

National study of US emergency department visits for acute allergic reactions, 1993 to 2004

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Background: The clinical epidemiology of acute allergic reactions in the emergency department (ED) is uncertain.

Objectives: To characterize ED visits for acute allergic reactions and to evaluate national trends in ED management.

Methods: The National Hospital Ambulatory Medical Care Survey was used to identify a nationally representative sample of ED visits between 1993 and 2004. Cases with a diagnosis of acute allergic reaction were identified by *International Classification of Diseases, Ninth Revision (ICD-9)* codes (9950, 9951, 9952, 9953, 9956).

Results: A total of 12.4 million allergy-related ED visits occurred from 1993 to 2004, representing 1.0% (95% confidence interval, 0.93%–1.10%) of all ED visits or 1.03 million ED visits per year. The number of allergy-related ED visits remained relatively stable, averaging 3.8 per 1,000 US population per year (95% confidence interval, 3.4–4.1; P for trend = .39). Although 63% of all visits were coded as urgent, only 4% required hospitalization. Anaphylaxis coding was rare (1%). ED staff prescribed medications in 87% of visits, especially histamine₁ blockers (62%; P for trend = .29). Increases were noted from 1993 to 2004 for corticosteroids (22% to 50%; $P < .001$), histamine₂ blockers (7% to 18%; $P < .001$), and inhaled β -agonists (2% to 6%; $P = .008$). Epinephrine use was infrequent and declining (19% to 7%; $P = .04$).

Conclusion: Between 1993 and 2004, significant variability has occurred in ED management of acute allergic reactions.

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INTRODUCTION

Little is known about the distribution and determinants of allergic reactions in US emergency departments (EDs). Despite the emergent nature and potential for morbidity and mortality associated with acute allergic reactions, limited data are available on their frequency and management in the ED.

Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.¹ Anaphylaxis therefore lies at the far end of a continuum of acute allergic reactions. Studies have shown that most anaphylaxis cases are treated in the ED.²

Earlier ED-based studies have attempted to evaluate the disease burden. In 1995, Klein and Yocum³ reported an incidence of anaphylaxis of 0.09% during a 4-month period in a single ED. Sheikh and Alves⁴ reported 17 cases of anaphylaxis per 100,000 ED visits in London between 1991 and 1995. More recently, Braganza and colleagues⁵ reported an incidence of 9.3 per 1,000 ED visits for generalized acute allergic reactions and 1 per 1,000 ED visits for anaphylaxis. Overall, the case fatality rate for anaphylaxis has been estimated at 4 deaths per 10 million people.⁶

The study of acute allergic reactions and anaphylaxis in the ED has been complicated for several reasons. First, the definition of anaphylaxis has been highly variable; an accepted clinical definition was lacking until recently.^{1,7} Also, clini-

cians often fail to differentiate between the singular presence of mucocutaneous signs and the additional occurrence of cardiovascular and respiratory symptoms, as in anaphylaxis. Similarly, when symptoms do not appear life threatening, physicians are more likely to categorize even multisystem complaints as either acute allergic reaction or urticaria.

The classification of allergic reactions and anaphylaxis has also evolved during the past several years. New codes to describe fatal anaphylactic reactions, including “anaphylactic shock due to adverse food reaction” and “anaphylactic shock, unspecified,” were developed in 2003.^{1,7} However, research has indicated that these codes are widely underused^{1,7} and that *International Classification of Disease (ICD)* codes might be limited in their ability to identify specific allergic reactions in the ED.⁸ Furthermore, newly introduced allergen-specific codes (such as those categorizing food allergies) do not account for other patient characteristics, such as the complexity or severity of the reaction.

Nevertheless, “acute allergic reactions” presumably encompass all of the anaphylaxis cases. Historically, the standard of care for severe allergic reactions has revolved around epinephrine and supportive care. In addition, agents such as histamine₁ (H₁) blockers and corticosteroids have been popular for treating mucocutaneous effects, whereas inhaled β -agonists have been used to treat respiratory symptoms. Other agents, such as H₂ blockers, have been used, but their effectiveness has yet to be fully elucidated.⁹

Our previous multicenter studies have suggested a large variation in the ED management of acute allergic reactions and anaphylaxis.^{10,11} The present study expands on these earlier efforts through use of nationally representative ED

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data during a 12-year period. Our objectives were to characterize US ED visits for acute allergic reactions (including anaphylaxis) and to evaluate national trends in ED management.

METHODS

The National Hospital Ambulatory Medical Care Survey (NHAMCS) data from 1993 to 2004 were combined for the current analysis.^{12–23} NHAMCS is a 4-stage probability sample of visits to noninstitutional general and short-stay hospitals, excluding federal, military, and Veterans Affairs hospitals, located in the 50 states and the District of Columbia.²⁴ NHAMCS is conducted annually and covers geographic primary sampling units, hospitals within primary sampling units, EDs within hospitals, and patients within EDs. Hospital staff collected data during a randomly assigned 4-week data period for each of the sampled hospitals approximately once every 15 months. Trained hospital staff performed visit sampling and data collection, and a Bureau of Census field supervisor performed review of data collection. Quality control included computer checks to evaluate inconsistencies with value ranges, a 2-way 10% independent procedure for medical and drug coding, and adjudication by the National Center for Health Statistics (NCHS) for ambiguous or illegible responses for fields, including reasons for visit and diagnosis. The nonresponse rate for most items was less than 5%, and error rates were less than 2% for items that required medical coding. In 2003, NCHS field representatives were trained on the Privacy Rule of the Health Insurance Portability and Accountability Act, and hospitals were encouraged to accept data use agreements between themselves and the NCHS.

When the data collection forms were completed, they were sent to Constella Group (Durham, NC), where they were coded using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. National estimates were obtained through use of a multistage estimation procedure with 3 basic components (inflation by reciprocals of the sampling selection probabilities, adjustment for non-response, and a population weighting ratio adjustment) and patient visit weights. A more detailed description of the NHAMCS data collection and estimation procedures is available for review in the technical notes section of each year's NHAMCS Emergency Department Survey.^{12–23}

We identified cases of acute allergic reactions and anaphylaxis by *ICD-9-CM* codes of 995.0 (other anaphylactic shock), 995.1 (angioneurotic edema), 995.2 (unspecified adverse effect of drug, medicinal, and biological substance [due] to correct medicinal substance properly administered), 995.3 (allergy, unspecified), and 995.6 (anaphylactic shock due to adverse food reaction) in any of the 3 diagnosis fields. Anaphylaxis cases were identified by an *ICD-9-CM* code of 995.0 or 995.6 in any of the 3 diagnosis fields.

US visit rates were computed using midyear age, sex, race, ethnicity, region, and metropolitan status-specific population estimates from the US Census Bureau; all rates were reported

per 1,000 individuals per year for the US resident population.²⁵

We analyzed ED visit rates by age, sex, race, Hispanic ethnicity, insurance status, metropolitan statistical area status of the hospital, and region (Northeast, Midwest, South, and West). Metropolitan statistical area and US region categories represent standardized geographical divisions defined by the US Bureau of the Census. We also examined ED visit rates by insurance status and season (January through March, April through June, July through September, October through December). Visits were further analyzed by admission status and the acuity of the medical problem (urgent/emergent) recorded at triage. To keep analyses between earlier and later years consistent, we coded visits that occurred after a change in coding in 1997 (1997–2004) as urgent/emergent if immediacy to be seen was recorded as less than 15 minutes or 15 to 60 minutes and as nonurgent if immediacy to be seen was recorded as more than 1 to 2 hours. Up to 5 medications were recorded per encounter from 1993 to 1994, up to 6 medications from 1993 to 2001, and up to 8 between 2002 and 2004, with medications coded as per published NCHS definitions.²⁶

We performed all analyses using Stata statistical software, version 9.0 (Stata Corp, College Station, TX). A masked ultimate cluster sample design was used to estimate variance. Analyses included the Pearson χ^2 test to evaluate differences between groups. Trends were analyzed using least squares regression. A 2-sided $P < .05$ was considered statistically significant.

RESULTS

A total of 12.4 million allergy-related ED visits occurred from 1993 to 2004, representing 1.0% (95% confidence interval [CI], 0.93%–1.10%) of all ED visits or 1.03 million ED visits per year (Table 1). The most commonly treated acute allergic reaction was unspecified allergy (57%; 95% CI, 55%–59%), followed by unspecified adverse effect of drug, medicinal, and biological substance due to correct medicinal substance properly administered (35%), angioneurotic edema (8%), other anaphylactic shock (0.9%), and anaphylactic shock due to adverse food reaction (0.2%).

Overall, the estimated annual rate of ED visits attributable to acute allergic reactions was 3.8 (95% CI, 3.4–4.1) visits per 1,000 people. The overall population rate per 1,000 people was relatively stable during the 12-year period (3.8 in 1993–1994 to 3.6 in 2003–2004; P for trend = .39). No significant temporal trends were found in ED visits for acute allergic reactions based on the following 4 major demographic subgroups: males (2.7–2.8; P for trend = .29), females (4.8–4.4; P = .44), whites (3.8–3.6; P = .71), and blacks (5.7–4.7; P = .44).

During the 12-year period, the mean age of patients was 35 years, and 64% were female. Approximately 78% were white, and 44% had private insurance. Although rates did not change over time, ED visits for acute allergic reactions varied according to age, sex, and race (Table 1). ED visits tended to be more common among patients aged 20 to 29 years, but this

Table 1. Estimated Numbers and Rates for Acute Allergic Reactions Between 1993 and 2004

Characteristics	Actual No. of visits	Estimated No. of visits	Rate per 1,000 US population (95% CI)	Rate per 1,000 ED visits (95% CI)
Overall	3,293	12,400,000	3.8 (3.4–4.1)	10.2 (9.3–11.0)
Age group, y				
<10	497	1,864,000	4.0 (3.5–4.5)	8.8 (7.7–9.9)
10–19	357	1,316,000	2.8 (2.4–3.2)	8.8 (7.6–10.1)
20–29	573	2,180,000	4.8 (4.2–5.4)	10.7 (9.3–12.0)
30–39	571	2,123,000	4.1 (3.5–4.7)	11.4 (9.8–12.9)
40–49	451	1,719,000	3.5 (3.0–4.0)	11.4 (9.7–13.1)
50–59	339	1,205,000	3.4 (2.9–4.0)	12.3 (10.3–14.2)
60–69	245	882,000	3.6 (2.9–4.2)	11.9 (9.8–14.0)
70–79	176	700,000	3.7 (2.9–4.5)	9.3 (7.3–11.3)
≥80	84	372,000	3.5 (2.5–4.4)	5.5 (4.0–7.0)
Sex				
Female	2,052	7,898,000	4.7 (4.3–5.1)	12.2 (11.1–13.4)
Male	1,241	4,464,000	2.8 (2.5–3.0)	7.8 (7.0–8.6)
Race				
White	2,513	9,626,000	3.6 (3.2–3.9)	10.4 (9.4–11.3)
Black	651	2,328,000	5.6 (4.7–6.4)	9.0 (7.7–10.4)
Other	129	407,000	2.3 (1.6–3.0)	12.2 (8.6–15.8)
Ethnicity*				
Hispanic	358	1,229,000	3.2 (2.7–3.6)	10.3 (8.7–11.9)
Non-Hispanic	2,337	8,844,000	3.0 (2.7–3.3)	10.2 (9.2–11.2)
US region				
Northeast	906	2,740,000	4.3 (3.7–5.0)	11.4 (9.8–13.0)
Midwest	731	2,901,000	3.8 (3.2–4.4)	9.4 (7.8–10.9)
South	1,008	4,355,000	3.7 (3.2–4.3)	9.7 (8.2–11.2)
West	648	2,366,000	3.2 (2.5–3.9)	10.8 (8.5–13.1)
Metropolitan area				
Metro	2,740	9,770,000	3.7 (3.3–4.0)	10.1 (9.1–11.1)
Nonmetro	553	2,591,000	4.0 (2.7–5.3)	10.2 (6.9–13.5)

Abbreviations: CI, confidence interval; ED, emergency department.

* A total of 19% of the sample was missing.

rate was not statistically higher than other age groups. Females had significantly more ED visits for acute allergic reactions, compared with males, for the rate per 1,000 US population and the rate per 1,000 ED visits (both $P < .001$). Blacks had a significantly higher rate of acute allergic reactions per 1,000 US population (5.6; 95% CI, 4.7–6.4) compared with whites (3.6; 95% CI, 3.2–3.9), but this race difference was not present for the rate per 1,000 ED visits. No differences were observed by Hispanic ethnicity, US region, or urban-rural status (Table 1). Furthermore, ED visit rates did not differ markedly by season, with 23% (95% CI, 21%–25%) of visits occurring in the winter, 26% (95% CI, 24%–28%) in the spring, 27% (95% CI, 25%–30%) in the summer, and 24% (95% CI, 21%–26%) in the fall.

Although 63% of all visits were coded as urgent/emergent at triage, only 4% were hospitalized. ED staff prescribed medications in 87% of visits. Trends in medication use are shown in Figure 1. Across the 12-year period, the most commonly prescribed medications were H_1 blockers (overall, 62%; 1993, 59% to 2004, 62%; P for trend = .29). Increases were noted for corticosteroids (overall, 38%; 1993, 22% to 2004, 50%; $P < .001$), H_2 blockers (overall, 11%; 1993, 7%

to 2004, 18%; $P < .001$), and inhaled β -agonists (overall, 4%; 1993, 2% to 2004, 6%; $P = .008$). By contrast, epinephrine use was infrequent (11% of all cases) and declining (from 19% to 7%; $P = .04$).

Anaphylaxis coding was rare (1%), and small sample size precluded any detailed analysis. The 52 actual cases represented approximately 12,000 visits per year (or approximately 143,000 anaphylaxis cases per 12.4 million total allergy cases during more than 12 years). In this subset with the most severe allergic reactions, 63% received an H_1 blocker, 61% a corticosteroid, and 38% an H_2 blocker. Only 50% of anaphylaxis cases received epinephrine, and 13% received a β -agonist. Only 33% of the patients who sought care in the ED and were coded as having anaphylaxis (ie, ICD-9 codes 995.0 or 995.6) were admitted overnight to the hospital.

DISCUSSION

Although a recent managed care study found that most anaphylaxis cases (71%) were treated in the ED,² relatively few studies have evaluated the ED-based frequency and management of acute allergic reactions, including anaphylaxis.^{2–5,10,11,27–32} The results of the present study, to our knowl-

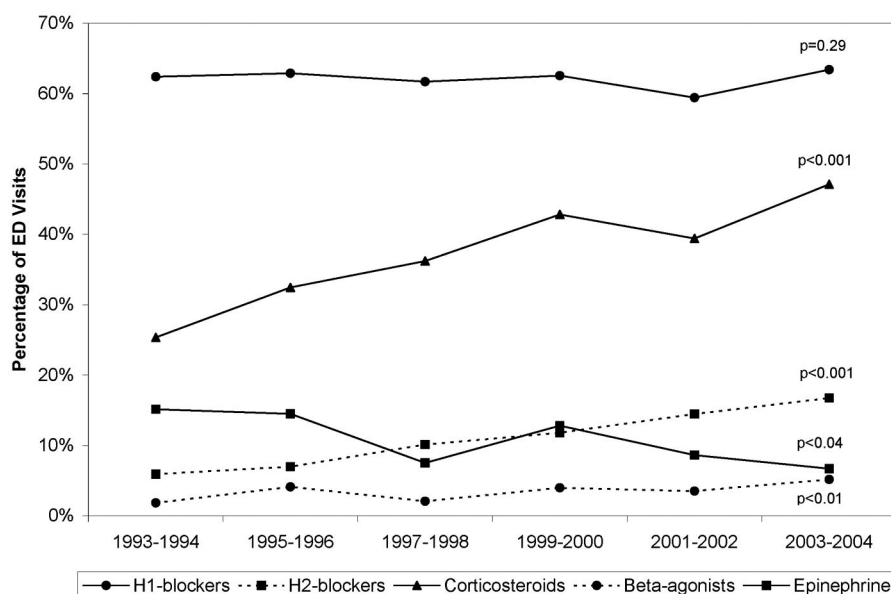


Figure 1. Trends in medications used to treat acute allergic reactions and anaphylaxis in the emergency department (ED) from 1993 to 2004. The intervals on the x-axis represent 2-year averages. H1 indicates histamine 1; H2, histamine 2.

edge the first of its kind, provide an important national perspective on this important topic. Between 1993 and 2004, a total of 12.4 million allergy-related ED visits occurred, accounting for 1.0% of all ED visits. Population rates suggested more frequent ED visits for acute allergic reactions among women than men and among blacks than whites but did not reveal significant differences by geographic location. The number of ED visits for acute allergic reactions did not significantly change during the 12-year study interval.

Anaphylaxis coding was rare, with only 1% of ED visits with acute allergic reactions receiving this designation (ie, 0.01% of all ED visits). This result is thought to significantly underestimate the true burden of anaphylaxis in the United States. Cases for the current study were identified using *ICD-9-CM* codes. It has been shown that codes to identify anaphylaxis are widely underused.^{1,7} Recent work by our research group also has shown that *ICD* codes might be limited in their ability to identify specific allergic reactions in the ED.⁸ Studies also have reported that a diagnosis of allergic reaction or acute allergic reaction often is used by ED physicians to diagnosis the conditions of patients with multisystem organ involvement who should instead be diagnosed as having anaphylaxis.^{2,3,10,11} For example, our study on the ED management of food-induced acute allergic reactions found that among 678 cases identified by *ICD-9* code, 51% were found to be anaphylaxis.¹⁰ A similar finding was observed in our insect sting allergy study, in which 31% of 617 patients were classified as having anaphylaxis.¹¹ If these 2 conditions are representative of all allergic reactions treated in the ED (ie, that 30% to 50% of the acute allergic reactions identified in the current study were indeed anaphylaxis), this

would lead to estimates of 310,000 to 517,000 ED visits for anaphylaxis each year.

In addition to the frequency and distribution of acute allergic reactions, there is much to be learned about the emergency management of this disorder. Although lesser reactions may be managed using antihistamines alone,³³ current recommendations for the treatment of severe reactions (including anaphylaxis) include ensuring a patent airway, administering supplemental oxygen, establishing intravenous access, and, most critically, administering intramuscular epinephrine.⁷ Although H₁ blockers and corticosteroids may be implemented as second-line treatments, experts generally agree that they should not serve as the sole treatment for severe allergic reactions and anaphylaxis, because their onset of action is much slower compared with that of epinephrine.³⁴

The NHAMCS data reveal that ED physicians rely on these second-line agents for the treatment of the most acute allergic reactions. During the 12-year study period, the most commonly prescribed medications were H₁ blockers and corticosteroids. Thus, our nationally representative data support the results of previous investigations that suggested this practice pattern. For example, Bellou and colleagues²⁹ identified 324 patients (1%) treated in an ED in the French region of Lorraine for suspected allergic disease. Overall, 36% of patients were treated with corticosteroids; of those patients who met the criteria for anaphylactic shock, 8% were treated with corticosteroids. Brown and colleagues²⁸ identified 142 cases of anaphylaxis treated in an Australian ED and found that most received H₁ antagonists (72%), H₂ antagonists (61%), and corticosteroids (75%). Braganza and colleagues⁵ reported that among 57 children diagnosed as having anaphylaxis in an

Australian ED, 51% were treated with an H₁ antagonist, 5% with an H₂ antagonist, and 49% with corticosteroids.

Two recent multicenter studies by our group evaluated the management practices in US academic EDs.^{10,11} Among 678 patients treated for food-induced acute allergic reactions, 72% received antihistamines and 48% received systemic corticosteroids.¹⁰ Among 617 patients treated for insect sting-induced acute allergic reactions, 11% were categorized as having mild systemic reactions and 31%, as having anaphylactic reactions. Among those patients with systemic reactions, 69% received antihistamines and 50% received systemic corticosteroids.¹¹ The results of the current study, as well as those of previous research, indicate that most patients presenting to US EDs receive H₁ blockers and corticosteroids as their treatment for acute allergic reactions, including anaphylaxis.

Although epinephrine is widely regarded as an essential treatment for anaphylaxis, but perhaps not lesser allergic reactions, it continues to generate the greatest confusion and concern among health care professionals.³⁵ Epinephrine's particular indications, dosing requirements, and route of administration remain a source of controversy, and these uncertainties hinder its appropriate use among health care professionals.^{34,35} The present analysis confirmed the rarity of epinephrine use in the larger group with acute allergic reaction, but it also revealed that epinephrine was administered in only 50% of identified anaphylaxis cases. The observed decline in epinephrine use during the 12-year study period is of particular interest.

A review of the literature revealed only one study that described 100% compliance with epinephrine in treating patients with anaphylactic shock²⁹; most found considerably lower use. In our own studies, only 13% of insect sting anaphylaxis patients and 24% of food anaphylaxis patients were treated with epinephrine.^{10,11} Stewart and Ewan²⁷ identified 24 cases of possible anaphylaxis and 9 cases of severe anaphylaxis during a 1-year period; among these 9 patients with severe anaphylaxis, only 3 were treated with epinephrine. Similarly, in the 142 anaphylaxis cases identified by Brown and colleagues,²⁸ only 18% received epinephrine in the prehospital setting and 27% in the ED. Cianferoni et al³² found that only 15% of patients treated in the ED for anaphylaxis were treated with epinephrine. Finally, in a recent pediatric study, only 12% of children treated for anaphylaxis in the ED received epinephrine.⁵ Taken together, our data provide strong evidence that even if one restricts allergic reactions to the most severe subset (ie, anaphylaxis) epinephrine is underused for severe acute allergic reactions in the ED.

Another area of controversy in the ED management of acute allergic reactions is the frequency and need for hospital admission after ED stabilization of anaphylaxis. Some criteria to consider when making this decision include symptom severity, anaphylaxis history, medical comorbidities (such as asthma), baseline medications used, access to medical care, unreliable home situation, and age.³⁵ If it is decided that a patient will not be admitted, it is still important that the

patient be observed for a sufficient time in the ED (at least several hours), because a risk of recurrent anaphylactic, or biphasic, reaction remains.³⁵ Indeed, some groups have suggested that patients who received epinephrine for treatment of anaphylaxis be observed for 24 hours,³⁰ which is unrealistic in the United States in this era of ED crowding and ambulance diversion.³⁶

We found that only 4% of all patients with acute allergic reaction were admitted to the hospital, which is consistent with the results from our prior multicenter studies.^{10,11} Furthermore, we found that only 33% of identified anaphylaxis patients were admitted to the hospital for overnight monitoring. Admission rates have varied in other reports, ranging from 3% to 41%.^{3,5,10,11,28–30} Brown et al²⁸ reported that 61% of patients with anaphylaxis were admitted to an observation unit, 3% to the general medical floor, and 3% to the intensive care unit. Braganza et al⁵ found that 39% of children with anaphylaxis were admitted to an observation unit and 7% were admitted to a general medical floor. As the research of Smit and colleagues³⁰ has suggested, because of the risk of biphasic reaction, practitioners might need to adopt much lower thresholds for ED observation and hospital admission.

In summary, our national study characterizes the epidemiology of patients with acute allergic reactions presenting to US EDs and provides further evidence of considerable practice variation in their management. The results are confined to ED visits and not all cases of acute allergic reactions in the general population, so readers should be cautious about generalizing our results to the population at large. Additionally, because we relied solely on *ICD-9-CM* coding to identify cases, it is probable that nonallergic reactions were included in the study population (eg, idiosyncratic drug reactions, *ICD-9-CM* code 995.2). It is also important to recognize that there are several confounders that may have limited the therapeutic options in the ED, namely, the patients' prior medical histories and medication use and medications administered en route to the hospital. Still, the present study surmounted the limitations of prior studies that had solely investigated ED visits in non-US countries or in US academic medical centers only. Our findings provide further support for the need to enhance diagnosis, documentation, and treatment-related guidelines for the care of patients with acute allergic reactions, and especially anaphylaxis, in the ED.

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