

Sudden-Onset Fatal Asthma

Current knowledge suggests that severe attacks of asthma may have a sudden or slow onset.¹ Slow-onset asthma attacks are associated with progressive difficulty with breathing, and fatalities occur in hours to days. Usually, affected patients have time to seek help. In contrast, sudden-onset asthma attacks are characterized by rapid development of airway obstruction, and death may occur within minutes.^{2,3} In 1990, a case-control study⁴ showed that sudden-onset asthma attacks were characterized by more severe acidosis and hypercapnia than slow-onset asthma and, surprisingly, that recoveries were more rapid from sudden-onset asthma attacks than from slow-onset asthma. Rapid recoveries from severe sudden-onset asthma attacks were also observed in an epidemic of asthma related to soybean dust in Barcelona, Spain;^{5,6} moreover, an association between increased levels of IgE to soybean dust and sudden-onset asthma attacks was noted.⁶ Another study of sudden-onset asthma attacks showed that 10 of 11 patients had positive results of prick skin tests and increased levels of IgE antibody to *Alternaria*.⁷ Overall, these studies suggest that sudden-onset asthma is a clinically distinct entity.

We studied tissues from patients who had died of asthma to determine whether the quality of inflammation in the airways differs between sudden-onset and slow-onset asthma. Lung specimens obtained at autopsy from seven patients who had died of asthma were analyzed.³ Three patients who had died within an hour after onset of an asthma attack were classified as having sudden-onset fatal asthma, and four patients who had died hours to days after onset of the asthma attack were classified as having slow-onset fatal asthma. The numbers of eosinophils and neutrophils were counted in the airway submucosa. In the four patients classified as having slow-onset fatal asthma, the numbers of eosinophils in the airway submucosa exceeded the numbers of neutrophils. In the three patients classified as having sudden-onset fatal asthma, however, the numbers of neutrophils exceeded the numbers of eosinophils. These findings suggest that immunohistologic differences exist between these two types of fatal asthma.³ Because of the relatively few cases studied, confirming these observations in a larger study will be important.

What Is Sudden-Onset Fatal Asthma and How Common Is It?—Two terms have been used—“sudden-onset asthma attacks” and “sudden-onset fatal asthma.” Sudden-onset asthma attacks have previously been defined as respiratory arrest or failure within 1½ hours⁵ or 3 hours⁴ after the

onset of the attack. Other labels that have been used to describe such asthma attacks are “sudden asphyxic asthma” and “sudden severe attacks out of a clear blue sky.”^{4,8} We and other investigators have defined sudden-onset fatal asthma as death within 1 hour after onset of the attack.^{3,8} The importance of sudden-onset fatal asthma depends on its incidence; historical evidence suggests that it may not be rare. For example, if sudden-onset fatal asthma is defined as death that occurs within 1 hour after the asthma attack,³ at least 15 to 26% of fatalities from asthma can be attributed to this type of asthma.^{9,10} In contrast, if sudden-onset fatal asthma is defined as death within 3 hours after onset of the terminal asthma attack, at least 29% (and possibly up to 40%) of all asthma-associated deaths can be attributed to it.¹¹ One study suggested that the incidence of sudden-onset fatal asthma may be increasing.¹² Finally, the actual incidence of sudden-onset fatal asthma may be even higher than our estimate because death certificate coding for asthma misses up to 50% of asthma-related mortalities.¹³

Who Is at Risk for Sudden-Onset Asthma Attacks and Sudden-Onset Fatal Asthma?—Inhalation of allergens may cause sudden-onset asthma attacks. In one study, exposure to castor bean dust from an oil-processing factory resulted in such episodes.¹⁴ Likewise, inhalation of *Alternaria* may have been a cause of sudden-onset asthma attacks in southern Minnesota.⁷ Considerable epidemiologic evidence and increased levels of soybean-specific serum IgE link the Barcelona asthma epidemic to exposure to soybean dust released from unloading of soybeans from ships in the city harbor.⁶ Collectively, these studies suggest that inhalation of large doses of allergen by patients with asthma and high levels of specific IgE to the allergen cause a sudden-onset asthma attack. Furthermore, some evidence suggests that sudden-onset fatal asthma is more likely to occur in patients with a history of sudden-onset asthma attack (or attacks) than in those without such a history. The British Thoracic Association reported that 65% of patients who had sudden-onset fatal asthma (death less than 1 hour after onset of the terminal episode) had a history of sudden-onset asthma attacks. In contrast, only 28% of patients whose death occurred more than 1 hour after the onset of the terminal episode had a history of sudden-onset asthma attacks.^{6,8} Therefore, because we found airway neutrophilia in patients with sudden-onset fatal asthma, should a bronchial biopsy be performed to determine which patients are at risk for sudden-onset fatal asthma? Although bronchial biopsy specimens are useful for research, performance of bronchial biopsies for diagnostic purposes in patients with any type of asthma is currently contraindicated. In general, asthma can be diagnosed on the basis of the clinical history and results of pulmonary function tests. In the future, controlled research

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studies may reveal immunohistologic differences in biopsy specimens from patients with sudden-onset and slow-onset types of asthma.

How Should Patients With a History of Sudden-Onset Asthma Attacks Be Treated?—For convenience, we have considered management of sudden-onset asthma in two parts. The first part relates to prophylactic management of acute severe episodes of breathing difficulty. We suggest that patients with such episodes wear a bracelet that describes their disease and advises immediate transfer to the emergency department. This measure could be of considerable importance if the patient became unconscious from a sudden severe attack. In addition, such patients should always carry with them an emergency department treatment plan (written by a clinician with expertise in treating asthma). This information would be useful for emergency department physicians who have not treated such patients regularly and either do not fully understand the severity of their disease or are unfamiliar with the potentially life-threatening nature of sudden-onset asthma. Because affected patients often are unable to reach an emergency department,^{3,8,10} we suggest that they carry injectable epinephrine with them (unless contraindicated). During an acute asthma attack, the patient should inject epinephrine subcutaneously and then seek help. The second part of the management plan relates to long-term treatment. Currently, no information exists to suggest that patients with sudden-onset asthma should be treated any differently from patients with the more common slow-onset asthma. Finally, noncompliance with medications, poor medical follow-up for various reasons, and psychologic factors have previously been identified as contributors to asthma-related mortality.¹

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