

Food-induced anaphylaxis

Foucard T, Malmheden-Yman I. Food-induced anaphylaxis.
Pediatr Allergy Immunol 2001; 12(suppl 14): 97–101. © Munksgaard 2001.

**Tony Foucard¹,
Ingrid Malmheden-Yman²**

¹Department of Paediatrics, University Hospital, Uppsala, Sweden, ²Research and Development, National Food Administration, Uppsala, Sweden

Key words: anaphylaxis; food; peanut; soy

Tony Foucard, Department of Pediatrics, University Hospital, S-751 85 Uppsala, Sweden

Introduction

Anaphylactic reactions belong to medical emergencies, but such reactions are fortunately fairly rare. On the other hand, it means that few doctors acquire medical experience of such reactions. Patients sometimes report a previous allergic shock, but when their records are checked they have had an allergic reaction with urticaria and perhaps Quincke oedema. Such a reaction should not be recorded as anaphylactic. Anaphylaxis should include acute symptoms from more than one organ system, and an anaphylactic shock should include a lowered blood pressure combined with a clouded consciousness due to mediator release. A vagal reaction with low blood pressure in association with, for instance, acute urticaria, can easily be mistaken for an anaphylactic shock.

Incidence and causes

The incidence of anaphylactic reactions has rarely been reported. In a population-based study in the United States the average annual incidence rate was reported to be 21 per 100 000 person-years (1), and in an Australian study of 4173 children 3–17 years of age, the rate of anaphylaxis was found to be 0.59 per 100 children (2).

Anaphylactic reactions are most often caused by foods. In hospital-based series of patients with anaphylaxis foods are involved in 25–60% of all anaphylactic reactions in which the cause has been established with reasonable certainty, followed by bee- or wasp-stings and drugs (3–8). In a

study from northern England the most severe anaphylactic reactions in 172 patients were reported (5). Of these 103 were caused by foods, 28 by bee or wasp venom, 15 by drugs and six by latex.

Although cow's milk and hen's egg white cause most anaphylactic reactions during infancy, the situation is different in older children and adults. When looking at the age distribution in the English study an interesting pattern was found. Almost four out of five patients were 18 years old or younger. In this age group three out of four food anaphylactic reactions were caused by peanuts and tree nuts, compared with one out of four in people older than 18 years. Why is allergy to peanuts and tree nuts so predominant in young people? There is little evidence that these allergies disappear just after the age of 18 years. Therefore, one may assume that the high frequency of severe reactions to peanuts and tree nuts depends on more risky behaviour in youngsters than in adults, or that youngsters are more reactive than older people. Alternatively, it may be an age cohort effect. If so, severe anaphylaxis to peanuts and tree nuts will probably also become more common among young adults.

A changing pattern of peanut allergy

Ewan investigated 62 consecutive cases referred because of a peanut or tree nut allergic reaction (9). Only 10 were adults and eight of these 10 were between 19 and 32 years of age. Peanut allergy

was found in 47 patients (76%). The most common tree nut allergy was against Brazil nut, in 18 patients. The most remarkable finding was the early appearance of peanut sensitisation. Before 1 year of age all 11 infants were allergic to peanuts but not to any other nut, and up to the age of 3 years 73% of the 33 children were allergic to peanut only. Although poorly studied previously, it seems likely that early sensitisation to peanut has become more common during the last one or two decades. There is also some indication that clinical peanut allergy has become more common during the last 20 years. Sampson reported 44% skin test positive reactions to peanut among 115 children with moderate to severe eczema in 1981–85. Sixteen percent were challenge positive. Ten years later the corresponding figures in a cohort of 155 children with moderate to severe eczema were 68% and 31%, respectively, indicating a 50% increase in sensitisation and a doubled prevalence of clinical peanut allergy in 10 years (10). Many Swedish paediatric allergologists consider severe peanut allergy to be more common nowadays than some decades ago. It is not unusual today to find peanut-allergic children reacting to indirect contact with peanuts. This impression is supported by a recent report by Emmet et al. (11). They found that 43% of peanut-allergic children but only 9% of peanut-allergic adults reacted to smell, touch or taste of peanut. Furthermore, they reported that 3 out of 4 adults with peanut allergy had reacted for the first time after 10 years of age but 56% of peanut-allergic children had reacted already during their first 2 years of life. It may, of course, mainly reflect an earlier introduction of peanuts in the child's diet. That peanut allergy has become more prevalent and severe seems to be true in the north-western Europe and in the United States. In other areas this does not seem to be the case. From Italy it was recently reported that only one out of 95 food anaphylactic reactions in 76 children was caused by peanut (7); nor is peanut anaphylaxis common in Singapore where bird's nest soup is the most common cause of food anaphylaxis (12). This low incidence may reflect a lower consumption of peanuts in Italy and Malaysia. Available figures indicate that about seven times more peanuts are consumed per person in the United States than in Italy (7, 13). This difference cannot explain the low incidence of anaphylaxis caused by peanuts in Italy, as severe reactions caused by peanut are common in Sweden, and the consumption of peanuts per person in Italy and Sweden is about the same – 0.7 kg per person per year.

Time-course and symptoms

The time-course of a food anaphylactic reaction may show great variations but three main types are seen (14). In the first the onset of symptoms is rather rapid and there is a gradual deterioration during minutes to hours. The second type shows initially mild to moderate symptoms followed by a latent phase for about half an hour up to a few hours, and then a rapid deterioration. In the third type there is only a late onset of severe symptoms. Infections, exercise or intake of cold beverage may trigger or aggravate an anaphylactic reaction caused by food (15, 16).

The symptoms of anaphylaxis are cutaneous, respiratory, gastrointestinal and cardiovascular. Cutaneous symptoms with urticaria and Quincke oedema occur in almost all patients but the respiratory and cardiovascular symptoms are the most dangerous ones. Almost all deaths caused by food anaphylaxis depend on cardiorespiratory failure due to anoxaemia caused by asthma. Only a few cases of fatal food anaphylaxis have been published.

Yunginger reported on seven deaths in food-related anaphylaxis, median age 19 years. The cause was peanuts in four cases, and pecan nut, crab and cod in one each (17). Sampson et al. reported on six deaths and seven near-deaths during a 3-year period in the Baltimore area (18). The median age was 13 years and the cause was peanuts in four cases, tree nuts in six cases, milk in two and egg in one case. One interesting aspect of the study was the time course in the fatal cases. Mild symptoms appeared within a few up to 30 minutes after intake but between 1 and 2.5 hours elapsed before the onset of severe symptoms in three out of the six fatal cases.

Fatal food anaphylaxis in Sweden

In 1993 a schoolgirl in Sweden died in a fatal asthma attack after having eaten a hamburger for school luncheon. She had only mild symptoms initially but after about half an hour she rapidly deteriorated and died within 20 minutes. She was strongly allergic to peanut but had never before reacted to soy. She suffered from mild asthma treated with only beta-2-agonist when needed. The following investigation found a high serum level of peanut-specific IgE antibody and a moderate level against soy. The hamburger contained 2% soy protein but no peanut protein, as measured with a rocket immunoelectrophoresis with a lowest detectable level of 50 p.p.m. peanut protein. The conclusion was that intake of soy in the hamburger was the probable cause of the fatal attack. As only

one case of fatal soy anaphylaxis was found in the literature (19) we found it hard to accept this conclusion. To see if this case was unique, and to obtain more experience of food anaphylaxis in general, the Allergy Section of the Swedish Paediatric Association and the National Food Administration began a study. All doctors were asked to report fatal and life-threatening reactions caused by food. During the first 3 years of the study 61 cases were reported, of which five were fatal (20). Only nine of the 61 cases were older than 17 years and there were twice as many boys as girls. A surprising finding in our study was that soy was found to be the second most common cause of severe food reactions, and only surpassed by peanuts. The connection between intake of soy and symptoms was not as clear-cut as between intake of peanuts or tree nuts and symptoms. This difference might depend on the fact that soy usually is an ingredient mixed with other ingredients in the food, and that the initial symptoms were mild in most cases. What made us believe that soy was the culprit in these cases was the similarity with a fatal peanut allergy reaction. Exactly the same time-course and symptoms as in the presumed soy reactions were observed. It was a 15-year-old boy with mild asthma and severe allergy to peanuts but tolerant to almonds. He ate a bun decorated with almond flakes, but after a few bites he experienced oral itch and realised that the bun contained something he did not tolerate. He cycled around in the area for about 30 minutes with no noticeable symptoms, and then he went home to change his clothes. At home he rapidly developed severe asthma symptoms. Asthma spray did not help and he failed probably to take his EpiPen. He telephoned his father who was in a house nearby but when the father came home his son was already unconscious, and when the ambulance arrived he was dead. Apparently, he had taken cold lemonade from the refrigerator when he came home, because a half-emptied bottle was found on the kitchen sink. Perhaps this cold beverage started the fatal reaction. Analysis of the almond flakes on the bun showed that they were peanut flakes.

One of our cases of fatal asthma caused by soy was a 10-year-old boy with mild asthma and allergy to cat, birch and nuts. He had a kebab, containing 7% soy protein, for school lunch. During the first lesson after the lunch break his teacher noticed that he had breathing difficulties. He was brought to the school nurse's office at the same floor but during the transport he rapidly deteriorated and on arriving there he was unconscious. He was dead when the ambulance came. The following investigation showed that he had a history of severe allergy to peanuts but not to other nuts or soy. His

serum had a high level of peanut-specific IgE antibody (>100 kU/L) and a moderate level against soy (29 kU/L). Soy protein but no peanut protein was found in his gastric content. The similarity between these two cases, and with no other plausible cause, made us believe that his intake of soy elicited his fatal asthma attack.

In 1992, the year before we started our study, a 17-year-old boy with mild asthma and severe peanut allergy was out with his friends and they had a hamburger from a street kitchen. He developed mild asthma but could walk at a normal pace to the subway. When they got to the end station after about half an hour he drank a cola and then his asthma deteriorated rapidly. He was more or less dragged home by his comrades and they called upon his father. Before the ambulance arrived the boy had died. He had a high concentration of peanut-specific IgE in post mortem blood (759 kU/L) (21).

We are also aware of another two cases of probable soy-elicited fatal asthma during the same time period as we had two cases of fatal asthma caused by peanut.

When looking at the most severe of the non-fatal food anaphylactic reactions, soy was found to be a common allergen also in these cases. Of 12 children with severe reactions, six had eaten soy-containing food. In contrast to the fatal cases five of the six children reacting after intake of soy-containing food had reacted to soy previously.

Has soy allergy become more severe?

Soy has, until now, been regarded as a rather weak clinical allergen and severe reactions are rarely reported (22). Our present experience indicates that this situation probably has changed. It seems that not only peanut allergy but also soy allergy has changed and that these allergens may cause more severe reactions than previously. All fatal cases and all six patients with a severe non-fatal reaction after intake of soy-containing food were also allergic to peanuts. As we have not analysed the consumed food in all cases we cannot completely exclude a contamination with peanut protein aggravating the reaction to soy. Speaking against such an explanation is the consistently negative result of a peanut ELISA performed on many hamburgers and other minced meat products at the National Food Administration. This ELISA can detect as low levels as 1–2 p.p.m. peanut. We did not find any peanut protein in the gastric content of two fatal cases with a somewhat less sensitive technique. In both cases the same residual batch of hamburger and kebab that caused the reaction was analysed, in addition to all ingredients used for the produc-

tion of the hamburger and kebab. Different soy ingredients (soy flour, soy isolate, soy concentrate and textured soy) used at the food facility for the production of kebab and hamburgers were also thoroughly analysed without any sign of peanut protein. Therefore, it seems unlikely that the severe reactions, presumably caused by soy, could be explained by a contamination with peanut protein. Most probably, the fatal reactions have been caused by peanut-specific IgE-antibodies cross-reactive with soy allergen in addition to a mild or moderate soy allergy not noticed or present before.

Practical considerations

Most of the fatal cases and severe non-fatal reactions had mild asthma and they had few allergies in addition to their peanut allergy. This fact creates a problem. Who, of all peanut-allergic children, should we warn against soy, and who should be furnished with EpiPen, steroids and antihistamine? As most of our cases with a fatal outcome had eaten soy protein before without any reaction many peanut-allergic patients may be alarmed. Although many peanut-allergic patients may have IgE to soy, only a few of them are clinically allergic to soy (23–25). A negative challenge is probably a guarantee for the time being, but not necessarily for the next year or later. In Sweden we have therefore applied a very pragmatic approach to the problem based on our experience with the fatal cases. Those who have such a severe peanut allergy that indirect contact is enough to elicit symptoms, and who suffer from asthma, even in mild forms, are advised not to eat hamburgers, meatballs or kebab containing soy. All our fatal cases had eaten these foods. All patients with a severe peanut or soy allergy should be furnished with EpiPen, corticosteroids and antihistamine, provided they are willing to carry these drugs with them. Concerning younger children, one has to consider practical prerequisites with parents and other caring people having knowledge of how to give, have the courage to give, and are willing to give these drugs.

What we have learnt from our experience is that we need to have some kind of registration of fatal and severe reactions caused by food to be able to observe changing patterns. It may be that our cases of severe reactions caused by soy represent a cluster occurring by chance, and that our fear that soy has become an important allergen is exaggerated. During the last 3 years only one case of fatal asthma probably caused by food has been reported so far. It occurred in a young boy with a severe peanut allergy and with no known soy allergy. Just

before the onset of the fatal attack he had eaten a hamburger and drunk a cola.

References

1. YOCUM MW, BUTTERFIELD JH, KLEIN JS, et al. Epidemiology of anaphylaxis in Olmsted county: a population-based study. *J Allergy Clin Immunol* 1999; 104: 452–6.
2. BOROS CA, KAY D, GOLD MS. Parent reported allergy and anaphylaxis in 4173 South Australian children. *J Paediatr Child Health* 2000; 36: 36–40.
3. YOCUM MW, KHAN DA. Assessment of patients who have experienced anaphylaxis: a 3-year survey. *Mayo Clin Proc* 1994; 69: 16–23.
4. KEMP SF, LOCKEY RF, WOLF BL, et al. Anaphylaxis: a review of 266 cases. *Arch Intern Med* 1995; 155: 1749–54.
5. PUMPHREY RSH, STANWORTH SJ. The clinical spectrum of anaphylaxis in north-west England. *Clin Exp Allergy* 1996; 26: 1364–70.
6. DIBS S, BAKER MD. Anaphylaxis in children: a 5-year experience. *Pediatrics* 1997; 99: E7.
7. NOVEMBRE E, CIANFERONI A, BERNARDINI R, et al. Anaphylaxis in children: clinical and allergological features. *Pediatrics* 1998; 101: E8.
8. MARGUET C, COUDERC L, BLANC T. Anaphylaxis in children and adolescents: apropos of 44 patients aged 2 months to 15 years. *Arch Pediatr* 1998; 6 (suppl 1): 72–8.
9. EWAN PW. Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations. *BMJ* 1996; 312: 1074–8.
10. SAMPSON HA. Epidemiology of food allergy. *Pediatr Allergy Immunol* 1996; 7 (suppl 9): 42–50.
11. EMMETT SE, ANGUS FJ, FRY JS, LEE PN. Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members. *Allergy* 1999; 54: 380–5.
12. GOH DLM, LAU YN, CHEW FT, et al. Pattern of food-induced anaphylaxis in children of an Asian community. *Allergy* 1999; 54: 84–6.
13. SAMPSON HA. Managing peanut allergy. *BMJ* 1996; 312: 1050–1.
14. STARK BJ, SULLIVAN TJ. Biphasic and protracted anaphylaxis. *J Allergy Clin Immunol* 1986; 78: 76–83.
15. CAFFARELLI C, TERZI V, PERRONE F, et al. Food related exercise induced anaphylaxis. *Arch Dis Child* 1996; 75: 141–4.
16. LIN YZ, HSIEH KH. Asthma induced by ice water ingestion in ethnic Chinese asthmatic children: a challenge. *Pediatr Allergy Immunol* 1997; 8: 11–16.
17. YUNGINGER J, SWEENEY KG, STURNER WQ, et al. Fatal food-induced anaphylaxis. *JAMA* 1988; 260: 1450–2.
18. SAMPSON HA, MENDELSON L, ROSEN JP. Fatal and near fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med* 1992; 327: 380–4.
19. YUNGINGER JW, NELSON DR, SQUILLACE DL, et al. Laboratory investigation of deaths due to anaphylaxis. *J Forens Sci* 1991; 36: 857–65.
20. FOUCARD T, MALMHEDEN-YMAN I. A study on severe food reactions in Sweden – is soy protein an underestimated cause of anaphylaxis? *Allergy* 1999; 54: 261–5.
21. EDSTON E, VAN HAGE-HAMSTEN M, JOHANSSON SGO. Trypsin – at last a useful diagnostic marker for anaphylactic death. *Allergy* 1996; 51: 443–5.

22. BRUNO G, GIAMPIETRO PG, DEL GUERCIO MJ, et al. Soy allergy is not common in atopic children: a multicenter study. *Pediatr Allergy Immunol* 1997; 8: 190–3.
23. BOCK SA, ATKINS FM, SAMPSON HA. Allergenic cross-reactivity among legume foods. *J Allergy Clin Immunol* 1988; 82: 310–12.
24. BERNHISEL-BROADBENT J, SAMPSON HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. *J Allergy Clin Immunol* 1989; 83: 435–40.
25. MONERET-VAUTRIN DA, RANCE F, KANNY G, et al. Food allergy to peanuts in France – evaluation of 142 observations. *Clin Exp Allergy* 1998; 28: 1113–19.