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### Further fatalities caused by anaphylactic reactions to food, 2001-2006

#### *To the Editor:*

In 2001 we reported a group of 32 individuals who died because of food-induced anaphylaxis. The cases were accumulated in a registry kept by members of the American Academy of Allergy, Asthma & Immunology and The Food Allergy and Anaphylaxis Network.<sup>1</sup> The registry, which does not represent a systematic or complete accounting of all fatal food-induced allergic reactions in this country, has been maintained continuously since the initial report. We have done so to determine whether there are any changes in the characteristics of subsequent fatalities and to determine whether recommended interventions with self-injectable epinephrine have changed.

Additional subjects have been recorded prospectively in the registry between 2001 and August 2006. Information about the deaths has been collected using the same questionnaire used in the original report.<sup>1</sup> This report lists the details of the new data that have been collected. Briefly, the family members of the individuals who died were contacted, and standardized information was collected by using a structured questionnaire to determine the likelihood that a food caused the fatal reaction, the identity of the food suspected, the presence or absence of asthma (and the status at the time of death where possible), previous history of reactions to the suspected food, location of the reaction, and whether epinephrine was administered in a timely manner. The cases included in this report from the registry have been as critically evaluated as possible to include only cases in which there is high certainty that the death was caused by a severe allergic reaction, there is high certainty that the correct culprit has been identified, and whatever history is available has been reviewed. We have tried to eliminate bias toward the most common culprit (peanut) by these measures. We did exclude some reports with incomplete information or where there was uncertainty about a likely culprit. It would have been helpful if every individual had been seen by an allergist and had undergone a complete evaluation that included skin testing, serum antibody levels, and blind food challenges. Diagnosis was not made by allergists for all patients. Diagnostic criteria used (for example, skin prick test, specific serum antibody levels, blind food challenges) were not consistent between health care providers for these patients. We do not have detailed information on the severity of previous allergic reactions to foods (except, of course, that none were fatal) in these

individuals. The history obtained during the interview reported the presence of a known allergy and information about previous reactions. Many of those who died had not previously been in the hospital for their reactions or needed epinephrine. Some of these families indicated that they had no idea that these reactions could be fatal. We acknowledge that we probably have a bias toward overprescription of self-injectable epinephrine because we tend to collect and be aware of more severe cases. However, the unpredictability of response to a known food allergen, especially in individuals with asthma and especially for the most predictable culprits, makes us comfortable with this approach.

Thirty-one additional subjects (Table I) were identified between 2001 and 2006. The individuals ranged from 5 to 50 years of age. There were 19 males (61%). Peanut accounted for 17 deaths, tree nuts for 8, milk for 4, and shrimp for 2. All subjects for whom there are data had asthma, although the severity and treatment at the time of death are poorly documented because of a lack of available details. The lack of readily accessible epinephrine remains substantial with only 4 individuals (where the information was available) appearing to have had epinephrine administered in a timely manner. The known locations where the deaths occurred included schools (3; including colleges), homes (12; including homes of friends), restaurants (8), work/office setting (4), and camp (2).

Maintaining the registry enables us to compare the characteristics of these ongoing tragic deaths with the course and deficiencies in previously observed cases and determine whether educational efforts have had any apparent effect on preventing these tragedies. Unfortunately, this group of fatal reactions has striking similarities to the original group, but there are also some differences that may be important. The median age and sex distribution are similar to the earlier group, with slightly more males in this group. However, there are more younger subjects (4 no more than 10 years of age vs 1 in the original report), and more older individuals (7 at least 30 years of age vs 1 in the original report). Nevertheless, it is clear that the greatest number of fatalities still occurs in adolescents and young adults. The foods primarily responsible for the deaths continue to be peanut and tree nuts, with more instances of reactions to milk (4 in this group, vs 1 in the previous report). The location and circumstances of the food reactions are similar as well, with ongoing examples of individuals with known food allergies consuming foods without asking about ingredients and then not having the proper treatment available. Twelve of the 31 fatalities were caused by individuals with peanut or tree nut allergy consuming desserts (candy and bakery products) prepared away from home, and without having properly inquired about the ingredients.

There are some similar reports in the literature. Moneret-Vautrin et al<sup>2</sup> reviewed 107 cases registered by the Allergy Vigilance Network in 2002. In this group there were 2 reported fatalities, one from "anaphylactic shock" caused by peanut in a 21-year-old man, and the other caused by soy in a child. Pumphrey<sup>3</sup> reported 37 food fatalities, and

TABLE I. Food fatalities 2001-2006

Patient no.	Age (y)	M/F	Date	Culprit	Asthma	Previous history	Food	Location	Timely epinephrine
1	32	M	3/11/2001	Nuts	Yes	Yes	Nut bowl	Restaurant	No
2	16	M	5/9/2001	Walnut	Yes	Yes	Chinese food	School, cooking class	Probably
3	9	M	5/18/2001	Peanut	Yes	Yes	Cookie	School outing	No
4	24	F	11/26/2001	Peanut	Yes	Yes	Chinese food	Home	No
5	25	F	10/30/2001	Nut meats	Yes	Yes	Candy	Home of friends	No
6	16	M	11/5/2002	Milk	Yes	Yes	Bread	Home	Unk
7	31	M	12/13/2002	Peanut	Yes	Yes	Catered food	Office party	No
8	50	M	12/24/2002	Nut	Yes	Yes	Cookie	Home	No
9	12	F	3/14/2003	Peanut	Unk	Unk	Egg roll	Unk	Unk
10	18	M	6/21/2003	Peanut	Unk	Unk	Wrap	Unk	Unk
11	32	M	3/15/2003	Shrimp	Yes	Yes	Meal	Restaurant	No
12	29	M	6/13/2003	Peanut	Yes	Yes	Meal	Restaurant	No
13	29	M	4/24/2000	Almond	Yes	Yes	Candy	Office	Yes
14	17	F	12/26/1986	Nuts	Yes	Yes	Cookie	Home of friends	No
15	21	F	10/9/2003	Peanut	Yes	Yes	Brownie	College	No
16	18	M	1/20/2004	Shrimp roll	Yes	Unk	Shrimp roll	Restaurant	No
17	27	M	2/1/2004	Peanut	Unk	Yes	Baked clam	Home	No
18	17	M	2/8/2004	Hazelnut	Yes	Yes	Candy	Home of friends	No
19	17	F	4/6/2004	Peanut	Yes	Yes	Peanut butter	Camp	No
20	34	F	5/29/2004	Peanut	Unk	Yes	Thai dish	Home	No
21	5	M	8/1/2004	Peanut	Unk	No	Peanuts	Home	No
22	9	M	7/22/2004	Milk	Unk	Unk	Milk	Camp	Yes
23	22	F	10/29/2004	Peanut	Yes	Yes	Dessert	Restaurant	No
24	14	F	1/22/2005	Peanut	Yes	Yes	Egg roll	Restaurant	No
25	36	M	3/21/2001	Peanut	Yes	Yes	Brownie	Work	No
26	17	M	3/5/2005	Milk/whey	Yes	Yes	Protein shake	Home	No
27	7	F	3/2/2005	Milk	Yes	Yes	Chocolate mix	Home	Unk
28	11	F	5/31/2005	Peanut	Unk	Yes	Candied apple	Carnival	Unk
29	40	M	2/8/2006	Tree nut	Unk	Yes	Cookie	Work	Yes
30	13	F	4/13/2006	Peanut	Yes	Yes	Wrap	Fast food in mall	No
31	16	M	8/1/2006	Peanut	Yes	Yes	Cookie	Home of friends	No

F, Female; M, male; Unk, unknown.

the foods incriminated had significant similarities to those reported here. The additional foods were chickpea, banana, and nectarine, but peanut and tree nuts predominated. Colvar et al<sup>4</sup> reported 9 children with severe reactions: 3 were fatal and 6 were “near-fatal.” Six subjects were known to be allergic to the food causing the reaction, and only 1 of 9 had never had a known food-allergic reaction. In the 3 fatal cases, peanut was the likely culprit in 1 and cow’s milk in the other 2. The 3 who died had a history of asthma. Uguz et al<sup>5</sup> reported 112 allergic reactions to implicated foods in subjects responding to a questionnaire in the United Kingdom Anaphylaxis Campaign. Although there were no fatalities reported in this group, the foods responsible for symptoms were similar to those in this report. In these reports, the foods culprits are similar, the locations where reactions occur are similar, and the importance of asthma is emphasized as a risk factor.

Several lessons have been learned and reinforced by the information collected in this portion of the registry. We have cited support from the literature where it exists for these lessons: (1) education of the medical profession to ask about food allergy, diagnose it, educate patients, and prescribe epinephrine continues to be inadequate<sup>6</sup>; (2)

patients’ education regarding diagnosis, allergen avoidance, symptom recognition, and discrimination between asthma flares and anaphylaxis remains very inadequate<sup>7,8</sup>; (3) patients need to inquire in detail about ingredients and avoid eating desserts and bakery goods, especially when away from home; (4) patients’ knowledge of and compliance with the importance of carrying epinephrine needs improvement<sup>9</sup>; (5) availability of epinephrine to emergency medical technicians and prompt dispatch of paramedics or emergency medical technicians who can carry and administer epinephrine needs to be improved in many locales; (6) school education including food preparation and staff training needs improvement; (7) public education about the potential fatal nature of food allergy needs to be disseminated; (8) restaurant education concerning the importance of accurate labeling and the full and complete disclosure of food ingredients must be stressed to the industry<sup>10</sup>; and (9) evaluation by an allergist with the identification of the specific food culprits, and detailed education of patients and their families and friends may be lifesaving.

In conclusion, the registry continues to receive reports of tragic fatalities caused by known food offenders. A lack

of education at all levels, a lack of preparedness of allergic individuals and their families to respond appropriately, and a lack of prompt reporting of the abrupt onset of serious allergic symptoms appears unchanged from our previous report. We believe that a concerted national effort, similar to the National Heart, Lung, and Blood Institute Guidelines on the Diagnosis and Management of Asthma,<sup>11</sup> is necessary to reverse the morbidity and mortality of this growing national problem.

S. Allan Bock, MD<sup>a</sup>  
Anne Muñoz-Furlong, BA<sup>b</sup>  
Hugh A. Sampson, MD<sup>c</sup>

From <sup>a</sup>the Department of Pediatrics, National Jewish Medical and Research Center, University of Colorado Health Sciences Center, Denver, Colo; <sup>b</sup>the Food Allergy and Anaphylaxis Network, Fairfax, Va; and <sup>c</sup>the Division of Allergy and Immunology, Department of Pediatrics, Mt Sinai School of Medicine, New York, NY. E-mail: Bockdoc@aol.com.

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## Further fatal allergic reactions to food in the United Kingdom, 1999-2006

To the Editor:

Since the original report on United Kingdom (UK) fatal anaphylaxis 1992-1998,<sup>1</sup> we have attempted to investigate every food-related anaphylactic death in the UK. In

addition to the previously described methods, all UK asthma deaths up to the age of 32 years were studied prospectively for a 12-month period during 2003-2004 to determine whether the fatal attack had been triggered by food allergy. Not all such cases were reported to the study prospectively, and retrospective analysis has not yet been completed; however, it now seems unlikely that many food-allergy-triggered asthma fatalities had been missed.

For each death, the probability that it was caused by anaphylaxis and the probability that the cause had been correctly identified were assessed. Despite detailed study of the medical history, results of allergy tests, events on the day of the reaction, microscopic examination of the stomach contents, and immunochemical analysis of remaining food, in one third of cases, it was not possible to be certain which food had caused the reaction. Deaths caused by an acute attack of asthma have only been included when strong evidence exists that the attack was triggered by eating a food to which the deceased patient had an allergy. We excluded 4 deaths caused by asphyxia from upper airway angioedema attributed to food allergy in those taking angiotensin converting enzyme (ACE) inhibitors because the proposed food allergy cause for the reaction seemed improbable; ACE inhibitors cause nonallergic angioedema in occasional patients,<sup>2</sup> which may prove fatal.<sup>3</sup> We have included a man with fish allergy who had eaten fish and begun to wheeze, who died from inhalation of vomit. He had consumed an alcoholic drink, but it was thought his vomiting was from his fish allergy, not the drink.

We report 48 additional deaths meeting these criteria from 1999 to 2006. Ages ranged from 5 months to 85 years, with a median age of 21 years. The age distribution is similar to that in the previous report, with 7 aged 0-10 years, 26 aged 11-30 years, and 15 aged more than 30 years. There were 22 men (46%) reacting to milk (4), peanuts (3), nuts (2), fish (1) shellfish (1), snail (1), sesame (1), egg (1), and uncertain (8); and 26 women reacting to milk (2), peanuts (6), nuts (7), tomato (1), and uncertain (10). The circumstances comprised at home (14), the home of friends or relatives (10) at work (1), at school (2), at nursery (1), in a restaurant (11 of which 4 were abroad), out and about (6, of which 4 were from takeout food), in camp (2), and a wedding reception (1). Two deaths were overseas visitors to the UK.

Epinephrine auto-injector pens had been provided to 19 (40%), including 11 of the 13 with previous severe reactions. Over half the deaths occurred in patients whose previous reactions had been so mild that it was unlikely that a doctor would have recommended they should carry a pen. Pens were (apparently) used correctly by 9 (but 2 had time-expired); 1 used 3 pens correctly but still died. For some, pens may have failed to deliver an intramuscular injection because of the depth of the subcutaneous adipose tissue, but this was not the case for at least 3. Pens not used correctly were used too late in the reaction (5), had not been carried on that occasion (4), or were misused (1). Recently, a 16-year-old girl with a nut allergy took the risk of eating a chocolate because she trusted her pen would save her. She used it immediately when she saw nuts in the chocolate but nonetheless died from her reaction.