

---

# Fatal anaphylaxis: postmortem findings and associated comorbid diseases

Paul A. Greenberger, MD; Brian D. Rotskoff, MD; and Barry Lifschultz, MD

---

**Background:** Anaphylaxis is an infrequent cause of sudden death. Death often results from circulatory collapse, respiratory arrest, or both.

**Objective:** To investigate the causes of death, anatomical findings, and comorbid diseases in cases of fatal anaphylaxis.

**Methods:** This is a retrospective case review of 25 unselected cases of documented fatal anaphylaxis. Each case report contained details of the fatal reaction, a review of the medical record, and laboratory and autopsy findings. Serum tryptase concentrations were measured in 7 cases.

**Results:** The anaphylactic deaths included 7 reactions to medications, 6 to radiocontrast material, 6 to Hymenoptera stings, and 4 to foods. The mean age was 59 years. The anaphylactic reaction began within 30 minutes of exposure in 21 of 25 cases, with death occurring within 60 minutes in 13 of 25 cases. Urticaria occurred in only 1 of 25 cases. Anatomical findings consistent with anaphylaxis were present in 18 of 23 patients undergoing autopsy. At least 1 significant comorbid disease was identified in 22 of 25 cases.

**Conclusions:** (1) Elderly patients with substantial comorbid conditions constituted a significant number of the anaphylactic fatalities; (2) the onset of severe anaphylaxis occurred in less than 30 minutes in nearly every case; (3) 18 of 23 cases were associated with specific anatomical findings of anaphylaxis; (4) self-administered epinephrine was used in just 1 of 5 cases; and (5) serum total tryptase concentrations were elevated markedly in 4 of 7 cases tested.

*Ann Allergy Asthma Immunol.* 2007;98:252–257.

## INTRODUCTION

*Anaphylaxis* describes an acute and potentially life-threatening IgE-mediated hypersensitivity reaction that results from the systemic release of inflammatory mediators from mast cells and basophils.<sup>1</sup> An anaphylactoid reaction may be clinically indistinguishable, but it results from non-IgE-mediated mechanisms.<sup>1</sup>

Anaphylaxis is of significant concern because of its potentially life-threatening nature. Death from anaphylaxis most often results from circulatory collapse, respiratory arrest, or a combination of the two.<sup>2–6</sup> If death results from circulatory collapse without airway obstruction, postmortem anatomical findings suggestive of anaphylaxis may not be present.<sup>2</sup> The finding that tryptase levels<sup>6,7</sup> are elevated during anaphylactic reactions may provide a useful adjunct to the diagnosis when other clinical or physical examination clues are not witnessed or are absent.<sup>3,5,8,9</sup> The purpose of this study was to review autopsy, clinical, and tryptase findings in 25 unselected cases of anaphylactic deaths of all causes.

## METHODS

Between March 1, 1989, and August 31, 2001, the Office of the Medical Examiner of Cook County, Chicago, IL,

established a general database for all deaths, from which 26 documented cases of fatal anaphylactic reactions were analyzed retrospectively. The cases were reviewed in careful detail. Each case was presented to 5 to 10 medical examiners for discussion before the final causes of death were reported. There had been no allergy-immunology input before the institution of this database. All the medical examiners' reports included a clinical history of the events surrounding the anaphylactic death and information regarding the medical history and previous allergic reactions when available. The sources of the information included in these reports were (1) telephone or in-person interviews of the patient's family, friends, or other witnesses of the events leading up to the fatal reaction by a lay professional from the Office of the Medical Examiner; (2) police or medical personnel responding to the scene; (3) nursing staff or physicians' accounts of their medical encounter with the patient; (4) postmortem findings, including gross pathology, toxicology, and laboratory reports; and (5) the hospital medical record. Laboratory testing on some, but not all, patients included routine postmortem chemistry analyses, toxicology reports, and postmortem serum total tryptase concentrations (in 7 patients). Before 2000, serum tryptase concentrations were not obtained routinely for suspected cases of anaphylaxis. Complete autopsy protocols were performed in 23 of the 25 cases in this study, with the patients' families refusing autopsy in the other 2 cases. This study was approved by the Northwestern University institutional review board.

---

Division of Allergy-Immunology, Departments of Medicine and Pathology, Northwestern University Feinberg School of Medicine, and the Office of the Medical Examiner of Cook County, Chicago, Illinois.

This study was supported by the Ernest S. Bazley Grant to Northwestern Memorial Hospital and Northwestern University.

Received for publication October 1, 2006.

Accepted for publication October 10, 2006.

### Classification of Definitions

The following classification system was used to separate the patients into 3 groups based on the likelihood that an anaphylactic reaction was the cause of death.

**Death from anaphylaxis.** Patients had 1 or more of the following: (1) a witnessed or documented exposure to an allergic trigger that provoked an immediate reaction with characteristic signs and symptoms of anaphylaxis; (2) physical examination and postmortem findings consistent with anaphylaxis along with a corroborative clinical history and the absence of other causes of death; and (3) markedly elevated serum tryptase concentrations in patients with clinical history, physical examination, and postmortem findings suggestive of anaphylaxis.

**Death probably from anaphylaxis.** Patients had 1 or both of the following: (1) an unwitnessed but likely exposure to a trigger that is known to cause an anaphylactic or anaphylactoid reaction with compatible physical examination and postmortem findings consistent with anaphylaxis (ie, a Hymenoptera-sensitive patient with upper airway edema who experienced an unwitnessed systemic reaction and sudden death in proximity to a bee hive) or (2) a clinical history suggesting the diagnosis of anaphylaxis and physical examination or postmortem findings corroborating anaphylaxis in the absence of an elevated serum tryptase concentration (ie, an opened bottle of ibuprofen is found in the bathroom of a patient who experiences sudden death and is noted to have significant upper airway edema on autopsy).

**Death possibly from anaphylaxis.** Patients had 1 or more of the following: (1) an unwitnessed and sudden death with possible exposure to an allergic trigger and nonspecific physical examination or postmortem findings; (2) a sudden death with a clinical history that does not conclusively support anaphylaxis, an unknown time of death from the onset of symptoms, and no obvious physical examination or postmortem findings specific for anaphylaxis; and (3) in the absence of conclusive support for anaphylaxis, a sudden death with other illnesses that could potentially explain the death, such as pulmonary or cardiovascular diseases.

### Pathological Definitions

**Pulmonary edema** was present when the lungs were aerated poorly on gross examination and when, on cut section, the lungs oozed blood in liquid form (not as clotted blood). **Pharyngeal and laryngeal edema** is the swelling of the lining of the pharynx and larynx due to fluid flowing into tissues out of the capillaries. **Pulmonary hyperinflation** is the term given to the pink, spongy lungs associated with air trapping in asthma. **Petechial hemorrhages** are small punctate hemorrhages in the mucosa of the vocal cords or trachea, usually associated with rupture of small blood vessels due to backing up of blood in asphyxial deaths. **Mucous plugging** is demonstrated by seeing thick mucous casts protruding from airways where the lungs are cut.

Laryngeal edema was graded from slight to severe by the panel of medical examiners. "Slight" describes mucosal

edema that was present only microscopically without distortion of the laryngeal structures. "Moderate" edema was present when there was gross swelling of the laryngeal structures with narrowing or obliteration of the ventricular folds but without obstruction of the air passages. "Severe" was the term used to describe marked swelling and distortion of the laryngeal structures with complete obstruction of the upper airways. *Ischemic heart disease* (IHD) was the term used to describe coronary artery occlusion of such severity that it likely contributed to death.

## RESULTS

### Demographics

The number of autopsies per year performed by the Office of the Medical Examiner was approximately 4,730; the 25 cases of anaphylaxis represent 0.044% of all cases during the 12 study years. The mean and median age of the patients included were 59 and 64 years, respectively, with the youngest patient being 17 years and the oldest 91 years. The demographic data are given in Tables 1 and 2. Most of the reactions occurred in a private residence (n = 12) or in an inpatient or long-term care facility (n = 7).

### Clinical History

This study included 25 of the 26 cases in the medical examiners' database, excluding 1 case because of insufficient information regarding the history of the possible anaphylactic reaction. Using the classification system for the clinicopathologic evaluation, 15 deaths were consistent with and 8

Table 1. Demographic Characteristics of 25 Anaphylactic Fatalities

| Characteristic                                 | Fatalities, No. |
|------------------------------------------------|-----------------|
| Patient age, y*                                |                 |
| <20                                            | 1               |
| 20–29                                          | 1               |
| 30–45                                          | 3               |
| 46–60                                          | 6               |
| >60                                            | 14              |
| Sex                                            |                 |
| M                                              | 13              |
| F                                              | 12              |
| Race                                           |                 |
| White                                          | 15              |
| Black                                          | 6               |
| Hispanic                                       | 3               |
| Asian                                          | 1               |
| Cases with autopsy                             | 23              |
| Location of the terminal episode               |                 |
| Private residence                              | 12              |
| Inpatient medical unit/long-term care facility | 7               |
| Outpatient procedure                           | 2               |
| Street                                         | 1               |
| Work                                           | 1               |
| Restaurant                                     | 1               |
| Physician's office                             | 1               |

\* Mean age, 59 years; median age, 64 years.

Table 2. Causes of Death and Time to Onset of Symptoms in 25 Anaphylactic Fatalities

| Case No./sex/<br>age, y | Comorbid diseases                      | Cause of death                 | Time to onset<br>of symptoms,<br>min | Time to death<br>after<br>exposure |
|-------------------------|----------------------------------------|--------------------------------|--------------------------------------|------------------------------------|
| 1/M/58                  | IHD, COPD                              | Contrast media                 | 0–30                                 | 0–60 min                           |
| 2/F/46                  | Urosepsis, pneumonia                   | Contrast media                 | 0–30                                 | 0–60 min                           |
| 3/M/66                  | IHD, ESRD, COPD                        | Contrast media                 | 0–30                                 | Unknown                            |
| 4/F/81                  | IHD                                    | Contrast media                 | 0–30                                 | 48 h                               |
| 5/F/82                  | IHD                                    | Contrast media                 | 0–30                                 | 84 h                               |
| 6/M/36                  | Extensive trauma (MVA)                 | Contrast media                 | 0–30                                 | 0–60 min                           |
| 7/M/49                  | None                                   | Hymenoptera                    | 0–30                                 | 0–60 min                           |
| 8/F/64                  | IHD                                    | Hymenoptera                    | 0–30                                 | 0–60 min                           |
| 9/M/58                  | IHD                                    | Hymenoptera                    | 0–30                                 | 1–6 h*                             |
| 10/F/70                 | None                                   | Hymenoptera                    | 31–60                                | 1–6 h*                             |
| 11/F/61                 | IHD                                    | Hymenoptera                    | 0–30                                 | <4 h*                              |
| 12/M/66                 | IHD                                    | Hymenoptera                    | 0–30                                 | 0–60 min                           |
| 13/M/64                 | Asthma, hypertensive heart disease     | Clams/seafood                  | 0–30                                 | 0–60 min                           |
| 14/M/35                 | Schizophrenia                          | Peanuts                        | 0–30                                 | 0–60 min                           |
| 15/F/91                 | IHD                                    | Ice cream, possibly peanuts    | 0–30                                 | 0–60 min                           |
| 16/F/17                 | Asthma                                 | Shrimp                         | 0–30                                 | 96 h                               |
| 17/M/41                 | Alcohol intoxication                   | Food (unknown)†                | Unknown                              | Unknown                            |
| 18/F/65                 | COPD, CHF, hypertensive heart disease  | Enalapril or clarithromycin    | Unknown                              | Unknown                            |
| 19/M/73                 | IHD, aortic stenosis                   | Tolmetin sodium                | 0–30                                 | 0–60 min                           |
| 20/M/67                 | COPD                                   | Methylprednisolone             | 0–30                                 | 0–60 min                           |
| 21/M/71                 | Severe mitral regurgitation, CHF, COPD | Ciprofloxacin                  | 0–30                                 | 0–60 min                           |
| 22/M/24                 | None                                   | Amoxicillin                    | 0–30                                 | 0–60 min                           |
| 23/F/50                 | CHF                                    | Tolmetin sodium                | 0–30                                 | <2 h*                              |
| 24/F/68                 | IHD, CHF                               | Probably hair coloring product | Unknown                              | Unknown                            |
| 25/F/57                 | ESRD, SLE, pneumonia                   | Probably insect repellent      | 0–30                                 | 24 h                               |

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; IHD, ischemic heart disease; MVA, motor vehicle accident; SLE, systemic lupus erythematosus.

\* Estimated time.

† The patient had a previous anaphylactic reaction to food (unspecified) and was found dead with recently administered self-injectable epinephrine nearby.

deaths were probably consistent with anaphylaxis. Two cases were considered as possible anaphylaxis because of the demise being complicated by alcohol intoxication (patient 17) and the issue of hair coloring as a trigger with an unknown time to the onset of symptoms (patient 24).

Of the 25 cases of anaphylactic deaths included in this study, 7 resulted from medication reactions, 6 from radiocontrast media, 6 from Hymenoptera stings, 4 from food reactions, and 1 each possibly from insect repellent and hair coloring product reactions (Table 2). Although the exact hair coloring product was not known, Cogen and Beezhold<sup>10</sup> reported a documented case of anaphylaxis caused by latex found in the glue used for cosmetic hair bonds and extensions. This report raises the possibility of a “hidden” allergen as the cause of anaphylaxis in this patient.

Acute respiratory distress and circulatory collapse were among the presenting features of anaphylaxis in all cases in which the history was known (n = 23). Six patients initially had circulatory collapse, and 9 patients had respiratory distress. Eight patients had both findings. Cutaneous manifestations included 3 cases of flushing or generalized pruritus, but just 1 case had the postmortem finding of urticaria. In 2 cases, periocular edema was described (Table 3).

Table 3. Initial Signs and Symptoms in 25 Anaphylactic Fatalities

| Initial sign/symptom (≥1 per patient) | Fatalities, No. |
|---------------------------------------|-----------------|
| Respiratory distress                  | 17              |
| Circulatory collapse                  | 14              |
| Flushing/generalized pruritus         | 3               |
| Facial/neck congestion                | 2               |
| Periocular edema                      | 2               |
| Numbness and tingling                 | 1               |
| Nausea and vomiting                   | 1               |
| Dizziness                             | 1               |
| Skin eruptions                        | 1               |
| Facial edema                          | 1               |
| Oral mucosal edema                    | 1               |
| Sudden death with unknown symptoms    | 6               |

The time from allergen exposure until onset of the anaphylactic reaction was 30 minutes or less in 21 patients, 31 to 60 minutes in 1 patient, and unknown in 3 patients (Table 2). The time elapsed from allergen exposure to death was 60 minutes or less in 13 patients, approximately 1 to 6 hours in 4 patients, and 24 to 96 hours in 4 patients (Table 2). The time

was unknown in 4 cases. The 4 patients who experienced a delayed death (24–96 hours) each developed an immediate and severe anaphylactic reaction that required mechanical ventilation and admission to the intensive care unit.

Previous allergic reactions to the implicated allergen were identified for 8 cases. One patient each had reacted previously to radiocontrast media, shrimp, clams, and penicillin. Three patients each had developed a previous systemic reaction to a Hymenoptera sting. In addition, 1 patient who had a previous food reaction was found dead in his residence with a recently administered self-injectable EpiPen (Dey Laboratories, Napa, CA) nearby. The allergen that triggered the fatal reaction was not known for this patient. Except for this last patient, none of the other 4 patients who died of anaphylaxis and had a previous anaphylactic reaction had epinephrine available for emergency use. It was not stated in the medical record whether the patient with a previous radiocontrast media reaction had been pretreated with systemic corticosteroids and diphenhydramine before the fatal anaphylactic reaction.

#### *Pathological Findings*

Postmortem examinations were performed in 23 of 25 cases. Nonspecific pulmonary congestion and pulmonary edema were present in 18 cases (78%) (Table 4). Specific pathological findings suggestive of anaphylaxis were present in 17 (85%) of 20 cases of immediate deaths. Of the 23 cases in which an autopsy was performed, upper airway edema was identified in 16 (80%) of 20 immediate deaths and in 16 (70%) of 23 deaths overall. Five immediate deaths (25%) were caused by severe upper airway edema, 4 (20%) by moderate edema, 5 (25%) by mild edema, and 2 (10%) by upper airway edema that was not graded. Of the 3 delayed deaths, none had upper airway edema. One immediate death did not have upper airway edema but did have petechial hemorrhages of the vocal cord and tracheobronchial tree, suggesting an asphyxial component of death. Overall, 6 patients (5 immediate deaths and 1 delayed death) developed petechial hemorrhage of the vocal cords or tracheobronchial tree. Acute pulmonary hyperinflation occurred in 3 cases (all immediate deaths) and was marked in 2 of them. One patient with a delayed anaphylactic death who had a history of asthma was found to have microscopic mucous plugging. Only 3 patients were noted to have increased mucous secretions in the tracheobronchial tree. One patient who did not have an autopsy performed was noted to have congestion of the face, neck, and shoulders, a finding suggestive of an asphyxial component of death. Histologic examination of the laryngeal mucosa in 1 patient with laryngeal edema demonstrated degranulated mast cells.

#### *Serum Tryptase Levels and Comorbid Conditions*

Serum total tryptase concentrations were elevated markedly in 4 of 7 patients in whom it was analyzed (200, 101, 63.2, and 78 ng/mL). In at least 1 of the negative cases, the anaphylactic death was delayed 8 to 10 hours, which would

Table 4. Pathological Findings in 23 Anaphylactic Fatalities With Completed Autopsy Examinations

| Pathologic finding (≥1 per patient)                          | Fatalities, No. |
|--------------------------------------------------------------|-----------------|
| Pharyngeal edema                                             | 6               |
| Not graded                                                   | 5               |
| Severe                                                       | 1               |
| Laryngeal edema                                              | 16              |
| Not graded                                                   | 5               |
| Slight                                                       | 3               |
| Moderate                                                     | 4               |
| Severe                                                       | 4               |
| Pulmonary congestion and edema                               | 18              |
| Increased tracheobronchial mucus secretions                  | 3               |
| Not graded                                                   | 1               |
| Slight                                                       | 1               |
| Severe                                                       | 1               |
| Acute pulmonary hyperinflation                               | 2               |
| Mucous plugging                                              | 2               |
| Bronchopneumonia                                             |                 |
| Unilateral                                                   | 2               |
| Bilateral                                                    | 2               |
| Petechial hemorrhages of vocal cord or tracheobronchial tree | 6               |
| Cardiovascular disease                                       | 19              |
| Ischemic heart disease                                       | 11              |
| Congestive heart failure                                     | 4               |
| Left ventricular hypertrophy                                 | 2               |
| Valvular heart disease                                       | 2               |

likely have been sufficient time for the serum tryptase concentration obtained from postmortem serum to have returned to normal.

Overall, 22 patients (88%) had 1 or more comorbid conditions identified pathologically at the time of death. Nine patients had 2 or more comorbid conditions. Clinically significant IHD was identified in 11 of 25 cases (Table 2). Other cardiovascular conditions included congestive heart failure, valvular heart disease, and hypertensive heart disease. Chronic obstructive pulmonary disease was identified in 5 cases. Two patients with food-induced anaphylaxis had a history of asthma (1 of these cases had microscopic mucous plugging, but the deceased patient had been intubated for nearly 5 days).

## DISCUSSION

Few studies have analyzed postmortem findings in unselected cases of fatal anaphylaxis. Major findings from this study include that (1) the onset of severe anaphylactic symptoms occurred in less than 30 minutes in nearly every case, (2) death from anaphylaxis occurred in less than 60 minutes in 13 of 25 cases, (3) 18 of 23 cases undergoing autopsy were associated with specific anatomical findings of anaphylaxis, (4) self-administered emergency epinephrine was given appropriately in 1 of 5 cases, and (5) serum total tryptase concentrations were elevated markedly in 4 of 7 cases tested.

We found that 20 of the 23 cases undergoing autopsy had at least 1 comorbid disease identified pathologically. Cardiovascular diseases were present in 15 of 23 cases. Chronic obstructive pulmonary disease was present in 5 cases. There was a previous history of asthma in 2 cases. These findings of such frequent comorbidity contrast with those of earlier studies in which postmortem findings of fatal anaphylaxis were analyzed. In another study that reported postmortem findings in 56 unselected cases of fatal anaphylaxis, Pumphrey and Roberts<sup>3</sup> reported that IHD was present in 4, chronic obstructive pulmonary disease in 1, and carcinoma of the breast in 2. Mosbech<sup>4</sup> reported clinical and pathologic findings in 26 cases of fatal Hymenoptera reactions; IHD was reported and may have contributed to death in 5 of these cases. Only 1 patient had a previous history of asthma.<sup>4</sup> Barnard<sup>11</sup> reported pathologic findings in 100 cases of fatal Hymenoptera reactions. Five of these cases were complicated by coronary occlusion.<sup>11</sup> Low and Stables<sup>6</sup> identified atherosclerotic cardiovascular disease in 10 (56%) of 18 cases.

We found that specific anatomical findings consistent with anaphylaxis were present in 18 of 23 cases undergoing autopsy, including 17 of the 20 immediate anaphylactic deaths. Upper airway edema was present in 16 of the 20 immediate deaths. The frequency of specific anatomical findings consistent with anaphylaxis in previous studies of fatal anaphylaxis has been variable. Pumphrey and Roberts<sup>3</sup> reported that 23 of 56 cases of fatal anaphylaxis had no macroscopic postmortem findings consistent with anaphylaxis. Delage and Irely<sup>2</sup> examined clinical and pathologic findings in 43 cases of medication- and diagnostic agent-induced fatal anaphylactic reactions and reported that upper airway edema and acute obstructive emphysema were present in 15 and 11 cases, respectively. It was not stated how many of these cases did not have specific anatomical findings consistent with anaphylaxis. In one of the earlier studies of fatal anaphylaxis, Lewis and Austen<sup>12</sup> reported that 5 of 6 cases had upper airway edema, and 3 of 6 cases had gross hyperinflation of the lungs. Low and Stables<sup>6</sup> reported the presence of laryngeal edema and pulmonary congestion in 5 and 13 of 18 cases, respectively.

The diagnosis of anaphylaxis can be made more easily when classic signs and symptoms of anaphylaxis develop after exposure to an allergen. In nonfatal anaphylaxis, in fact, up to 88% of the cases are associated with urticaria and angioedema, and wheezing and dyspnea are present in up to 47% of the cases.<sup>1</sup> However, with severe anaphylactic reactions, there is often a short interval between allergen exposure and the onset of acute respiratory distress or anaphylactic shock.<sup>2,13</sup> Some of the more readily recognized signs and symptoms of anaphylaxis may be absent, unrecognized, or not documented. In fatal cases of anaphylaxis, acute respiratory distress and circulatory collapse are frequently the sole initial features and may occur with such rapidity that the classic features do not develop.<sup>2-4</sup> All the patients in the present study presented with acute respiratory distress, circulatory collapse, or both, often with no other presenting fea-

tures. Delage and Irely<sup>2</sup> reported that acute respiratory distress and circulatory collapse were the most frequent initial features of patients experiencing anaphylactic shock, occurring in 16 and 14 of the 43 total cases, respectively. Pumphrey and Roberts<sup>3</sup> reported that there was a history of collapse in all 56 cases after allergen exposure.

The finding that concentrations of serum  $\beta$ -tryptase and total tryptase, a neutral protease of human mast cells, may be elevated during an anaphylactic reaction provides clinicians and pathologists with an indicator of mast cell activation.<sup>3,5-9,14</sup> Although postmortem serum tryptase concentrations taken from suspected anaphylactic deaths have been shown to be elevated, the specificity of serum tryptase concentrations has been questioned when used alone to diagnose anaphylaxis.<sup>15-17</sup> Randall et al<sup>16</sup> reported that of 49 autopsy cases in which death was considered to be of non-anaphylactic origin, the serum tryptase concentration was greater than 10 ng/mL in 5 (10%). Edston and van Hage-Hamsten<sup>15</sup> measured serum  $\beta$ -tryptase concentrations in 193 cases, including 176 with a known cause of death, 20 with unexplained death, and 7 with anaphylactic or anaphylactoid death. When the investigators used 10 ng/mL as the cutoff value for anaphylaxis, sensitivity was 86% and specificity was 88%. When the cutoff level was increased to 20 ng/mL, sensitivity decreased to 71% but specificity increased to 93%.<sup>15</sup> In the present study, postmortem serum total tryptase concentrations were elevated in 4 of 7 cases tested, with a range from 63.2 to 200 ng/mL. Pumphrey and Roberts<sup>3</sup> reported elevated serum tryptase concentrations in 14 of 16 anaphylactic deaths (their data were not presented).

Serum tryptase concentrations may not be elevated for up to 30 minutes after the onset of an anaphylactic reaction.<sup>7</sup> Concentrations typically peak in 1 to 2 hours and have a half-life of 90 to 120 minutes or longer.<sup>16</sup> Serum tryptase concentrations can be elevated for 1 to 4 hours after a non-fatal anaphylactic event, or even longer depending on the magnitude of peak tryptase concentrations.<sup>16</sup> Serum tryptase concentrations remain stable in postmortem sera for at least 1 year when stored at  $-20^{\circ}\text{C}$ .<sup>15</sup> Patients experiencing a sudden and rapidly fatal anaphylactic reaction may not have elevated postmortem tryptase values. In addition, tryptase concentrations may have normalized in patients whose death is delayed for more than several hours before the serum tryptase concentration is obtained, thus reducing the sensitivity.<sup>16</sup>

Ingestion of an amount of food (such as peanuts) on the order of milligrams to grams can trigger life-threatening anaphylaxis.<sup>18</sup> One such patient in the present series was a 17-year-old girl with a history of asthma and a previous anaphylactic reaction to shrimp. The patient was reported to have consumed a "minute" quantity of shrimp and within minutes developed immediate respiratory distress and used her albuterol, but circulatory collapse proved fatal. Five patients in the present study had a previous IgE-mediated hypersensitivity reaction to the allergen that was implicated in their fatal reaction. Only 1 of these patients had administered epinephrine. In a study by Bock et al,<sup>19</sup> 19 of 21 patients who

had fatal food-induced anaphylaxis had a previous systemic reaction to the food implicated in their death. Only 2 of these subjects had received timely administration of epinephrine.<sup>19</sup> Pumphrey<sup>13</sup> reported that just 20% of patients who succumbed to anaphylaxis had received epinephrine before the fatal arrest.

Patient 20 had received methylprednisolone and was believed to have had fatal anaphylaxis. Immediate-type reactions have been described after intravenous methylprednisolone exposure,<sup>20,21</sup> and even generalized urticaria, syncope, and shock have been reported after intra-articular triamcinolone use.<sup>22</sup> We do not know whether this patient had undergone skin testing to methylprednisolone or had had a previous reaction to a corticosteroid.

Two patients were considered to have had possible anaphylaxis using the classification system in this article. The analysis of patient 17, who had a history of food allergy, was complicated by alcohol intoxication and an unknown time course, but self-injectable epinephrine was found nearby. Patient 24 was considered to have possible anaphylaxis because of the cause being attributed to a hair coloring product. Other anatomical causes of death had not been identified.

In summary, the fatal episodes of anaphylaxis had rapid progression, with 13 of 25 deaths occurring within 1 hour of the onset of the reaction. Comorbidities were frequent, consisting primarily of IHD. Specific anatomical findings were present in 18 of 23 autopsy examinations, but urticaria was identified in only 1 case. Epinephrine administration by the patient seemed to have occurred in just 1 of 5 cases. Serum total tryptase concentrations were elevated markedly in 4 of 7 cases.

## REFERENCES

- Lieberman PL. Anaphylaxis and anaphylactoid reactions. In: Adkinson NF Jr, Yunginger JW, Busse WW, Bochner BS, Holgate ST, Simons FER, eds. *Middleton's Allergy: Principles and Practice*. 6th ed. St Louis, MO: Mosby; 2003:1497–1522.
- Delage C, Irely NS. Anaphylaxis deaths: a clinicopathologic study in 43 cases. *J Forensic Sci*. 1972;17:525–540.
- Pumphrey RS, Roberts IS. Postmortem findings after fatal anaphylactic reactions. *J Clin Pathol*. 2000;53:273–276.
- Mosbech H. Death caused by wasp and bee stings in Denmark 1960–1980. *Allergy*. 1983;38:195–200.
- Riches KJ, Gillis D, James RA. An autopsy approach to bee sting-related deaths. *Pathology*. 2002;34:257–262.
- Low I, Stables S. Anaphylactic deaths in Auckland, New Zealand: a review of coronial autopsies from 1985 to 2005. *Pathology*. 2006;38:328–332.
- Schwartz LB, Metcalfe DD, Miller JS, et al. Tryptase levels as an indicator of mast-cell activation in systemic anaphylaxis and mastocytosis. *N Engl J Med*. 1987;316:1622–1626.
- Nishio H, Takai S, Miyazaki M, et al. Usefulness of serum mast cell-specific chymase levels for postmortem diagnosis of anaphylaxis. *Int J Legal Med*. 2005;119:331–334.
- Ansari MQ, Zamora JL, Lipscomb MF. Postmortem diagnosis of acute anaphylaxis by serum tryptase analysis: a case report. *Am J Clin Pathol*. 1993;99:101–103.
- Cogen FC, Beezhold DH. Hair glue anaphylaxis: a hidden latex allergy. *Ann Allergy Asthma Immunol*. 2002;88:61–63.
- Barnard JH. Studies of 400 Hymenoptera sting deaths in the United States. *J Allergy Clin Immunol*. 1973;52:259–264.
- Lewis PJ, Austen KF. Fatal systemic anaphylaxis in man. *N Engl J Med*. 1964;270:597–603.
- Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy*. 2000;30:1144–1150.
- Yunginger JW, Nelson DR, Squillace DL, et al. Laboratory investigation of deaths due to anaphylaxis. *J Forensic Sci*. 1991;36:857–865.
- Edston E, van Hage-Hamsten M.  $\beta$ -Tryptase measurements post-mortem in anaphylactic deaths and in controls. *Forensic Sci Int*. 1998;93:135–142.
- Randall B, Butts J, Halsey J. Elevated postmortem tryptase in the absence of anaphylaxis. *J Forensic Sci*. 1995;40:208–211.
- Horn KD, Halsey JF, Zumwalt RE. Utilization of serum tryptase and immunoglobulin E assay in the postmortem diagnosis of anaphylaxis. *Am J Forensic Med Pathol*. 2004;25:37–43.
- Yunginger JW, Sweeney KG, Sturmer WQ. Fatal food-induced anaphylaxis. *JAMA*. 1988;260:1450–1452.
- Bock SA, Munoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol*. 2001;107:191–193.
- Mendelson LM, Meltzer EO, Hamburger RN. Anaphylaxis-like reactions to corticosteroid therapy. *J Allergy Clin Immunol*. 1974;54:125–131.
- Brugdorff R, Venemalm L, Vogt T, et al. IgE-mediated anaphylactic reaction induced by succinate ester of methylprednisolone. *Ann Allergy Asthma Immunol*. 2002;89:425–428.
- Karsh J, Yang WH. An anaphylactic reaction to intra-articular triamcinolone: a case report and review of the literature. *Ann Allergy Asthma Immunol*. 2003;90:254–258.

Requests for reprints should be addressed to:  
 Paul A. Greenberger, MD  
 Division of Allergy-Immunology  
 Northwestern University Feinberg School of Medicine  
 676 N St Clair  
 Suite 14018  
 Chicago, IL 60611  
 E-mail: p-greenberger@northwestern.edu