

# Incidence of Anaphylaxis in the Emergency Department: A 1-Year Study in a University Hospital

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**SUMMARY** The aim of this study was to estimate the incidence of anaphylaxis in an emergency department, identify rate and risk factors of recurrent anaphylaxis, and describe its clinical features and management. A retrospective study of patients who attended the emergency department at Thammasat University Hospital was conducted during 2003-2004 with anaphylactically related ICD-9 and ICD-10 terms. There were 64 patients who experienced 65 anaphylactic episodes during the 1-year period. The anaphylaxis occurrence rate was 223 per 100,000 patients per year. The most common manifestations were cutaneous symptoms and signs, followed by respiratory expression. Food allergy was the most common cause of anaphylaxis. Eighty-five percent of admitted cases had monophasic anaphylaxis. Patients with and without biphasic reactions did not differ significantly in terms of epinephrine and steroid usage. In conclusion, anaphylaxis is not rare. Epinephrine and steroid usage did not prevent biphasic reactions.

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Anaphylaxis is an acute and potentially fatal systemic reaction. The clinical features can vary in terms of onset, appearance and severity.<sup>1</sup> Awareness of the clinical features of anaphylaxis and its causes are important. The exact occurrence rate of anaphylaxis from all triggers is unknown.<sup>2</sup> Few reports have described the incidence of anaphylaxis in the general population. The epidemiologic study of anaphylaxis is difficult and usually underestimated. Factors that might lead to the underreports on the real incidence of anaphylactic attacks are as follows: (1) anaphylaxis might have been unrecognized, especially during surgery; (2) patients with sudden death might not have been included; (3) very mild anaphylaxis might not have been recognized.<sup>3</sup> In the US population, the occurrence rate is higher than 1%.<sup>4</sup> Although the majority of episodes were treated in the emergency department (ED), little information is known about

clinical characteristics at presentation and treatment. The purposes of this study were (1) to determine the occurrence rate of anaphylaxis in the emergency department; (2) to describe the clinical features and management of anaphylaxis; (3) to identify rate and risk factors of recurrent anaphylaxis.

## MATERIALS AND METHODS

### Study population

A retrospective case study was performed of all patients who attended the Emergency Department

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at Thammasat University Hospital, Thammasat University, Thailand, from December 1, 2003 to November 30, 2004. We selected the patients' charts based on the International Classification of Diseases (ICD), 9<sup>th</sup> and 10<sup>th</sup> version, using the discharge diagnostic codes of the following: allergic reaction; anaphylaxis; urticaria; angioedema; laryngeal edema; syncope; shock; insect sting; food allergy and drug allergy. To confirm the diagnosis, the medical records obtained from the database were reviewed. Anaphylaxis was established on the basis of the presence of one symptom of generalized mediator release such as flushing; pruritus or paresthesias of lips, axilla, hands, or feet; general pruritus; urticaria or angioedema; lip tingling; and conjunctivitis or chemosis, including at least one symptom involving the oral and gastrointestinal, respiratory, or cardiovascular systems.<sup>5</sup> The study was approved by the Ethical Committee of the Faculty of Medicine, Thammasat University.

### Medical record review

The medical records were reviewed to collect demographic data e.g. age and sex. The date of onset, symptoms and signs, treatment, and history of atopy were also obtained. Patients were classified atopic if they had a history of asthma, allergic rhinitis, or eczema.

### Statistical analyses

The Statistical Package for the Social Sciences (SPSS), version 11.0 for Windows (SPSS Inc, Chicago, IL) was used for all statistical calculations. Chi-square testing was performed for a univariate analysis of the relationship between dichotomous clinical variables and the outcome variable of biphasic reactions. The unpaired *t* test was used for the univariate analysis of continuous clinical predictor variables and the outcome variable of biphasic reactions.

## RESULTS

One hundred and two records identified by the database search were reviewed, of which 64 satisfied our inclusion criteria. Since there were 28,699 attendances of patients of all age groups at the emergency department during this 1-year period, the occurrence rate of anaphylaxis in the emergency department was 223 per 100,000 patients per year. A

total of 65 episodes of anaphylaxis were identified in 64 patients. One case had two episodes from wheat anaphylaxis. Demographic data and the presence of associated atopy are presented in Table 1. Fig. 1 shows the age distribution of the patients with anaphylaxis. One patient with a history of cardiovascular disease died in the ICU. She developed shock and wheezing after a blood transfusion and a recurrent anaphylactic reaction after 2 hours. The mortality rate was 1.6%.

### Clinical features and causative agents

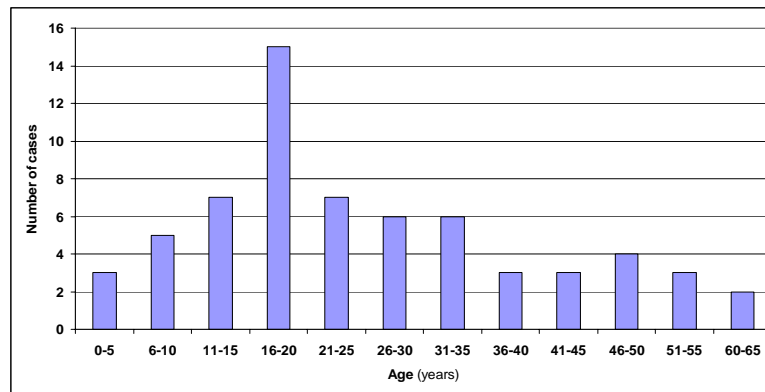
The clinical features of these 64 patients with anaphylaxis are shown in Table 2. Sixty patients (93.8%) had cutaneous manifestations while 49 patients (76.6%) experienced a respiratory expression. One patient had cyanosis, shock, seizure and nausea/vomiting after a benzathine injection without any cutaneous feature. The first presenting symptoms and signs are shown in Table 3. The causative agent was known in 83% of the patients with anaphylaxis (Table 4). The most common causes were food items (40%); followed by drugs (36%) and insects (5%). Twenty six cases had developed anaphylaxis from food. There were 22 cases with seafood allergy, 3 cases with cow milk allergy and one with wheat allergy. Drug-induced anaphylaxis included nonsteroidal anti-inflammatory agents (NSAIDs) (8 cases), penicillin (9 cases) and other medications such as antituberculous drugs and muscle relaxants. One patient developed urticaria and wheezing 5 minutes after contrast media injection.

### Treatments and investigations

The majority of anaphylactic events (83%) occurred at home. Fifty-two patients (81%) were

**Table 1** Demographic data

Male/Female (%)	34/30 (53/47)
Age (years) (median)	26 (1month-65 years)
Atopy (%)	35 (55)
-Allergic rhinitis	13 (20)
-Atopic dermatitis	4 (6)
-Asthma	8 (13)
-Urticaria	7 (11)
-Drug/food allergy	17 (27)



**Fig. 1** Distribution of the number of patients with anaphylaxis according to age (n = 64).

admitted to the hospital. Medications used in the treatment of anaphylaxis are shown in Table 5. However, only eight patients received epinephrine for autoinjection for anaphylactic events after discharge. Skin test and specific IgE to food were performed in 17 and 2 patients, respectively. An oral food challenge test was done in one patient.

### Biphasic reactions

Fifty-two cases resolved after the initial anaphylactic symptoms. A biphasic reaction occurred in 8 cases. Table 6 shows the comparison of patient characteristics between patients with monophasic and biphasic reactions. There were no significant differences in any characteristic between the two groups although the time interval between the onset of symptoms and the initial dose of epinephrine was longer for patients who had biphasic reactions.

## DISCUSSION

According to our knowledge, the present study is the first report of anaphylaxis occurring at an ED in Thailand. Our results show that anaphylaxis is not rare. The annual incidence (1 in 448 ED cases) presented in our study was consistent with a study from Australia,<sup>6</sup> but higher than in other studies.<sup>7,8</sup> Our mortality rate of anaphylaxis was 1:64 (1.6%), which is in agreement with results reported by Helbling<sup>9</sup> and Bunsawansong and colleagues.<sup>10</sup> However; this fatality rate appeared to be higher than those of previous studies.<sup>5,6</sup> Our finding and others<sup>11</sup> show that anaphylaxis can be found in all

**Table 2** Symptoms and signs of anaphylaxis

Symptoms and signs	Number of patients (%)
<b>Cutaneous</b>	60 (94)
Urticaria	50 (78)
Angioedema	40 (63)
Pruritus	40 (63)
Flushing	21 (33)
Conjunctivitis or chemosis	9 (14)
<b>Respiratory</b>	49 (77)
Dyspnea	39 (71)
Wheezing	23 (36)
Throat tightness	32 (50)
Rhinitis	6 (9)
Laryngeal edema	1 (2)
Hoarseness of voice	4 (6)
<b>Oral and gastrointestinal</b>	44 (69)
Intraoral angioedema	11 (17)
Oral pruritus	9 (14)
Dysphagia	6 (9)
Nausea	27 (42)
Abdominal cramps	13 (20)
Diarrhea	10 (16)
<b>Cardiovascular</b>	31 (48)
Tachycardia	9 (14)
Hypotension	17 (27)
Syncope	9 (14)
Chest tightness	7 (11)
Shock	16 (25)
Seizure	1 (2)

ages of both sexes. Fifty-five percent of our patients had a history of allergy which is close to the 53 % of patients reported in Olmsted County.<sup>5</sup> A history of asthma was documented in 13% of our patients which is similar to the prevalence of asthma reported in the central<sup>12</sup> and north-eastern part of Thailand.<sup>13</sup> However, our study found only one case with asthma which developed food allergy in contrast to the report of Sampson<sup>14</sup> which found that asthma increased the risk of food anaphylaxis.

Food was the most common cause of anaphylaxis in our study consistent with other studies.<sup>8,15,16</sup> Seafood is the most common food allergy in Thailand contrary to a study from Japan which demonstrated that more than 60% of food allergies were caused by egg, cow milk and wheat.<sup>17</sup> We did not find any patients with peanut allergy in our study suggesting that peanut allergy is uncommon in Thailand similar to other studies conducted in the Asia Pacific region.<sup>17-19</sup> While peanut is the main cause of severe anaphylaxis in USA and Europe,<sup>20-22</sup> wheat allergy causes the most severe form of anaphylaxis in Thailand.<sup>23</sup> We found that one patient developed two severe anaphylactic episodes from wheat. In addition, our study demonstrated that cow milk allergy mainly occurred in young children, whereas drug allergy mainly occurred in adults. This study confirmed that NSAIDs and beta-lactam antibiotics were the drugs most commonly associated with allergy.<sup>6</sup> The incidence of wasp venom allergy was lower than in previous reports.<sup>9,24</sup> All cases with venom anaphylaxis had severe reactions (hypotension and wheezing). Based on the medical history, skin prick test, specific IgE test and food challenge, precipitating allergens were identified in 83% of cases which was in the range of other studies.<sup>8,25</sup> However, the incidence of idiopathic anaphylaxis reported in our study was lower than in previous reports.<sup>5,6</sup>

It should be noted that 94% of our patients had cutaneous manifestations in agreement with another study.<sup>6</sup> We also found that patients with acute anaphylaxis might not have cutaneous markers. It is possible that they were partially treated or a spontaneous resolution of cutaneous symptoms and signs occurred before the patient presented to the hospital. Seizure is an uncommon manifestation and may be the cause of delayed diagnosis.<sup>26</sup> In our study, one

**Table 3** The first anatomical site where symptoms and signs of anaphylaxis was presented

Symptoms and signs	Number of patients (%)
Cutaneous	48
Respiratory	8
Gastrointestinal	7
Nervous	1
Cardiovascular	0

**Table 4** Causes of anaphylaxis

Cause	Number of patients (%)
Foods	26 (40)
Drugs	23 (36)
<i>Hymenoptera</i>	3 (5)
Radiocontrast agent	1 (2)
Unidentified	11 (17)

**Table 5** Drugs used in patients with anaphylaxis

Treatment	Number of patients (%)
Epinephrine	57 (89)
-Intramuscular	40 (62)
-Subcutaneous	16 (25)
-Intravenous	1 (2)
H <sub>1</sub> -antagonists	64 (100)
H <sub>2</sub> -antagonists	39 (61)
Corticosteroids	49 (77)
Beta-agonists	15 (23)

case developed seizure and cyanosis immediately after a benzathine injection and a delayed epinephrine injection.

The use of H<sub>1</sub> antihistamines was high as expected, and even higher than epinephrine use (100% and 89%). The use of intramuscular epinephrine in our study was higher than in previous studies.<sup>6,8</sup> A few patients (2%) with mild anaphylaxis received intravenous epinephrine in an intramuscular preparation dose (1: 1,000). Intravenous epinephrine should be reserved for extreme emergencies when there is inadequacy of the circulation since inappro-

**Table 6** Clinical characteristics of patients with monophasic and biphasic reaction

Patient characteristics	Monophasic reaction N = 44	Biphasic reaction N = 8
Male gender	24 (54.5%)	4 (50%)
Mean age (year)	28	22.6
Atopy	22 (50%)	4 (50%)
Shock in initial phase	10 (22.7%)	3 (37.5%)
Mean time after allergen exposure (minutes)	39	48
Epinephrine injection	40 (90.9%)	8 (100%)
Steroid use	35 (79.5%)	7 (87.5%)
Median time to initial dose of epi- nephrine (minutes)	82	263

All parameters,  $p > 0.05$

priate treatment with epinephrine precipitates ventricular tachycardia.<sup>27</sup> Steroids were used in 77% of patients with anaphylaxis which was similar to a study in Australia.<sup>6</sup>

In the present study, we found that 15% of patients developed a biphasic reaction. Stark and Sullivan<sup>28</sup> reported biphasic reactions in 20% of anaphylactic patients. However, the occurrence rate of the biphasic reaction in our study was relatively high compared to a previous report in children.<sup>15</sup> The limitation of the study was that not all anaphylactic patients were admitted to the hospital. Thus, the exact occurrence of biphasic reactions could not be estimated. Since there was no significant difference in epinephrine and steroid usage between patients with and without biphasic reactions, steroid usage did not prevent biphasic anaphylaxis. The lack of efficacy of steroids in preventing biphasic reactions has also been reported by other researchers.<sup>15,27</sup> In contrast to the study reported by Lee and Greenes,<sup>15</sup> our data show that although the median time from the onset of symptoms to the initial administration of epinephrine in the patients with biphasic reactions was longer than in those without a biphasic reaction, it did not reach statistical significance. Even in the event of an early treatment with epinephrine, all anaphylactic patients should be admitted to monitor the possibility of a biphasic reaction. However, administering epinephrine as early as possible after the ini-

tial onset of symptoms may help to prevent other complications of anaphylaxis.<sup>29</sup>

To identify the causes of anaphylaxis, a referral to allergy specialists is recommended. There is a wide variation in reported referral rates to allergy clinics, ranging from 0%<sup>29</sup> to as high as 79%.<sup>25</sup> In our study, the referral rate to allergists was relatively low (30%). More attention is needed to identify the causative factors associated with anaphylaxis. Particularly, in patients with unknown etiology a proper investigation should be performed. Skin testing and/or specific IgE analysis should be included wherever appropriate.

In this study it is possible that most patients have a low compliance of epinephrine usage at home for anaphylactic treatment. Since instruments for auto-epinephrine injection such as Epipen<sup>®</sup> are not available in the country, an ampule/syringe/needle technique is being taught to the patients for anaphylaxis that occurs outside the hospital. This measure is relatively uncomfortable to the patients compared to the epinephrine self-injector. Since the nationwide prevalence of anaphylaxis including risk factors is still unknown in Thailand, more epidemiological studies of anaphylaxis are required. The outcome of our study should be, at least, provides some information to physicians who see patients with anaphylaxis in an emergency department and, hopefully, prompt

them to properly investigate and treat anaphylaxis and refer the patients to allergy specialists.

### ACKNOWLEDGEMENT

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