Anaphylaxis in the United States
An Investigation Into Its Epidemiology
Alfred I. Neugut, MD, PhD; Anita T. Ghatak, MPH; Rachel L. Miller, MD

Background: Anaphylaxis is a severe, life-threatening allergic reaction that affects both children and adults in the United States. However, data regarding the incidence and prevalence of anaphylaxis and the number of deaths caused by it are limited.

Objective: To provide a better understanding of the magnitude of the problem of anaphylaxis in the United States.

Methods: A thorough review of the current medical literature was conducted to obtain prevalence estimates on each of the 4 major subtypes of anaphylaxis (food, drugs, latex, and insect stings). We calculated an overall estimate of the risk of anaphylaxis by using only estimates that are specifically derived from epidemiologic studies measuring anaphylaxis in the general population.

Results: Known rates or cases of anaphylaxis were 0.0004% for food, 0.7% to 10% for penicillin, 0.22% to 1% for radiocontrast media, and 0.5% to 5% after insect stings. There were 220 cases after latex exposure. Considering the 1999 US population of 272 million, the population at risk for anaphylaxis from food is 1099, from penicillin is 1.9 million to 27.2 million, from radiocontrast media is 22000 to 100000, from latex is 220, and from insect stings is 1.36 million to 13.6 million. These calculations yield a total of 3.29 million to 40.9 million individuals at risk of anaphylaxis.

Conclusion: The occurrence of anaphylaxis in the US is not as rare as is generally believed. On the basis of our figures, the problem of anaphylaxis may, in fact, affect 1.21% to 15.04% of the US population.

Arch Intern Med. 2001;161:15-21
fore, is not an appropriate screening method by which high-risk individuals can be identified. The most effective and reliable method of identifying individuals at risk of anaphylaxis is through a documented history of previous anaphylactic episodes and/or allergic or systemic reactions to known anaphylaxis triggers, ie, individuals who have had previous anaphylactic reactions may be at risk of future anaphylactic reactions. A history or known previous exposure can be used as a somewhat reliable indicator of risk, although it should be noted that some individuals may die from their first and only known anaphylactic reaction.

The incidence rates of anaphylaxis of all types have experienced upward trends in the United States in recent years, creating cause for serious alarm in the public health community. This rise has been linked primarily with the increased introduction of certain allergenic agents into various US settings. Some examples include the increased use of peanuts (one of the most common offending allergens in both adults and children) in the American food supply and the recent widespread use of latex gloves in the health care industry. There is also evidence that the westernization/industrialization process leads to increased incidence of anaphylaxis. Additional information on the nature and extent of this relationship is limited and unclear.

**MECHANISMS**

Anaphylaxis is caused by the interaction of a foreign antigen with specific IgE antibodies found on tissue mast cells and peripheral blood basophils. The subsequent release of histamine and other bioactive mediators caused by this interaction results in smooth-muscle spasm, bronchospasm, mucosal edema and inflammation, and increased capillary permeability. These systemic changes characteristically show clinical manifestations within seconds or minutes of antigen exposure. Closely related to anaphylaxis is an anaphylactoid reaction, caused by the release of mast cell and basophil mediators triggered by non-IgE-mediated events. For the most part, the reaction suffered by the patient and the treatment of the reaction by clinicians is identical to that of anaphylaxis.

**PREVENTION AND TREATMENT**

The basic approach to prevention is strict elimination and avoidance of offensive substances known to have allergenic potential. With widespread education, this strategy has enormous potential. Recurrence of anaphylaxis is largely based on repeated contact with or ingestion of the allergen; therefore, with caution and constant supervision, future reactions are preventable. However, avoidance is not always possible. In the event of accidental ingestion or contact, prompt treatment with epinephrine immediately after allergen exposure is effective, as it is with all subtypes of anaphylaxis.

**SYMPTOMS**

The clinical manifestations of anaphylaxis can vary in onset, appearance, and course. Common symptoms usually include weakness, dizziness, flushing, angioedema, urticaria of the skin, congestion, and sneezing. More severe symptoms include upper respiratory tract obstruction, hypotension, vascular collapse associated with angioedema and urticaria, gastrointestinal distress, cardiovascular arrhythmias, and/or arrest. Any combinations of these symptoms (common vs severe) have been observed among patients who have suffered an anaphylactic reaction. Common symptoms do not always precede the more severe symptoms as a warning or indication of a possible oncoming anaphylactic reaction. However, generally, the time to onset of symptoms is a good indicator of the severity of the reaction, ie, the faster the onset, the more severe the reaction.

**CASE DEFINITION**

On the basis of the above information, a proper case definition of anaphylaxis usually includes bronchial contractions in conjunction with hemodynamic changes. A good example is as follows: acute mucocutaneous signs (pruritus, flushing, urticaria, angioedema) coupled with any of (1) respiratory obstructive symptoms, such as glossal edema, pharyngeal edema, laryngeal edema, and bronchospasm; or (2) cardiovascular symptoms, such as hypotension substantiated by blood pressure measurement, syncope, or orthostatic hypotension; or (3) gastrointestinal symptoms, such as nausea, vomiting, diarrhea, or cramps. Although this type of definition is commonly found in published literature, there is no standard accepted definition; therefore, a great deal of confusion still exists regarding anaphylaxis among both lay people and medical professionals. It is commonly believed by some that anaphylaxis is limited to a subset of allergic reactions that are always severe and life threatening, while others consider anaphylaxis to be any type of systemic allergic reaction. The lack of a standard definition is one of several causes of much of the variability and uncertainty in incidence and prevalence studies of anaphylaxis.

Epidemiologic studies of anaphylaxis are also affected by the small study groups of patients selected and studied. Results of these small studies are used to produce estimates, which are often later used as national statistics, based on extrapolations of their individual findings. If estimates are to be of any real value on a national level, it is necessary for extensive efforts to be made nationwide. At this time, there are no national health statistics from which it is possible to generate incidence and prevalence estimates of anaphylaxis. A national registry mandating the reporting of anaphylactic reactions by individual institutions at the local or state level might help to resolve this problem. Incidence and prevalence estimates could then be easily generated in a timely and convenient manner.

In the face of these obstacles, there is clearly a need for further research on anaphylaxis. Additional epidemiologic studies must be undertaken to provide better insight to both clinicians and the general population, if further cases of anaphylaxis are to be understood and prevented. Realizing this need, we have undertaken this investigation. Un-
til such large-scale information, as previously mentioned, is available, our efforts in this study are merely a first step toward a better understanding of the problem.

**CAUSES OF ANAPHYLAXIS**

Agents that most commonly cause anaphylaxis are nearly identical among adults and children. They include foods, drugs, insect stings, and latex. Idiopathic anaphylaxis and food-dependent exercise-induced anaphylaxis have also been observed in some adults, although rarely in children. Although both of these subtypes are considered clinically significant, the incidence rates are low and therefore will not be investigated in this article. Below, we discuss the specific subgroups.

**Foods**

Foods are fairly common agents in anaphylactic reactions. Approximately 1% to 2% of the general population, or 2.7 million to 5.4 million Americans, suffer from food allergies. Nearly all published literature on food-related anaphylaxis uses this statistic. However, a few small studies have been conducted and have attempted to show incidence rates in selected populations and extrapolated their results to the entire US population. One such study showed that approximately 0.0004%, or 1080 Americans, have a severe allergic or anaphylactic reaction each year. Approximately 100 food-related anaphylactic deaths occur each year. The most common agents in food allergies include peanuts, tree nuts, shellfish, fish, milk, eggs, soy, and wheat. Of these, peanuts and tree nuts are the leading causes of severe food-induced anaphylaxis. In 1999, was an official code (995.0, anaphylaxis; E947.9, anaphylactic shock) established. Therefore, cases had to be attributed to other causes, such as general anaphylaxis, adverse food reactions, food intolerance, urticaria, angioedema, or unspecified allergic reaction, or even respiratory or cardiac arrest. Without laborious individual medical chart abstraction, such estimates remain unclear and are largely based on extrapolation.

In addition, these restraints affect our ability to assess trends in food-related anaphylaxis accurately. Recent upward trends could be attributable to a number of different reasons, some of which follow. The American diet has expanded during the past few decades to include more varied and foreign foods, many of which are known allergens. Some of these, especially peanuts, are often introduced to children at an early age, when the immune systems are immature. As the market continues to introduce such substances into the US food supply, more individuals will have the opportunity for increased and early exposure to allergens, with the potential to cause anaphylaxis. In addition, the Food and Drug Administration does not mandate the labeling of trace amounts of ingredients by US food manufacturing companies. As a result, inadvertent and unexpected exposures are possible.

**Drugs**

Hundreds of agents have been documented to cause anaphylaxis; Table 1 lists several of them. Drugs that most often cause anaphylaxis include β-lactam antibiotics (including penicillin), radiocontrast media (RCM), intravenous anesthetic drugs, aspirin and other noncorticosteroidal anti-inflammatory agents, and opioid analgesics. Among hospitalized patients, 2% to 3% experience allergic drug reactions and 1 in every 2700 suffers drug-induced anaphylaxis. Incidences of drug-induced anaphylaxis from all drug types are reportedly rising. This phenomenon may best be explained by the increased development and frequent use of newer protein-based medications.

Among the drugs that most commonly cause anaphylaxis, antibiotics, especially penicillin, and RCM cause the most serious anaphylactic reactions, with a rate of about 1 per 5000 exposures. Of all allergens, penicillin is the most frequent cause of anaphylaxis in hu-

### Table 1. Selected Medications Causing Anaphylaxis*

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Chemotherapeutic Agents</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin and derivatives</td>
<td>Asparaginase</td>
<td>Aspirin</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Vincristine sulfate</td>
<td>Noncorticosteroidal anti-inflammatory agents</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Cyclosporine</td>
<td>Allergy extracts</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Methotrexate</td>
<td>Immune globulin</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>Fluorouracil</td>
<td></td>
</tr>
<tr>
<td>Ciprofl oxacin</td>
<td></td>
<td>Insulin</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td></td>
<td>Heparin</td>
</tr>
<tr>
<td>Vancomycin hydrochloride</td>
<td></td>
<td>Vaccines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dextran</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opiates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protamine sulfate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Local anesthetics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucocorticosteroids</td>
</tr>
</tbody>
</table>

*Reprinted with permission from Kagy and Blaiss.©2001 American Medical Association. All rights reserved.
mammals and accounts for approximately 75% of fatal anaphylactic cases in the United States each year. Penicillin has been shown to cause fatal anaphylaxis at a rate of 0.002% among the general population or only those receiving the medicine, with 500 to 1000 deaths per year. If accurate, this would change the previously mentioned projection of 500 to 1000 deaths annually for anaphylaxis. Estimates of nonfatal drug-induced anaphylaxis to penicillin range from 0.7% to 10% among the general population, or 1.9 million to 27.2 million Americans. Anaphylaxis to penicillin most commonly occurs in adults aged 20 to 49 years, but it has been observed in all age groups.

Conventional RCM are used in more than 10 million procedures in the United States each year. The frequency of anaphylactoid reactions is reported to be between 0.22% and 1% of patients who receive RCM. In 1975, fatalities were estimated to occur in as many as 900, or 0.009%, of patients receiving RCM; these figures may be out of date. Newer, lower-osmolarity RCM are reported to cause fewer anaphylactoid reactions, cause less pain at the site of injection, and have fewer adverse effects. Adverse reactions in patients receiving lower-osmolar RCM are reported to occur at a rate of 3.13%, whereas in patients with conventional RCM the rate is 12.66%. The rate of anaphylactoid death caused by lower-osmolar RCM is also significantly reduced and is as low as 1 in 168,000 administrations. The frequency of reactions is equally distributed between males and females. Most patients who suffer from anaphylactoid RCM reactions are between the ages of 20 and 50 years. Reactions are less frequent in children and the elderly but are generally more severe. Of patients with a history of anaphylactoid reactions to conventional RCM, 16% to 44% are at risk of a recurrent reaction on reexposure. Incidence and severity of recurrent reactions can be reduced with pretreatment drug regimens or use of lower-osmolarity RCM. In addition, an increased risk and severity of anaphylactoid reactions to RCM has been linked to the concomitant use of β-blocker drugs. One study found that risk of moderate to severe anaphylactoid reaction was 2.6 times higher in patients taking β-blocking agents than in those who were not taking these medications.

Latex

During the past 10 to 15 years, the incidence of latex allergies has risen dramatically. With the spread of infectious diseases such as the acquired immunodeficiency syndrome and hepatitis, the use of latex-containing rubber gloves in the health care industry rose exponentially. This increased exposure led to the sensitization of millions of individuals, especially patients and occupational health care workers. Latex sensitivity has been documented in individuals with spina bifida, congenital urinary tract problems, and/or multiple surgeries and in health care workers. Studies have shown the incidence of latex allergy to be as high as 67% in patients with spina bifida, 6.5% in patients who have undergone multiple surgeries, and between 1% and 6% in the general population. These figures would indicate, based on assumptions, that there are presently more than 5.5 million health care workers in the United States and 272 million Americans in the current US population, that an estimated 440,000 to 935,000 health care workers, or 2.7 million to 16 million Americans, may suffer from some type of allergic reaction to latex.

Allergic reactions to latex may manifest as dermatitis initially and progress to a more severe reaction if exposure is repeated or continued. Because exposure to latex is possible through topical or mucosal contact, inhalation, and intravenous injection, latex-sensitive individuals should avoid latex completely, if possible. However, with more than 40,000 consumer products containing latex, avoidance may be difficult. Some suggested avoidance measures include using powder-free or low-allergen-content gloves and medical supplies or nonlatex-type alternative products. Sensitive individuals should also work in an environment where latex is not present. Proper content labeling of manufactured goods is also needed now if additional cases are to be prevented.

Widespread educational campaigns have been attempted, but the incidence of latex allergy continues to rise. Between 1988 and 1993, the Food and Drug Administration received more than 1100 reports of latex anaphylaxis, including 15 anaphylactic deaths. On the basis of this information, the annual incidence of latex-induced anaphylactic reactions is estimated to be 220. More recent information is unavailable.

Hymenoptera Stings

Stinging insects, belonging to the Hymenoptera order, include honeybees, bumblebees, sweat bees, yellow jackets, hornets, wasps, and ants. On the basis of population studies conducted in the United States, anaphylaxis from Hymenoptera stings is estimated to occur in 0.5% to 5% of the general population, or 1.36 million to 13.6 million Americans, and more commonly occurs in adults than in children. The reported incidence of death from insect sting anaphylaxis is between 40 and 100 per year, but this number is believed to be severely underestimated.

Accurate estimates of anaphylaxis to insect stings are difficult to determine, because systemic reactions are often not clearly differentiated from local reactions and toxic reactions. In many cases, the signs and symptoms of each of these types are identical, making diagnosis complicated. Skin testing and IgE measurements are unable to make these distinctions. Also, most affected individuals rarely seek treatment, so medical records do not provide an accurate estimate of the frequency of reactions. Reactions to stings occur with greatest frequency in individuals who are highly exposed, so those groups who are at highest risk are likely to be children, men, and outdoor workers or sportsmen.

Venom immunotherapy immediately after a sting is extremely effective and is recommended for up to 3 to 5 years after the incident. In adults with a history of anaphylaxis caused by Hymenoptera sting who do not receive im-
munotherapy, the risk of anaphylaxis from future stings lies between 30% and 60%, whereas in patients who do receive immunotherapy, the risk is less than 3%. Also, venom immunotherapy is generally very well tolerated, because only 6% of patients develop allergic reactions to the injections. Sting avoidance is advised through the use of appropriate apparel, insect repellent, and caution. In the event of a sting, prompt treatment with epinephrine is suggested.

PREVALENCE ESTIMATES

The objective of this investigation was to provide a better understanding of the magnitude of anaphylaxis in the United States. As stated previously, the scope of anaphylaxis is currently unclear. A thorough review of the current medical literature was conducted to obtain prevalence estimates on each of the 4 major subtypes of anaphylaxis (food, drugs, latex, and stings). Using those estimates, we have calculated an overall estimate to estimate the US population at risk for anaphylaxis (Table 2).

The total in this chart indicates that between 8.7 million and 62.6 million Americans are at risk of anaphylaxis. On closer examination, it is apparent that these calculations are largely based on estimates of populations who are allergic, not specifically anaphylactic. Theoretically, we might apply these numbers to show that a certain percentage of the US population suffers from allergies and therefore is at potential risk of anaphylaxis. However, only a small group will actually suffer an anaphylactic reaction. Therefore, this number is clearly an overestimate.

A better approach to estimating the US population at risk of anaphylaxis would use only estimates specifically calculated from epidemiologic studies measuring anaphylaxis in the general population. Those revised calculations appear in Table 3.

This chart (Table 3) now suggests that 3.3 to 43 million Americans may actually experience anaphylaxis, which is a narrower band than the one listed above. These values, we believe, are a better representation of the magnitude of anaphylaxis in the United States, as they are based solely on estimates presented by researchers in past epidemiologic studies of anaphylaxis (and not allergy). The wide range of values computed is of particular importance, for it further emphasizes and demonstrates the obvious limitations, as previously discussed, in this field of research.

One final figure of clinical significance is the number of deaths that occur annually as a result of anaphylactic reactions. Using the reported rates and totals from the studies used in Tables 2 and 3, we have calculated the number of deaths and present them in Table 4.

Given these values, it is now evident that the occurrence of anaphylaxis is not so rare as previously thought. In fact, these numbers suggest that from 1.24% to 16.8% of the total US population may suffer from an anaphylactic reaction and that 0.002% may die. Clearly, the magnitude of the problem is serious and poses a substantial health problem. Further investigation in this area is imperative to fully understand the scope of anaphylaxis in the United States.

STUDY LIMITATIONS

The estimates of anaphylaxis currently available in the literature, we expect, are greatly affected by underreporting. There are several explanations for this. During the course of an anaphylactic reaction, there are patients who choose not to seek medical advice or treatment. Other patients may also elect to take over-the-counter medications, which are widely available and come at low cost. Obviously, for such episodes, no record shall ever be documented. In ad-

### Table 2. Estimate of US Population at Potential Risk of Anaphylaxis

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Prevalence in US Population</th>
<th>Population at Risk of Anaphylaxis, Millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
<td>1%-2% allergic*</td>
<td>2.7-5.4</td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>0.7%-10% anaphylactic12</td>
<td>1.9-27.2</td>
</tr>
<tr>
<td>RCM†</td>
<td>0.22%-1% of US patients allergic21-22</td>
<td>0.022-0.1</td>
</tr>
<tr>
<td>Latex</td>
<td>1%-6% allergic23,24,25</td>
<td>2.7-16.3</td>
</tr>
<tr>
<td>Stings</td>
<td>0.5%-5% anaphylactic19</td>
<td>1.4-13.6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>8.7-62.6</td>
</tr>
</tbody>
</table>

*These rates are based on 1999 US population of 272 million.
†These rates apply to numbers of patients receiving radiocontrast media (RCM) based on 10 million procedures annually.

### Table 3. Revised Estimates of US Population at Potential Risk of Anaphylaxis*

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Known Estimated Occurrences in US Population</th>
<th>Population at Risk of Anaphylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
<td>0.76%14-10</td>
<td>1088-2 067 200</td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>0.7%-10%12,13</td>
<td>1 904 000-27 200 000</td>
</tr>
<tr>
<td>RCM</td>
<td>0.22%-1%21-23,26</td>
<td>22 000-100 000</td>
</tr>
<tr>
<td>Latex</td>
<td>NA</td>
<td>220</td>
</tr>
<tr>
<td>Stings</td>
<td>0.32%-5%34</td>
<td>1 360 000-13 600 000</td>
</tr>
<tr>
<td>Revised Total</td>
<td>3 287 308-42 967 420</td>
<td></td>
</tr>
</tbody>
</table>

*RCM indicates radiocontrast media; NA, not available.

### Table 4. Estimates of Number of Deaths Occurring Annually Attributable to Anaphylaxis

<table>
<thead>
<tr>
<th>Subtypes</th>
<th>Anaphylactic Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
<td>100</td>
</tr>
<tr>
<td>Drugs</td>
<td>400</td>
</tr>
<tr>
<td>Penicillin</td>
<td>900</td>
</tr>
<tr>
<td>RCM*</td>
<td>3</td>
</tr>
<tr>
<td>Latex</td>
<td>40-100</td>
</tr>
<tr>
<td>Stings</td>
<td>1443-1503</td>
</tr>
</tbody>
</table>

*RCM indicates radiocontrast media.
Table 5. Patient Diagnosis and Clinical Manifestation Information*  

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Clinical Manifestations</th>
<th>Original ED Diagnosis (ICD-9 Code)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pruritus, wheezing (subjective)</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>2</td>
<td>Urticaria, wheezing (subjective), gastrointestinal</td>
<td>Allergic reaction (995.3), possible viral gastroenteritis (008.8)</td>
</tr>
<tr>
<td>3</td>
<td>Urticaria, wheezing (objective), hypotension</td>
<td>Idiopathic urticaria (708.1), syncope episode (780.2)</td>
</tr>
<tr>
<td>4</td>
<td>Urticaria, wheezing (subjective)</td>
<td>Anaphylactic reaction (995.0)</td>
</tr>
<tr>
<td>5</td>
<td>Angioedema, wheezing (subjective)</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>6</td>
<td>Angioedema, urticaria, wheezing (subjective)</td>
<td>Allergic reaction (995.3), bronchospasm (519.1)</td>
</tr>
<tr>
<td>7</td>
<td>Angioedema, pruritus, wheezing (subjective)</td>
<td>Mild anaphylaxis (995.0)</td>
</tr>
<tr>
<td>8</td>
<td>Urticaria, angioedema, wheezing (subjective)</td>
<td>Angioedema (995.1)</td>
</tr>
<tr>
<td>9</td>
<td>Angioedema, wheezing (subjective)</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>10</td>
<td>Urticaria, wheezing (subjective)</td>
<td>Hives (708.9)</td>
</tr>
<tr>
<td>11</td>
<td>Urticaria, pruritus, syncope</td>
<td>Anaphylactic reaction (995.0)</td>
</tr>
<tr>
<td>12</td>
<td>Urticaria, pruritus, angioedema, hypotension, gastrointestinal</td>
<td>Anaphylaxis (995.0)</td>
</tr>
<tr>
<td>13</td>
<td>Angioedema, wheezing (subjective)</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>14</td>
<td>Urticaria, pruritus, wheezing (subjective)</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>15</td>
<td>Urticaria, angioedema, gastrointestinal</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>16</td>
<td>Urticaria, gastrointestinal</td>
<td>Allergic reaction (995.3)</td>
</tr>
<tr>
<td>17</td>
<td>Angioedema, wheezing (subjective)</td>
<td>Angioedema (995.1)</td>
</tr>
</tbody>
</table>

*ED indicates emergency department; ICD-9, International Classification of Diseases, Ninth Revision.14 Reprinted with permission from Klein and Yocum.7

condition, not all emergency departments will report or refer the patient to a specialist for further evaluation, medical treatment, or proper diagnosis. These cases will remain unreported as well. Finally, errors in the detection of anaphylaxis may occur if the patient is examined during the initial onset of symptoms. At the start of an anaphylactic reaction, symptoms can be limited to bronchospasm and upper respiratory tract obstruction. Without further medical observation and examination, such cases could easily be misdiagnosed as some other condition, such as asthma. It is believed that part of this problem could be alleviated with universal guidelines and definitions relating to the diagnosis and proper treatment of anaphylaxis.

Furthermore, incidence and prevalence estimates are limited without a national network of case reporting. Such values could be ascertained through extensive surveying of US hospitals and emergency facilities with the use of questionnaires, but this would require additional resources of time, money, and personnel. Moreover, information for particular diagnoses (hives, breathing difficulties, drop in blood pressure, etc) would necessitate laborious retrospective medical chart review on a case-by-case basis. An alternate method might consist of database searches of computerized hospital records by International Classification of Diseases, Ninth Revision, codes. This would entail searching hundreds or thousands of records for a particular keyword or set of keywords (e.g., urticaria, upper respiratory tract obstruction, or cardiovascular collapse). As one can imagine, this type of search would result in a countless number of matches. To avoid false-positive findings, each case would then have to be reviewed to ensure that the patient had actually experienced the symptom as a result of anaphylaxis. Given the wide range of symptoms associated with anaphylaxis, obtaining such an estimate would require an extensive amount of work.

Yocum and colleagues5 conducted the only study of the overall incidence of anaphylaxis in a defined community by performing a retrospective analysis of the medical records of 1255 Olmstead County, Minnesota, residents during a 5-year period (1983-1987). They used computer-linked, medical diagnostic indexes to identify residents who were seen with anaphylaxis. In this study, 155 anaphylactic episodes occurred, yielding an average annual incidence rate of anaphylaxis of 21 per 100,000 person-years and occurrence rate of 30 per 100,000 person-years. The case-fatality rate was 0.65% during the 5-year period. While this study may underestimate the true incidence of anaphylaxis because of underdiagnosis of the episodes, attacks occurring outside Olmstead County, and the fact that the study preceded the widespread use of latex in the health care industry, it provides a useful analysis in a defined general population.

Some studies have undertaken such measures to estimate the incidence of emergency department visits for anaphylaxis in US emergency departments. One such study, conducted in 1995 by Klein and Yocum from the Mayo Clinic,7 attempted to estimate incidence rates, while at the same time providing excellent insight into the limitations associated with research in this field. A retrospective analysis was conducted in the emergency department of a rural tertiary care medical center in the city of Rochester, Minn (1995 population, 71,000), that receives nearly 80% of the total emergency department visits within the city. The emergency department records of 19,122 patient visits, all those occurring during a particular 4-month period, were reviewed. On the basis of information documented in emergency department records, a total of 17 cases were diagnosed as anaphylaxis. Therefore, the 4-month period incidence of anaphylaxis was 0.09% (17/19,122). By extrapolation, it might then be possible to approximate the annual (or 12-month) incidence of emergency department visits related to anaphylaxis, perhaps even on a national level.

Table 5 provides detailed information on each of the 17 patients with a diagnosis of anaphylaxis, including the original emergency det-
partment diagnosis and clinical symptoms present at the time of the emergency department visit. The most commonly reported original diagnosis was allergic reaction (9/17 [53%]). Given that 13 (76%) of 17 cases of anaphylaxis were undocu-

mented by emergency department physicians at this one location, one can only imagine how often this o-
curs elsewhere. Underreporting and misdiagnosis of anaphylaxis because of confusion with other condi-
tions are widely recognized both among clinicians and in the litera-
ture. Despite this, very few researchers have addressed the problem and attempted to estimate its magnitude.

Few studies have attempted to provide an overall estimate of the total number of cases attributable to all causes of anaphylaxis. We calculate, on the basis of estimates of persons allergic to the most typical allergens known to trigger anaphylaxis, that between 3.3 and 43 million Americans may be at risk of anaphylaxis. As such, we conclude that the occurrence of anaphylaxis in the United States is not as rare as is believed. On the basis of our figures, the problem of anaphy-
laxis may, in fact, potentially affect 1.24% to 16.76% of the US popula-
tion.

Accepted for publication July 5, 2000. This study was supported in part by the DEY Corp, Napa, Calif.

Corresponding author: Alfred J. Neugut, MD, PhD, Department of Medi-
cine, College of Physicians and Surgeons, Columbia University, 630 W 168th St, Room PH18-127, New York, NY 10032 (e-mail: ain1@columbia.edu).

REFERENCES

3. Stark B, Sullivan TJ. Biphasic and protracted anaphy-

5. Yocum MW, Butterfield JH, Klein JS, Volcheck GW, Schroeder DR, Silverstein MD. Epidemiology of ana-
6. Centers for Disease Control and Prevention. Vital and Health Statistics, National Ambulatory Medi-
7. Klein JS, Yocum MW. Underreporting of anaphyl-
12. Kagi L, Biais MS. Anaphylaxis in children. Pa-
14. World Health Organization. International Classifi-
16. Assell G, Tweedie MCK, West CR, et al. The cur-
rent status of reactions to intravenous contrast me-
17. Weiss ME, Adkinson NF. Immediate hypersensi-
tivity reactions to penicillin and related antibiot-
(suppl):S465-S528.
19. Sue MA, Nontake DT, Klaustermeyer WB. Peni-
cillin anaphylaxis: fatality in elderly patients with-
20. Anderson JA. Allergic reactions to drugs and biolo-

verse reactions to ionic and nonionic contrast me-
22. Lieberman P. Anaphylactoid reactions to radio-
24. Greenberger PA, Patterson R. The prevention of immediate generalized reactions to radiocon-
25. Bush WH. Treatment of systemic reactions to con-
26. Bush WH, Swanson P. Acute reactions to intra-
vascular contrast media: types, risk factors, rec-
ognition, and specific treatment. AJR Am J Roent-
27. Toogood JH. Risk of anaphylaxis in patients re-
28. Lang D, Alpern M, Visintainer P, et al. Increased risk of anaphylactoid reaction from contrast media in pa-

29. Kelly KJ, Kurup VP, Rejula KE, Fink JN. The di-
31. Watts DN, Jacobs RR, Forrester B, et al. An evalua-
32. Arellano R, Bradley J, Sussman G. Prevalence of latex sensitization among hospital physicians oc-
cupationally exposed to latex gloves. Anaesthe-
33. Liss GM, Sussman GL, Deal K, et al. Latex al-
lergy: epidemiological study of 1351 hospital work-
34. Omby DR, Omby HE, McCullough J, et al. The prevalence of anti-latex IgE antibodies in 1000 vol-
35. Sussman GL, Bensholtz DH. Allergy to latex rub-
36. Valentine MD. Anaphylaxis and stinging insect hy-
38. Hollingsworth H. Preventing insect sting anaphy-

©2001 American Medical Association. All rights reserved.