

# Fatal and near-fatal asthma questionnaire: Prelude to a national registry

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**Background:** Asthma mortality rates continue to be unacceptably high in the United States. As a follow-up to the initiatives proposed by the Asthma Mortality Task Force in 1987, the Committee on Asthma Mortality of the American Academy of Allergy, Asthma, and Immunology developed a questionnaire on fatal and near-fatal asthma.

**Objective:** This study assessed completeness of answers from participating physicians and described characteristics of patients with fatal and near-fatal asthma.

**Methods:** There were 111 survey items intended to characterize patients with fatal or near-fatal exacerbations of asthma. The questionnaire was sent to the members of the American Academy of Allergy, Asthma, and Immunology (approximately 3900), and a total of 143 usable questionnaires were received. **Results:** Responding physicians had information on most items in the questionnaire; the mean number of responses was 120 of 143 possible, with a median of 128 and a range of 40 to 143. Patient demographics, description of the event, identification of overall risk for the event, use of medications, and characteristics of asthma management had the most complete responses (median response rates were 126-143). Presence of factors contributing to the event had fewer responses (range, 44-125). The physicians frequently had information on some psychologic characteristics (eg, 108 responses for depression and/or hopelessness and 127 responses for social support) but less information on several others (eg, 62 responses for family dysfunction). Statistical analysis of the completed surveys indicated that only 2 characteristics distinguished fatal from near-fatal asthma: progression in minutes (adjusted odds ratio, 4.89; 95% confidence interval, 2.05-12.90) and absence of a past history of intubation (adjusted odds ratio, 3.55; 95% confidence interval, 1.55-8.97).

**Conclusions:** There is a need to gather further data on patients with fatal and near-fatal events to design appropriate prospec-

tive studies on asthma morbidity and mortality rates. Physicians can contribute important information about these patients. Gathering such data would be enhanced by establishing a national registry on fatal and near-fatal asthma. (*J Allergy Clin Immunol* 1999;104:763-8.)

**Key words:** Asthma mortality, fatal asthma, near-fatal asthma, questionnaire, rapidity of asthma progression, severe asthma, risk factors, asthma medications

Asthma mortality rates remain unacceptably high,<sup>1,2</sup> particularly in specific patient populations.<sup>3-7</sup> The rate of asthma deaths among children and young adults has more than doubled between 1980 and 1993.<sup>8</sup> Fatalities from asthma can be sudden and unexpected,<sup>9,10</sup> and even patients with mild disease may be at risk of fatal or near-fatal exacerbations of asthma.<sup>11,12</sup> In 1987, the Asthma Mortality Task Force, a joint endeavor of the American Thoracic Society and the American Academy of Allergy and Immunology, was formed to address the causes of increased asthma mortality rates in the United States and to plan a strategy for changing this trend.<sup>13</sup> The obvious need to educate physicians about asthma management gave birth to the National Asthma Education and Prevention Program.<sup>14</sup> The Asthma Mortality Task Force recommended that more information be obtained about the characteristics of individuals who died from asthma and how these patients differed from those who experienced near-fatal events. Therefore a committee of the American Academy of Allergy, Asthma, and Immunology (AAAAI) developed a questionnaire that was distributed to their membership for the purpose of gathering data on fatal and near-fatal asthmatic events. This was viewed as the first step toward the development of a national registry on fatal and near-fatal asthma.

## METHODS

The questionnaire was developed by the Committee on Asthma Mortality of the AAAAI based on a review of the available literature describing characteristics of patients who died of asthma. The survey items asked respondents to describe: (1) patient demographics (age, sex, race, class of residence, insurance status, and occupation); (2) description of the event (date and time); (3) location; (4) progression of events; (5) whether the event was unexpected; (6) whether the event was respiratory or cardiac in nature; (7) whether patient management was involved; (8) where the patient was treated; (9) identification of overall risk for the event (whether at risk for a fatal or near-fatal exacerbation, severity of asthma, change in severity over time, and histories of respiratory failure, emergency visits, hospitalizations, and significant nocturnal symptoms); (10)

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**Abbreviations used**

AAAAI: American Academy of Allergy, Asthma, and Immunology  
 CI: Confidence interval  
 NSAID: Nonsteroidal anti-inflammatory drug  
 OR: Odds ratio

use of medications (both asthma and other medications); (11) presence of factors contributing to the event (eg, upper respiratory infection, allergen or irritant exposure, paradoxical bronchospasm after use of inhaled drugs, allergen immunotherapy, emotional stress, family dysfunction, depression, and presence of significant life stress); and (12) characteristics of asthma management (delay in seeking help; recognition of severity by patient, family, and physician; adherence and self-care; delay in seeking help for asthma symptoms; and social support for asthma). There were a total of 111 items, 81 with specific responses and 30 items for comment or providing categories for specific areas.

Questionnaires were mailed to the 3897 physician members of the AAAAI, soliciting information on their experience with asthmatic patients who had undergone fatal or near-fatal events. A total of 143 usable questionnaires describing fatal or near-fatal events were returned within 8 months of the mailing. These 143 questionnaires described 89 fatal and 54 near-fatal events.

Statistical analysis of the completed surveys included a summarization of all items by using percentages for categorical responses and means and standard errors for continuous responses. For purposes of analysis, many multiple-level categorical responses were collapsed into fewer categories. Comparisons of responses between strata were performed by using  $\chi^2$  tests for categorical variables and independent sample *t* tests for continuous variables. For those categorical responses in which there were small expected cell sizes, the Fisher exact test was used. To assess the risk of events being fatal compared with being near fatal, logistic regression was used to compute odds ratios (ORs) and their 95% confidence intervals (CIs) for selected potential risk factors. Multiple logistic regression was used to identify subsets of selected risk factors that concurrently contributed to the risk of an event being fatal and to compute adjusted ORs. All tests were 2-tailed, and individual *P* values are reported. Because of the large number of tests performed, only those significant at the .01 level were considered statistically significant.

## RESULTS

### Use of the questionnaire by responding physicians

Of the 143 analyzable events, 89 were fatal, and 54 were near fatal. Reports were based on records from private practice clinics (91), hospital inpatient charts (65), hospital outpatient records (31), and case management records (6); in some cases more than one source was identified. No autopsy data were included. Of the 143 responses, 118 were from physicians whose primary practice was in allergy and immunology. Seventy-three percent of patients received their primary care from an allergist-immunologist, with 25% being predominantly treated by a primary care physician.

Responses to the 81 questions requesting specific information were reviewed for completeness. The number of responses varied from 40 to 143 of the 143 possible, with a mean of 120 and a median of 128. Table I

shows selected characteristics from the questionnaire, with the percentages of questionnaires containing an answer for the characteristics. Most categories had a high percentage of responses: demographics (median, 143; range, 131-143), description of the event (median, 131; range, 79-143), identification of overall risk for the event (median, 132; range, 123-142), use of medications (median, 127; range, 98-139), and characteristics of asthma management (median, 126; range, 111-138). The physicians frequently had information on some psychologic characteristics (eg, 108 responses for depression and/or hopelessness, 127 responses for social support, and 131 responses for capacity to ask for help for symptoms). Presence of factors contributing to the event had fewer responses (median, 108; range, 44-125). Physicians had the most difficulty answering questions on time of day of the event (79 responses), role of patient management in outcome (93 responses), doses of inhaled steroids being used (98 responses), relationship of nonasthma medicines to the event (eg, 83 responses for the role of aspirin and nonsteroidal anti-inflammatory drugs [NSAIDs]), recent irritant exposure (42 responses), and paradoxical bronchospasm after inhaled drugs (45 responses). They also had difficulty providing information about some of the psychologic characteristics (eg, 49 responses for recent emotional stress, 62 responses for family dysfunction, and 40 responses for presence of life stress).

### Selected characteristics of patients undergoing fatal and near-fatal events

There were no statistically significant differences between the fatal and the near-fatal groups with regard to age, sex, race, residence, or insurance type. The majority of patients were white and had private insurance, probably reflecting sampling bias. Of the reports that listed an occupation, 34% were listed as students (consistent with the age of the group) without a statistically significant difference between the fatal and near-fatal groups.

Only one event feature and one historical feature were different between the fatal and near-fatal groups at a .01 level (Table I). The event feature was rapidity of progression, with deterioration in minutes for 46% of the fatal group compared with only 15% of the near-fatal group (*P* = .0026). The majority of both the fatal and near-fatal events were characterized as deteriorating over a period of less than 12 hours, with no difference between the groups. The historical feature was prior intubation, with a significantly higher percentage in the near-fatal group (48%) compared with the fatal group (19%; *P* = .0003). However, only 28% of the overall group had been intubated. Hypoxic seizures had occurred previously in 13 patients, 8 in the fatal group and 5 in the near-fatal group (*P* = .91; data not shown).

A majority (83%) of both fatal and near-fatal events were unexpected by the physician. A majority (62%) of both fatal and near-fatal events occurred at home (Table I). Respondents considered all events in both groups to be respiratory in nature. Only a small number of patients

**TABLE I.** Selected characteristics of patients undergoing fatal and near-fatal events

| Characteristic                   | Total* (n = 143) | Fatal† (n = 89) | Near fatal† (n = 54) | P value‡ |
|----------------------------------|------------------|-----------------|----------------------|----------|
| Demographics                     |                  |                 |                      |          |
| Age (y)                          | 100              | 32.3 ± 2.1      | 29.5 ± 2.5           | .41      |
| Sex (M)                          | 99               | 48              | 49                   | .93      |
| Race (white)                     | 99               | 72              | 70                   | .47      |
| Residence (urban)                | 99               | 47              | 33                   | .07      |
| Insurance (private)              | 92               | 80              | 71                   | .28      |
| Event features                   |                  |                 |                      |          |
| Progression of event (min)       | 95               | 46              | 15                   | .003     |
| Event unexpected                 | 92               | 83              | 82                   | .85      |
| Location of event (home)         | 100              | 60              | 67                   | .40      |
| Patient management related       | 91               | 27              | 35                   | .39      |
| Historical features              |                  |                 |                      |          |
| Intubation                       | 93               | 19              | 48                   | .00003   |
| Asthma severity (severe)         | 99               | 58              | 65                   | .61      |
| Asthma worse in previous year    | 98               | 23              | 26                   | .84      |
| Emergency visit in previous year | 86               | 72              | 75                   | .78      |
| Hospitalized in previous year    | 94               | 52              | 62                   | .30      |
| At risk for an event             | 95               | 71              | 76                   | .46      |
| Risk factors                     |                  |                 |                      |          |
| Recent urinary tract infection   | 93               | 51              | 62                   | .23      |
| Recent allergen exposure         | 73               | 48              | 49                   | .95      |
| Recent irritant exposure         | 29               | 14              | 8                    | .35      |
| Family dysfunction§              | 43               | 30              | 34                   | .73      |
| Depression-hopelessness          | 76               | 27              | 24                   | .76      |
| Recent emotional stress          | 34               | 19              | 43                   | .66      |
| Significant life stress          | 28               | 29              | 32                   | .84      |
| Social support fair or poor      | 89               | 39              | 40                   | .91      |
| Patient recognized severity      | 92               | 34              | 31                   | .68      |
| Family recognized severity       | 78               | 45              | 57                   | .21      |
| Extremely adherent to treatment  | 97               | 15              | 23                   | .11      |
| Adequate response (often)        | 91               | 56              | 41                   | .04      |

\*Numbers in this column represent the percentage of responses about this characteristic from the 143 questionnaires.

†Numbers in these columns represent the percentage of responses in each of the fatal and near-fatal groups, with the denominators being the number of responses received for each of the categories.

‡The P value is from a test of the hypothesis that the fatal and near-fatal events are different.

§In the year before the event, there were 13 reports of marital discord, 6 of drug or alcohol abuse in the family, 16 of financial instability, and 17 of lack of consistent support for medical treatment.

||There were 14 patients who were described as having expressed a feeling of hopelessness, 4 expressed a wish to die, and 2 had given direct or indirect references to suicide within 1 month of the event.

**TABLE II.** Asthma medication use

| Type of medication         | Respondents* | Use† | No use† | Pattern of use† |          |         |         |
|----------------------------|--------------|------|---------|-----------------|----------|---------|---------|
|                            |              |      |         | Episodic        | Underuse | Regular | Overuse |
| Oral $\beta$ -agonist      | 131/127      | 34%  | 66%     | 13%             | 1%       | 14%     | 6%      |
| MDI $\beta$ -agonist       | 142/98       | 95%  | 5%      | 36%             | 3%       | 53%     | 2%      |
| Nebulized $\beta$ -agonist | 131/124      | 64%  | 36%     | 32%             | 3%       | 19%     | 10%     |
| MDI salmeterol             | 95/91        | 52%  | 48%     | 6%              | 0%       | 42%     | 3%      |
| Oral corticosteroid        | 139/129      | 88%  | 12%     | 48%             | 14%      | 24%     | 2%      |
| Inhaled corticosteroid     | 135/131      | 85%  | 15%     | 8%              | 19%      | 58%     | 0%      |
| Nedocromil or cromolyn     | 259/250      | 23%  | 77%     | 4%              | 4%       | 15%     | 0%      |
| Theophylline               | 139/135      | 67%  | 33%     | 11%             | 8%       | 47%     | 1%      |

\*Number of respondents to question/number with knowledge of use (of a possible 143).

†Percentages in the table are based on only those patients for whom there was knowledge about the use of the medication.

were considered to have had a cardiac component (10 in fatal and 2 in near-fatal events, data not shown). Problems with patient management were identified as contributing in only about one third of each group.

Consistent with the event being unexpected, 76% of

the respondents indicated that the patient's asthma had remained the same or improved in the year before the event. In addition, 25% had no history of an urgent visit, and 45% had no history of hospitalization in the previous year. On the other hand, 73% of the patients were con-

sidered to have been at risk for a severe exacerbation of asthma, and approximately 60% were believed to have had severe disease, with no differences between the fatal and near-fatal groups.

Overall, risk factors for the fatal and near-fatal episodes were not different between the groups (Table I). Approximately one half of the patients were thought to have had a recent exposure to a respiratory viral infection or exposure to an allergen or irritant. Between 19% and 34% of the patients were considered to have had psychologic risk (family dysfunction, depression and/or hopelessness, recent emotional stress, or a significant life occurrence). The patient's social support was classified as fair or poor in 40%. In general, physicians judged patients and families as not able to recognize the severity of asthma. The patient recognized the severity of illness in only 25% of cases, and the family recognized the severity of illness in only 46% of cases. Adherence was characterized as extremely adherent in only 21%, neglectful in 23%, and inconsistent in 35%. The patients had an adequate response to previous problems in only 38%. In spite of these identified problems, only 31% of the events were thought to have been related to patient management (not shown).

Logistic regression analysis was performed with risk factors believed to possibly be related to fatal versus near-fatal events. Individual variables were collapsed as follows: residence, urban versus other; progression, in minutes versus longer; asthma severity, mild or moderate versus severe; intubation, no versus yes; emotional stress, no versus yes; and history of adequate response to symptoms, often versus other. The 2 strongest effects were progression in minutes, with an OR of 4.77 (95% CI 2.09-12.03) and absence of prior intubation, with an OR of 4.07 (95% CI 1.89-9.07). Multiple logistic regression analysis indicated that when these variables were modeled together, they remained highly significant. The adjusted ORs were 4.89 (95% CI 2.05-12.90) for progression in minutes and 3.55 (95% CI 1.55-8.47) for absence of prior intubation. The associated *P* values for these effects were .00002 and .0026, respectively. None of the other variables listed contributed significantly to the model at the .01 level.

### Use of asthma medications

The majority of patients were taking asthma medications (Table II). There was no significant difference between the near-fatal and fatal groups in regard to general or specific use of asthma medications. Almost 50% of patients were reported to have been reluctant to use asthma medications (data not shown). There was no significant difference in this regard between the fatal and near-fatal subsets of patients.

The majority of patients were using inhaled  $\beta_2$ -agonists delivered by metered-dose inhaler (95%). In most cases, the respondents had information on the pattern of  $\beta_2$ -agonist use. Fifty-six percent of patients were thought to have used the metered-dose inhaler on a regular basis. The majority of patients were also thought to have used

nebulized  $\beta_2$ -agonists (64%). Ten percent of respondents knowledgeable in the use of this type of medication reported that nebulized  $\beta_2$ -agonists were being overused. The majority of patients were also thought to be receiving corticosteroids; 58% used inhaled corticosteroids regularly. Of those receiving inhaled corticosteroids, about 60% were believed to be using greater than 800  $\mu$ g per day.

There was a determination made by 71% of the respondents that the event reported was not related to the patient's use of asthma medications (data not shown). Nevertheless, physicians thought medication may have played a role in 20 cases, with concern about salmeterol in 7, short-acting  $\beta$ -agonist (overuse) in 9, and corticosteroids (inadequate use) in 4. The questionnaire sought only suspicion. These results must be interpreted in the context of physician difficulty in knowing and reporting details of factors contributing to the events but do provide suggestion for future inquiry about deaths.

Eighty-six patients were reported to have been taking aspirin, and 87 were reported to have been taking NSAIDs. However, in only 2 patients taking aspirin and 1 patient taking an NSAID was the event judged to have been definitely related to use of this type of medication. There were 2 patients whose treatment with a  $\beta$ -adrenergic blocking agent was considered definitely related to the event.

### DISCUSSION

There is a need to gather information on the characteristics of patients who experience fatal and near-fatal exacerbations of asthma because of unacceptably high asthma mortality rates in this<sup>15-19</sup> and other countries.<sup>20-29</sup> The questionnaire developed and distributed by the Committee on Asthma Mortality of the AAAAI was returned by practicing physicians with extensive information about the patients and the fatal and near-fatal events. Physicians had difficulty providing answers in only a small number of areas represented by the 81 questions. Even for questions regarding psychologic status of the patients and families, which yielded the fewest responses, physicians provided significant detailed information about family dysfunction. Thus asking detailed questions about patients and families appears to produce useful information.

There are inherent limitations on conclusions that can be drawn from the database generated by the questionnaire described in this report; that is, a nonrandom sample of 89 deaths from a pool that probably would have exceeded 8000 over the approximately 18-month interval included in the reports. However, some interesting findings emerge from this limited data set. Although rapid progression of fatal or near-fatal asthma has been described previously,<sup>30,31</sup> it was alarming to see that 33% of the events were described as progressing to a fatal or near-fatal outcome within minutes. It is even more striking for the fatal events of which 46% were described as occurring with this rapidity. The insidious nature of these

events was reflected in the reply by 80% of the respondents that the event was unexpected despite the fact that 69% reported that the patient was at risk for this type of event. It is also reflected in the fact that approximately 75% of the patients were described as stable or improving in the year before the event. The general lack of distinguishing characteristics that separate patients who experience fatal and near-fatal exacerbations of asthma has been described previously.<sup>28,32</sup>

The findings of this questionnaire indicated that patients who had required assisted ventilation in the past were less likely to have a fatal episode than those who had not. This is different than other reports in which previous assisted ventilation was a risk for fatality.<sup>33-36</sup> Two possible explanations for this apparent paradox deserve consideration in future surveys. First, patients identified as having the potential for a fatal outcome by previous respiratory failure receive more immediate attention because of their prior event in institutions familiar with care of severe asthma in which mortality in asthma patients with respiratory failure is largely avoidable.<sup>37</sup> Second, some of the surviving patients who had been intubated may have had vocal cord dysfunction, a nonfatal condition that mimics and complicates asthma.<sup>38</sup> The clinical presentation of vocal cord dysfunction is often dramatic, and its misdiagnosis has led to both intubation and tracheostomy.<sup>38-40</sup>

There is strong evidence that inhaled corticosteroids reduce asthma morbidity and mortality rates.<sup>41-44</sup> Other studies have suggested that gross underuse of inhaled corticosteroids in patients with severe asthma leads to increased asthma morbidity and mortality rates.<sup>44,45</sup> Eighty-four percent of the patients reported here had been prescribed inhaled corticosteroids, with most of these prescribed greater than 800 µg per day. Other studies have demonstrated that patients with asthma may not be protected from fatal exacerbations of asthma simply because they are prescribed inhaled corticosteroids.<sup>46</sup> Consideration of the information on medication use must acknowledge the fact that prescribing medications does not establish that patients were actually taking these medications because there are a number of studies documenting highly variable adherence with medication use.<sup>47-51</sup> Physicians reported that only a small percentage of patients were adherent to medication use (Table I), which is consistent with underuse of prescribed medication, including inhaled steroids.

The database generated by this questionnaire has raised questions more than providing answers. It should be viewed as the first step toward the formation of a national registry for fatal and near-fatal events. An expanded database is likely to identify issues relating to asthma morbidity and mortality that can provide direction for well-designed prospective studies. In addition, such a registry could serve as an outlet for those treating patients with asthma. Anecdotally, health care providers have often expressed the need to believe that information about these events can be used to prevent asthma morbidity and mortality in the future.

This paper describes a database which was generated by a questionnaire distributed by the American Academy of Allergy, Asthma, and Immunology to the membership of that organization. The questionnaire was developed by the Committee on Asthma Mortality of the American Academy of Allergy, Asthma, and Immunology and distributed to the membership after review by the Board of Directors of the Academy.

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