visits and/or allergy/immunology consultations. Among all those diagnosed with a code specific for anaphylaxis, 67 of 216 (31%) were accepted as probable or possible anaphylaxis.

Among the codes that were not specific for anaphylaxis, 4 of the 6 codes (989.5, toxic effect of venom; 708.0, allergic urticaria; 995.1, angioneurotic edema; and 995.3, allergy unspecified) yielded accepted cases of anaphylaxis. For these four codes, the proportion of reviewed cases that was accepted as anaphylaxis ranged from 1.3% (995.3, allergy unspecified) to 7.4% (angioneurotic edema).

Based on the 67 accepted cases of anaphylaxis among those diagnosed with the most specific codes during a total

TABLE III. Incidence rates by age, sex, and year*

	No. of cases	Person-years	Rate (/100,000 person-years) (95% CI)
Age			
0-4	15	151,197	9.9 (5.6, 16.4)
5-9	13	175,425	7.4 (4.0, 12.7)
10-14	22	196,601	11.2 (7.0, 16.9)
15-17	17	117,101	14.5 (8.5, 23.2)
Sex			
F	27	311,720	8.7 (5.7, 12.6)
M	40	328,604	12.2 (8.7, 16.6)
Year			
1991	6	79,222	7.6 (2.8, 16.5)
1992	10	92,408	10.8 (5.2, 19.9)
1993	9	89,580	10.1 (4.6, 19.1)
1994	10	92,358	10.8 (5.2, 19.9)
1995	13	94,457	13.8 (7.3, 23.5)
1996	9	95,974	9.4 (4.3, 17.8)
1997	10	96,326	10.4 (5.0, 19.1)

*Restricted to cases diagnosed with the most specific ICD-9 codes (995.0, 995.6, 999.4, 995.4).

of 640,324 person-years of follow-up, we estimate the incidence rate and 95% confidence interval of provider-diagnosed anaphylaxis in this population to be 10.5 per 100,000 person-years (95% CI, 8.1 per 100,000 person-years to 13.3 per 100,000 person-years). Rates of anaphylaxis were highest in the 15- to 17-year-old age group and were 40% higher among boys than among girls. These differences were not statistically significant. There was no evidence of an increase in rates over time (Table III).

Extrapolating from the samples that were drawn from codes not specific for anaphylaxis, an estimated 371 episodes of anaphylaxis may have received these other diagnoses during the study period. Inclusion of these codes would increase the estimated incidence rate from 10.5 per 100,000 person-years, based on the most specific diagnosis codes only, to 68.4 per 100,000 person-years (95% CI, 5.1 per 100,000 person-years to 917.6 per 100,000 person-years), including both specific and non-specific codes.

Table IV displays descriptive features of the confirmed episodes of anaphylaxis. A total of 85 episodes in 80 individuals were classified as "probable" (n = 39) or "possible" (n = 46) anaphylaxis (5 subjects had 2 anaphylactic episodes each). The median age at the time of the episode was 12 years, with a range of 7 months to 17 years (data not shown).

Mucocutaneous signs and symptoms were the most common and occurred in 94% of cases. Respiratory signs and symptoms were the second most common, affecting 88% of cases. Smaller proportions of cases (21% and 22%, respectively) had cardiovascular or gastrointestinal manifestations.

The time interval from exposure to onset of signs and symptoms was recorded in 60 (71%) of the anaphylactic episodes. Among these, symptoms occurred immediately (within 5 minutes) in 30% of the episodes. Seventy-nine percent of the episodes were treated with epinephrine, 51% with parenterally administered antihistamines, and 34% with parenterally administered corticosteroids. In

addition to the medications listed in Table IV, 30 episodes were treated with oral or unspecified antihistamines and 10 episodes were treated with oral corticosteroids.

The most frequent posited cause of the anaphylactic episode was food, followed by hymenoptera stings and medications. The most common food-related causes were peanuts and tree nuts. Ten episodes were attributed to peanuts, 7 were attributed to tree nuts, and 5 were attributed to unspecified nuts. The second most common food-related cause was shellfish (n = 3; one reaction was attributed to crustaceans, one to mollusks and crustaceans, and one to shellfish). Medication-associated anaphylaxis was attributed to trimethoprim sulfamethoxazole (n = 4), ibuprofen (n = 2), ibuprofen or aspirin (n = 1), amoxicillin (n = 1), erythromycin (n = 1), and compazine (n = 1). The cause was unknown in 10 (12%) episodes.

Seventy-one percent of the anaphylactic episodes were seen in the emergency department or urgent care, and 19% were seen in an outpatient clinic. Nine episodes (11%) resulted in hospitalization. Cases classified as "probable" were more likely to be treated in the hospital or emergency department than cases classified as "possible." There were no deaths.

A history of atopic signs and symptoms was present in 48 (60%) of the 80 subjects who had anaphylaxis. The prevalence of atopy appeared to vary by cause of the anaphylactic episode and was higher among cases of anaphylaxis caused by food (72%) and unknown causes (70.0%) than among cases caused by hymenoptera sting (44%) or medications (30%) (data not shown).

DISCUSSION

We have described the incidence and clinical characteristics of anaphylaxis in a large population of child and adolescent HMO enrollees. A previous study of anaphylaxis from all causes in a large general population was conducted by Yocum et al, who described the underlying causes of anaphylaxis in Olmsted County, Minnesota,

TABLE IV. Descriptive features of the anaphylactic episodes*

	Probable episodes n (%) n = 39	Possible episodes n (%) n = 46	Total episodes n (%) n = 85
Age (y)			
0-4	8 (20.5)	8 (17.4)	16 (18.8)
5-9	11 (28.2)	8 (17.4)	19 (22.4)
10-14	10 (25.6)	17 (37.0)	27 (31.8)
15-17	10 (25.6)	13 (28.3)	23 (27.1)
Signs and symptoms			
Urticaria	24 (61.5)	24 (52.2)	48 (56.5)
Pruritis	25 (64.1)	21 (45.7)	46 (54.1)
Angioedema	20 (51.3)	24 (54.2)	44 (51.8)
Erythema	21 (53.9)	17 (37.0)	38 (44.7)
Rhinorrhea or nasal congestion	3 (7.7)	4 (8.7)	7 (8.2)
Conjunctivitis	3 (7.7)	3 (6.5)	6 (7.1)
Rash	3 (7.7)	3 (6.5)	6 (7.1)
Sneezing	2 (5.1)	1 (2.2)	3 (3.5)
Lip or mouth tingling	0 (0.0)	2 (4.4)	2 (2.4)
Drooling/salivation	0 (0.0)	1 (2.2)	1 (1.2)
Any mucocutaneous	39 (100.0)	41 (89.1)	80 (94.1)
Dyspnea	21 (53.9)	26 (56.5)	47 (55.3)
Wheezing	22 (56.4)	19 (41.3)	41 (48.2)
Stridor	6 (15.4)	4 (8.7)	10 (11.8)
Swelling of the uvula, tongue, or pharynx	6 (15.4)	10 (21.7)	16 (18.8)
"Tight," "thick," or "burning" throat; "lump in throat"	4 (10.3)	4 (8.7)	8 (9.4)
Cyanosis	4 (10.3)	1 (2.2)	5 (5.9)
Laryngeal edema	2 (5.1)	1 (2.2)	3 (3.5)
Laryngospasm	2 (5.1)	1 (2.2)	3 (3.5)
Cough	1 (2.6)	1 (2.2)	2 (2.4)
Bronchospasm	0 (0.0)	1 (2.2)	1 (1.2)
Respiratory arrest	1 (2.6)	0 (0.0)	1 (1.2)
"Chest tightness"	0 (0.0)	1 (2.2)	1 (1.2)
Any respiratory	37 (94.9)	38 (82.6)	75 (88.2)
Hypotension	6 (15.4)	2 (4.4)	8 (9.4)
Tachycardia	4 (10.3)	4 (8.7)	8 (9.4)
Syncope or collapse	1 (2.6)	3 (6.5)	4 (4.7)
Shock	1 (2.6)	0 (0.0)	1 (1.2)
Any cardiovascular	11 (28.2)	7 (15.2)	18 (21.2)
Vomiting	6 (15.4)	3 (6.5)	9 (10.6)
Nausea	5 (12.8)	3 (6.5)	8 (9.4)
Cramping abdominal pain	4 (10.3)	2 (4.4)	6 (7.1)
Diarrhea	1 (2.6)	0 (0.0)	1 (1.2)
Any gastrointestinal	13 (33.3)	6 (13.0)	19 (22.4)
Time from exposure to onset			
<5 min	15 (38.5)	3 (6.5)	18 (21.2)
5 to 59 min	21 (53.9)	11 (23.9)	32 (37.7)
1 to 4 h	3 (7.7)	4 (8.7)	7 (8.2)
>4 h	0 (0.0)	3 (6.5)	3 (3.5)
Unknown	0 (0.0)	25 (54.4)	25 (29.4)
Treatment			
Epinephrine	35 (89.7)	32 (69.6)	67 (78.8)
Parenterally administered antihistamines	23 (59.0)	20 (43.5)	43 (50.6)
Parenterally administered corticosteroids	17 (43.6)	12 (26.1)	29 (34.1)
Intravenous fluids	13 (33.3)	5 (10.9)	18 (20.2)
Bronchodilators	15 (38.5)	8 (17.4)	23 (27.1)
Oxygen	13 (33.3)	5 (10.9)	18 (21.2)
Any of the above	39 (100.0)	38 (82.6)	77 (90.6)
Posited cause			
Food	20 (51.3)	16 (34.8)	36 (42.4)
Hymenoptera sting	12 (30.8)	7 (15.2)	19 (22.4)
Drug	2 (5.1)	8 (17.4)	10 (11.8)
Vaccine	0 (0.0)	0 (0.0)	0 (0.0)
Allergy immunotherapy	4 (10.3)	0 (0.0)	4 (4.7)
Exercise	0 (0.0)	1 (2.2)	1 (1.2)
Latex	0 (0.0)	1 (2.2)	1 (1.2)
Other	1 (2.6)	3 (6.5)	4 (4.7)
Unknown	0 (0.0)	10 (21.7)	10 (11.8)
Setting			
Outpatient clinic	1 (2.6)	15 (32.6)	16 (18.8)
Emergency department/urgent care	31 (79.5)	29 (63.0)	60 (70.6)
Hospital	7 (18.0)	2 (4.4)	9 (10.6)

*Among all accepted cases, regardless of diagnosis code.

from 1983 through 1987.² In that study, which considered a broad range of diagnoses, 154 episodes of anaphylaxis occurred among 133 residents. The occurrence rate (which included new and recurrent cases) was 30 per 100,000 person-years, and the incidence rate (which included new cases only) was 21 per 100,000 person-years. Age-specific results were not presented. An estimate of the prevalence of a history of anaphylaxis among children comes from a school-based study conducted in Australia, which found a history of anaphylaxis in 0.59% of children 3 to 17 years of age.³

Our estimated rate of 10.5 per 100,000 person-years is lower than that observed in the Olmsted County study, but the restricted set of diagnosis codes on which we based our incidence calculations and the different age structure and lack of age-specific results in the Olmsted County study make direct comparisons difficult. Although our study captures the rate of anaphylaxis diagnosed by providers, it is undoubtedly an underestimate of the rate of all anaphylaxis occurring in our population, as evidenced by the larger (68.4 per 100,000 person-years) though imprecise estimate that we obtained when we incorporated information from the samples of less specific diagnosis codes.

There was no apparent increase in the incidence of anaphylaxis during the study period (1991 to 1997). Although time trends for anaphylaxis are not well understood, our finding differs from two studies based on hospital discharge statistics in England. The first of these reported that the rate of hospitalizations for anaphylaxis (per 100,000 hospital discharges) had increased roughly 2-fold between 1991 and 1995.¹² A second, similar analysis reported that rates had increased further by 1998 to 1999.¹³ We had too few hospitalized cases to evaluate time trends in anaphylaxis hospitalizations.

The most common causes of anaphylaxis in our population were food, hymenoptera sting, and medications. The relative importance of each cause of anaphylaxis is difficult to determine, given our sampling of the nonspecific ICD-9 codes. For example, given 1714 diagnoses of 989.5 (toxic effect of venom) and a positive predictive value for anaphylaxis of 4.6% (10 cases accepted of 216 reviewed), we would expect to find 69 additional cases of anaphylaxis caused by hymenoptera sting if we reviewed all 1714 diagnoses of 989.5. The additional number of cases from other causes among the other sampled ICD-9 codes is difficult to estimate, given the nonspecific nature of these codes. Food, medications, and hymenoptera stings were also reported as the most common causes of anaphylaxis in a study of children referred to the allergy and immunology unit of a children's hospital in Italy.⁶ The proportion of idiopathic anaphylaxis in our study (12%) is lower than that reported by some studies^{2,14} but similar to or higher than the proportions reported by two studies of anaphylaxis in children.^{5,6}

Several previous studies have suggested that patients with anaphylaxis have a higher prevalence of atopy than would be expected in the general population,^{2,14-16} although this may vary by cause of the anaphylactic

episode. In the current study, we found a history of atopy in 60% of subjects with anaphylaxis. Although we had no control group with which to compare this estimate, it is higher than the estimated prevalence of allergy in the United States of 1 in 6 persons (17%).¹⁷ History of atopy was most common among those with food-related or idiopathic anaphylaxis and less common among those with anaphylaxis caused by hymenoptera stings or drugs. The suggestion that history of atopy is more common among cases of food-related anaphylaxis than among cases of hymenoptera-related anaphylaxis is consistent with at least two previous studies.^{6,18}

A potential limitation of our study was our reliance on medical records for information about the characteristics of the anaphylactic episode. It is possible that chart documentation could have been incomplete. An additional limitation is that the list of nonspecific codes that we reviewed was not exhaustive, and additional cases of anaphylaxis may have been identified if additional codes (eg, ICD-9 995.2, unspecified adverse effect of drug, medicinal, and biological substance; or ICD-9 989.82, toxic effect of latex) were reviewed. Adding these codes would not change the incidence estimate based on the specific codes but might increase the estimate based on all diagnoses.

A challenge to the study of anaphylaxis is the lack of a standard case definition.^{19,20} Although this and several previous studies use definitions that incorporate information about the number and type of signs and symptoms^{2,6,10,11,21} and the time interval between exposure and symptom onset,^{6,11,21} the specific elements of the definitions vary. Our algorithm was intended to exclude minor reactions, and a majority of cases classified as "probable" or "possible" anaphylaxis were treated in the emergency department or urgent care. However, given the range of reactions consistent with our definition of "possible" anaphylaxis, our algorithm may have resulted in some false-positive diagnoses. In the arena of vaccine safety, the process of standardizing a case definition for anaphylaxis may be aided by initiatives such as the Brighton Collaboration, an international collaboration with the mission of establishing case definitions for adverse events after vaccination.²²

Possibly related to the lack of a standard definition is the lack of consistent diagnosis of anaphylaxis. Previous studies of anaphylaxis^{10,11} as well as the current one found cases of anaphylaxis coded as a variety of other conditions. Although thorough investigation of these other codes does appear to be important for complete capture of anaphylaxis (and description of true incidence), their high frequency and low predictive value poses a challenge. One approach to solving this problem is to review all medical records, regardless of the diagnosis. Klein and Yocum¹⁰ used this approach in a study of all patients seen at a community emergency room during a 4-month period. Among 19,122 visits, the authors identified 17 cases of anaphylaxis, only 4 of which had received a diagnosis of anaphylaxis. Another approach is to review all diagnoses thought to be related to anaphy-

laxis. This approach was used in the Olmsted County study.² Among 1255 persons with diagnoses related to anaphylaxis, 133 were determined by medical record review to have had at least one episode of anaphylaxis. Given the potentially large number of records to review, these approaches are most feasible when restricting to a limited time period or population. Since one of our objectives was to explore trends over several years in a large population, the current study focused on a fairly restricted and specific set of diagnosis codes, with the interpretation being that the estimates represent provider-diagnosed disease. We then sampled from among codes not specific for anaphylaxis. It would be interesting to know whether cases diagnosed with the less specific codes present with different symptoms or receive different treatment or follow-up, but we reviewed too few cases with nonspecific diagnoses to answer these questions.

To conclude, available data do not support an increase in the incidence of anaphylaxis during the years 1991 to 1997 for the population of children and adolescents served by this HMO. A majority of the identified episodes (71%) were treated in the emergency department or urgent care. Consideration of a broad range of diagnoses appears to be important for complete case identification. Future studies could build on these findings, exploring the basis and implications of differing diagnostic practices for anaphylaxis.

Study subject coordination

This study was approved by the Group Health Cooperative's Institutional Review Board.

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