

Food-induced anaphylaxis

To date, there are no population-based epidemiologic studies providing information about the prevalence of food-induced anaphylaxis. However, statistics from the United Kingdom demonstrated an increase of anaphylaxis from 5.6 cases per 100 000 hospital discharges in 1991–92 to 10.2 cases in 1994–95. The increase for the subcategory of food-induced anaphylaxis was above the overall increase in anaphylaxis. In the UK register of fatal anaphylactic reactions, all food-induced fatalities have been accompanied by respiratory problems with respiratory arrest. Atopic individuals with bronchial asthma and prior allergic reactions to the same food are at a particularly high risk. Not only peanuts, seafood and milk can induce severe, potentially lethal, anaphylaxis, but indeed a wide spectrum of foods, according to the different patterns of food sensitivity in different countries. Foods with “hidden” allergens and meals at restaurants are particularly dangerous for patients with food allergies. Similarly, schools, public places and restaurants are the major places of risk. However, the main factor contributing to a fatal outcome is the fact that the victims did not carry their emergency kit with adrenaline (epinephrine) with them. Therefore, we suggest that the pharmaceutical industry should reintroduce an adrenaline inhaler that is more effective, especially in asthmatic reactions.

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Anaphylaxis is a generalized and potentially life-threatening clinical syndrome resulting from the release of biologically active mediators from mast cells and basophils. Food allergies are, besides drugs and insect stings, the single most common cause of anaphylaxis seen in hospital emergency departments, accounting for about one third to a quarter of cases seen (1, 2). To date, there is no epidemiologic study providing information about the prevalence of food-induced anaphylaxis. Anecdotal evidence and daily work at an allergy unit with a large number of patients, however, suggest that the incidence of acute anaphylaxis to food is increasing. Reasons for the suspected increase are poorly understood. The well documented increase of pollen and latex sensitizations with associated allergies to fruits, nuts and vegetables, the problem of “hidden” allergens and the globalization with the widespread consumption of exotic foods or the increasing consumption of packaged food with many different, often undeclared, ingredients, have all been implicated. In a recent paper, Sheikh & Alves (3) investigated the trend in hospital admissions for acute anaphylaxis using routinely collected national hospital discharge statistics in England from 1991 to 1995. In 2424 of a total of 32.4 million discharges, the primary diagnosis was anaphylaxis. There was an increase from 5.6 cases of anaphylaxis per 100 000 discharges in 1991–92 to 10.2 cases in 1994–95 ($P < 0.001$). The etiology was recorded for 1248 cases (51%); the most common causes of anaphylaxis were

therapeutic drugs (772; 62%), food (193; 15%) and insect venoms (138; 11%). These percentages remained fairly constant throughout the 4 years. The increase for the subcategory of food-induced anaphylaxis (unspecific and other foods) was above the overall increase in anaphylaxis.

Fatal food anaphylaxis

The first documented case of a fatal reaction was described in 1926 by a pediatrician (4). A 1½-year-old boy with atopic eczema experienced three episodes of generalized allergic reactions at home after intake of a few spoons of mashed peas. In the hospital setting an oral challenge with carrots/mashed peas was performed under the supervision of a chief nurse. Immediately after the intake of the test meal the child developed angioedema, cyanosis and collapsed. He died despite emergency treatment. In 1948, Wergeland described three cases of a suspected familial allergy to human milk (5). All three babies of the same family had since birth experienced squirting and watery stools after each feeding. All three cases ended in mortality, despite appropriate treatment. The pathogenetic mechanism of these cases remains unclear. Fries, who described in 1982 a number of anaphylactic reactions to peanuts (6), stated that “there is no documentation of fatal or near fatal anaphylactic reaction in the medical literature to peanuts, although explosive allergic reactions to the

ingestion of the botanically related chickpea (garbanga bean) have been described". Six years later, Evans et al. (7) described the first fatal reaction to peanut antigen in a 24-year-old peanut-allergic woman after eating an almond icing contaminated with peanuts. The first series on fatal food-induced anaphylaxis, however, was not published until 1988 (8). Over a period of 26 months, Yunginger et al. identified seven cases (five males and two females) aged 11–43 years: all victims were atopic with multiple prior anaphylactic episodes following ingestion of the incriminating food: peanuts (4), pecan nuts (1), crab (1) and fish (1). In 1992, Sampson et al. (9) reported six fatal anaphylactic reactions in children, aged 2–17 years. Five of the six fatal cases occurred in schools or public places. All children were asthmatics and all had suffered from previous anaphylactic reactions to the same food, i.e. after intake of peanuts, cashew nuts, walnuts, pecan nuts, eggs and milk. In the UK, six fatal cases of food allergy to peanuts occurred in 1993 (10). In 1998, Patel described two fatal cases caused by seafood (11). Foucard & Malmheden Yman (12) reported six fatal cases in Sweden from 1992 to 1996: two deaths were caused by peanuts and four by soy. All four youngsters who died from soy anaphylaxis were asthmatics with a known severe allergy to peanuts but no previously known allergy to soy. The authors concluded that soy has probably been underestimated as a cause of food anaphylaxis. Fatal anaphylactic reactions have regularly been registered in the UK since 1992 (2, 13). The register holds details of 164 fatalities that occurred from 1992 to 1998 and for which dates of birth and death, sex, putative allergen and location of death are known. Approximately half of the fatal reactions recorded each year were iatrogenic and a quarter were induced by food or insect venom. The 37 fatalities to food were caused by: peanut (10), nuts (10), walnut (5), seafood (3), milk (2), chickpea, banana, nectarine (1 each) and uncertain (4). The fatalities occurred at a restaurant/bar (13), take-away (6), home (6), canteen (3), school (2) and other (5). All fatal reactions judged as food-induced have been accompanied by respiratory problems and, in 86%, even by respiratory arrest. In 14% (5) a "combined" mode (combination of shock and respiratory arrest) was assumed. In none was shock alone recorded as the cause of death.

Life-threatening reactions to food

Beside these fatal cases, life-threatening reactions to food occur more frequently than commonly assumed. In the UK, anaphylactic reactions of 172 patients, aged 5 months to 69 years, were documented in 1994 (14). Food was the most frequent cause of anaphylaxis, accounting for 60% of the cases. Peanuts (24%) and other nuts (13%) played a predominant role. Eriksson

and colleagues (5) studied the cases of patients treated for anaphylaxis at the country hospital of Halland, Sweden, over a period of 13 years. Foods were the most important eliciting factor of anaphylaxis (45%), followed by drugs (29%) and insect stings (21%). Among the foods, tree nuts and peanuts dominated, but many other foods, such as eggs, celery, wheat, milk, poppy seeds, sunflower seeds and rice, were also involved. In 1991–92, a French multicenter survey (20) reported on 794 anaphylactic shock reactions; food-induced anaphylaxis represented 10.2% of the cases. More than 15 food allergens were detected: egg (11.6%), fish (10.4%), crustaceans (10.4%) and milk (6.5%), followed by the fruit-latex group, peanuts and other leguminosae (soy, peas, lentils, guar gum), as well as celery and garlic. Rohrer et al. (17) analyzed clinical data, causative agents and follow-up in 118 subjects (68 females and 50 males, mean age 41) with severe anaphylaxis who were referred to the Allergy Unit in Bern from May 1994 to October 1996. The following causative agents were identified: drugs in 34% of cases, insect stings (24%), foods (19%), exercise and food (8.5%), latex (8%) and immunotherapy with pollen extracts (1%). Of the 22 individuals with food-induced anaphylaxis, 17 were females. The causative foods were celery root in nine individuals (40.9%), nuts (hazelnuts and walnuts) and shrimps in three cases each (13.6%), followed by banana, papaya, chestnut, peanut, sesame seed, honey and olive in one case each. Results from a 10-year statistical analysis of all cases of food allergy diagnosed at our allergy unit in Zurich also showed that celery root, or celeriac, was the most important food allergen, mainly triggering severe anaphylaxis (18). In the meantime, the clinically relevant sensitization to celery could be confirmed by double-blind placebo-controlled food challenge (19). Among 124 cases of food-induced anaphylaxis identified in Singapore, the most common food allergen was the Chinese delicacy birds's nest soup (double-boiled edible nest of swift, *Collocalia* spp.) (27%), followed by crustaceans (24%), eggs and cow's milk (13% each), and various traditional Chinese herbs (7%) (20). Interestingly, no cases of allergy to peanuts or tree nuts were observed.

Documentation of the different patterns of food sensitivity observed in the different populations will improve our understanding of food allergy as a whole. These differences will also be of importance in the selection of relevant ingredients for food product labeling in the different countries (21).

Lesson for management of anaphylaxis from the past

The main risk factor for a fatal anaphylaxis was that the victims did not carry their emergency kit with adrenaline, antihistamines and steroids with them. A recent study (22) demonstrated that in children the EpiPen

device was only used in 29% of recurrent anaphylactic reactions. Children in whom the EpiPen device was used were less likely to be given epinephrine in hospital or to require subsequent hospital admission. Pumphrey (2) reported that only 22% of patients with food-allergic fatalities had suffered from previous severe reaction, suggesting that for most high-risk patients, an adrenaline self-treatment kit is not available. In nine out of the 14 patients (64%), however, with previous severe reactions who did have self-medication, the emergency kit proved to be unsuccessful for many reasons (used kit for another person, had not replaced it; found kit was out of date, subsequent treatment unsuccessful, may have collapsed too quickly to use kit, etc.). And two people with lethal anaphylaxis to food used two and

three doses, respectively, correctly (0.3 mg adrenaline) without benefit. Unfortunately, although the risk of unexpected exposure to food allergens can be reduced, it can never be completely eliminated. Milligram quantities of nut may be sufficient to elicit an anaphylaxis (23). Despite dietary counseling, accidental exposure may cause repeated reactions. There is also cross-reactivity between different types of nut (24). At least three fatal reactions in the study of Pumphrey (2) were probably due to a type of nut that had not previously caused a reaction. The author concluded from these observations that anyone allergic to one nut should be tested for allergy to all nuts. Nonetheless, the dietary advice should generally be to avoid all nuts.

References

1. WÜTHRICH B. Lethal or life-threatening allergic reactions to food. *Invest Allergy Clin Immunol* 2000;**10**:59–65.
2. PUMPHREY RSH. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy* 2000;**30**:1144–1150.
3. SHEIKH A, ALVES B. Hospital admission for acute anaphylaxis: time trend study. *Br Med J* 2000;**320**:1441.
4. VON STARCK. Primäre spezifische Allergie und idiosynkratischer Schock. *Monatsschr Kinderheilkd* 1926;**32**: 119–127.
5. WERGELAND H. Three cases of probable familial allergy to human milk. *Acta Paediatr (Uppsala)* 1948;**35**:321–335.
6. FRIES JH. Peanuts: allergic and other untoward reactions. *Ann Allergy* 1982;**48**:220–226.
7. EVANS S, SKEA D, DOLOVITCH J. Fatal reaction to peanut antigen in almond icing. *Can Med Assoc J* 1988;**139**: 232–233.
8. YUNGINGER JW, SWEENEY KG, STURNER WQ, GIANNANDREA LA, TEIGLAND JD. Fatal food-induced anaphylaxis. *JAMA* 1988;**260**:1450–1452.
9. SAMPSON HA, MENDELSON L, ROSEN JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med* 1992;**327**:380–384.
10. HIDE D. Fatal anaphylaxis due to food. *Br Med J* 1993;**307**:1427.
11. PATAL F. Seafood-induced fatal anaphylaxis. *Med Sci Law* 1998;**38**:354–357.
12. FOUCARD T, MALMHEDEN YMAN I. A study on severe food reactions in Sweden – is soy protein an underestimated cause of food anaphylaxis? *Allergy* 1999;**55**:261–265.
13. PUMPHREY RSH, ROBERTS ISD. Postmortem findings after fatal anaphylactic reactions. *J Clin Pathol* 2000;**53**:273–276.
14. PUMPHREY RSH, STANWORTH SJ. The clinical spectrum of anaphylaxis in north-west England. *Clin Exp Allergy* 1996;**26**:1364–1370.
15. ERIKSSON NE, HENRICSON KA, JEMSBY P. Factors eliciting anaphylaxis in 50 Swedish patients. *Allergy* 1996;**51** (Suppl 31):52.
16. MONERET-VAUTRIN DA, KANNY G. L'anaphylaxie alimentaire. Nouvelle enquête multicentrique française. *Ann Gastroentérol Hépatol* 1995;**31**: 256–263.
17. ROHRER CL, PICHLER WJ, HELBLING A. Anaphylaxie: Klinik, Ätiologie und Verlauf bei 118 Patienten. *Schweiz Med Wochenschr* 1998;**128**:53–63.
18. WÜTHRICH B. Zur Nahrungsmittelallergie: Häufigkeit der Symptome und der allergieauslösenden Nahrungsmittel bei 402 Patienten – Kuhmilchallergie – Nahrungsmittel und Neurodermitis atopica. *Allergologie* 1993;**16**:280–287.
19. BALLMER-WEBER BK, VIETHS S, LÜTTKOPF D, HEUSCHMANN P, WÜTHRICH B. Celery allergy confirmed by double-blind, placebo-controlled food challenge: A clinical study of 32 subjects with a history of adverse reactions to celery root. *J Allergy Clin Immunol* 2000;**106**:373–378.
20. GOH DLM, LAU YN, CHEW FT, SHEK LPC, LEE BW. Pattern of food-induced anaphylaxis in children of an Asian community. *Allergy* 1999;**55**:78–92.
21. BOUSQUET J, BJÖRKSTÉN B, BRUINZEEL-KOONEN CAFM, et al. Scientific criteria and the selection of allergenic foods for product labelling. Prepared under the guidance of the ILSI Europe Food Allergy Task Force. *Allergy* 1998;**53**:3–21.
22. STEVEN GOLD M, SAINSBURY R. First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen). *J Allergy Clin Immunol* 2000;**106**:171–176.
23. HOUIRANE JO'B, KILBURN SA, NORDLEE JA, HEFLE SL, TAYLOR SL, WARNER JO. An evaluation on the sensitivity of subjects with peanut allergy to very low doses of peanut protein: A randomized, double-blind, placebo-controlled food challenge study. *J Allergy Clin Immunol* 1997;**100**:596–600.
24. PUMPHREY RSH, WILSON PB, FARRAGHER EB, EDWARDS SR. Specific IgE to peanut, hazelnut and brazil nut in 731 patients: similar pattern found at all ages. *Clin Exp Allergy* 1999;**29**: 1256–1259.