

Anaphylaxis and reactions to foods in children – a population-based case study of emergency department visits

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Summary

Background Information about acute reactions to foods among children is limited.

Objective To describe the overall incidence of anaphylaxis in a paediatric emergency department (ED) setting and to describe reactions to foods in relation to sex and age, clinical characteristics and management.

Methods In a review of medical records, children with ED visits at any of three paediatric hospitals in Stockholm County during 2007 were targeted. Inclusion criteria were any adverse reaction to foods or anaphylaxis.

Results 383 children fulfilled the inclusion criteria of which 371 had had reactions to foods. The incidence of anaphylaxis was 32 per 100 000 person years irrespective of cause and food was involved in 92%. Tree nuts, particular cashew, and peanut were the most common eliciting foods, and in children under 3 years, reactions to these two food allergens were as common as reactions to milk and egg. Pollen-allergic children seemed to be admitted due to food-induced anaphylaxis more often during the deciduous tree pollen season compared with the rest of the year ($P = 0.015$). Symptoms from the lower airways occurred in 49% of children with anaphylaxis but without underlying asthma compared with 72% of children with anaphylaxis and asthma, $P < 0.01$.

Conclusions and Clinical Relevance Reactions to peanut and tree nuts are as common as reactions to milk and egg in early life. Concomitant exposure to airborne allergens seems to increase the risk of anaphylaxis to foods. Among children with anaphylaxis, wheeze is prevalent even in children without asthma diagnosis.

Keywords anaphylaxis, children, emergency department, food allergy

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Introduction

An increase in the incidence of anaphylaxis has been suggested in several papers and in a recent review [1–4]. Food has been considered the dominating cause of anaphylaxis, in particular among children [5–11], and represents a major health issue since anaphylaxis caused by food may contribute towards mortality particularly among patients with asthma [12].

The true incidence of anaphylaxis among children on a population basis has not yet been established [11]. This may partly be explained by the lack of universal agreement on the definition and criteria for diagnosis

of anaphylaxis. At the time of this study, the suggested definition encompassed a serious allergic reaction with rapid onset and at worst with life-threatening severity [13]. To date, few studies have primarily investigated acute allergic reactions, including anaphylaxis, among children [6, 7, 14], and there are even fewer studies on children that focus primarily on acute reactions to foods, conducted in an emergency department (ED) setting [15].

The purpose of this population-based case study was to describe the incidence of anaphylaxis irrespective of cause, as well as reactions to foods in relation to how the symptoms present themselves and which foods elicit

them among children admitted to any of three paediatric EDs in Stockholm [16].

Methods

Study design

Clinical records were reviewed of all 0- to 18-year-old patients visiting any of the EDs of three paediatric hospitals in Stockholm County, Sweden, with an acute reaction to food, or anaphylaxis irrespective of underlying cause. The study period was from 1 January through 31 December 2007, and the hospitals' catchment area was Stockholm County. A total of more than 50 000 visits were recorded at the three EDs during the study period. The study was approved by the Regional Ethical Review Board, Stockholm, Sweden.

Identification of cases

To identify patients with anaphylaxis irrespective of cause or with suspected acute reactions to foods, we searched for 19 possible discharge codes selected from the *International Classification of Disease, Tenth Revision (ICD-10)* (Table 1) [16]. We performed a pre-review of records of children who had ICD codes J45, L20, L24.6, L27 or K52.2 as the only diagnosis and who had been admitted to Sachs' Children's Hospital during the first 3 months of 2007 or during another randomly selected 3 months of the same year. Since we did not identify any child with food-induced anaphylaxis in this group of children, records with these ICD codes as only diagnosis were not further reviewed.

All medical records including notes taken during ambulance transportation and by the nurse in charge at admission were reviewed in detail by three physicians (D. H., C. F., M. V.). In case of uncertainty, trained paediatric allergists (D. H., M. W.) took the decision on inclusion. If a child had had repeated ED visits during 2007, we included only the first record unless the child had reacted to different foods on different occasions, in which case we included one record per eliciting food. This was done in order not to oversample symptoms to a specific food. The only exception was during calculation of the incidence of anaphylaxis.

All recorded symptoms and signs from the ED visits were entered a database. Symptoms and signs were those objectively registered by ambulance and health care staff at the ED. As to vomiting and diarrhoea, these symptoms were entered in the database even when only reported by the patient or parents if such symptoms had occurred just prior to admission. Subjective symptoms reported by patients and described in the clinical records (i.e. abdominal pain, dyspnoea, oral pruritus) were also registered. In addition, patient's sex,

Table 1. The discharge codes initially used for retrieval of clinical emergency department records (*International Classification of Disease, Tenth Revision (ICD-10)*)

Code	Diagnosis
J45	Asthma
K52.2	Allergic and dietetic gastroenteritis and colitis
L20	Atopic dermatitis
L27	Dermatitis due to substances taken internally
L24.6	Irritant contact dermatitis due to food in contact with skin
L50.0	Allergic urticaria
L50.9	Urticaria, unspecified
T63	Toxic effect of contact with venomous animals
T78.0	Anaphylactic shock due to adverse food reaction
T78.1	Other adverse food reactions, not elsewhere classified
T78.2	Anaphylactic shock, unspecified
T78.3	Angioneurotic oedema
T78.4	Allergy, unspecified
T78.8	Other adverse effects, not elsewhere classified
T78.9	Adverse effect, unspecified
T80.5	Anaphylactic shock due to serum
T88.1	Other complications following immunization, not elsewhere classified
T88.6	Anaphylactic shock due to adverse effect of correct drug or medicament properly administered
T88.7	Unspecified adverse effect of drug or medicament

age, history of any allergy-related disease including known underlying food allergy, probable current eliciting foods, pharmacological treatment (at home, in the ambulance and at the hospital) and observation time at the hospital were extracted from the clinical records. We also had access to referral letters written at discharge after the visit as well as the complete medical records of each patient including in- and outpatient visits prior to and after the ED visit. The eliciting agent was recorded as 'mixed food' if no single food could be identified.

Classification of anaphylaxis

Children with reactions to foods were allocated into two groups: those who fulfilled the criteria for anaphylaxis and those who did not. The criteria for anaphylaxis were those presented in the EAACI Task Force Anaphylaxis paper by Muraro et al. [17], but slightly modified by us [16]. In brief, anaphylaxis was defined as an acute allergic reaction involving two or more organ systems after exposure to a likely allergen, or hypotension alone after exposure to a known allergen for that patient.

Statistical analysis

Both incidence and prevalence were calculated. The incidence per person years, i.e. the total number of

years that our study population was under observation, was calculated from the population of all children 0–18 years of age living in Stockholm during 2007, in total 447 739 [18]. Prevalence rates of eliciting foods, symptoms and treatment are presented as proportions. Data are also expressed in total numbers, but as mean or median when appropriate. Differences in proportions between groups were analysed with either the chi-square analysis or Fisher's Exact Test. The One-Sample Kolmogorov–Smirnov test was used for comparisons of distribution between variables. The data were analysed with the statistical program PASW Statistics version 18.0 (SPSS Inc, Chicago, IL, USA). To control for errors of mass significances a P -value ≤ 0.01 was considered to be significant.

Results

Study population

Five hundred and thirty-one (531) clinical ED records were identified and manually reviewed. During the study period, 385 children met the inclusion criteria (Fig. 1). Two children were excluded owing to incomplete documentation. Of the remaining 383 children, 371 had had acute reactions to foods. Another 12 children with anaphylaxis not likely caused by food were identified. Among the 371 children with reactions to foods, 23 were found to have had more than one ED visit caused by allergic reaction to foods, of which 10 had had reactions to different foods, leaving 381 records for final analysis. These 371 children were allocated into two different groups: patients fulfilling ($n = 128$) or not fulfilling ($n = 243$) the criteria of anaphylaxis. Among the 243 children who did not fulfil

the criteria, 70 had been given adrenaline at home, during transportation with ambulance or on arrival to hospital; this might have prevented anaphylaxis. The remaining 173 children neither fulfilled the criteria for anaphylaxis nor had been given adrenaline. Thus, our study population ultimately consisted of three groups: group A/anaphylaxis ($n = 128$), group B/no anaphylaxis, but adrenaline administered ($n = 70$) and group C/no anaphylaxis, no adrenaline administered ($n = 173$) (Fig. 1).

Incidence of anaphylaxis

Anaphylaxis irrespective of cause was found among 140 (128 + 12) children of whom 128 reacted to food. Another three children had repeated ED visits during 2007 caused by the same food and were classified as having had a mild allergic reaction at their first ED visit but anaphylaxis at re-admission. Thus, 143 children had anaphylaxis and food was the inciting agent for 92%. With a population of 447 739 children/adolescents 0–18 years of age in Stockholm during 2007, the total incidence of anaphylaxis that year was 32 per 100 000 person years, whereas the incidence of food-related anaphylaxis was 29 per 100 000 person years [18].

Demographic data and co-morbidity

Table 2 presents the three groups in terms of demography, co-morbidity and known contacts with health care prior to the ED visit. Of the 371 children with reactions to foods, 183 (49%) were in the age group 0–3 years (Fig. 2). In this age group, only 28% (52/183) had anaphylaxis compared with 40% (76/188) in children

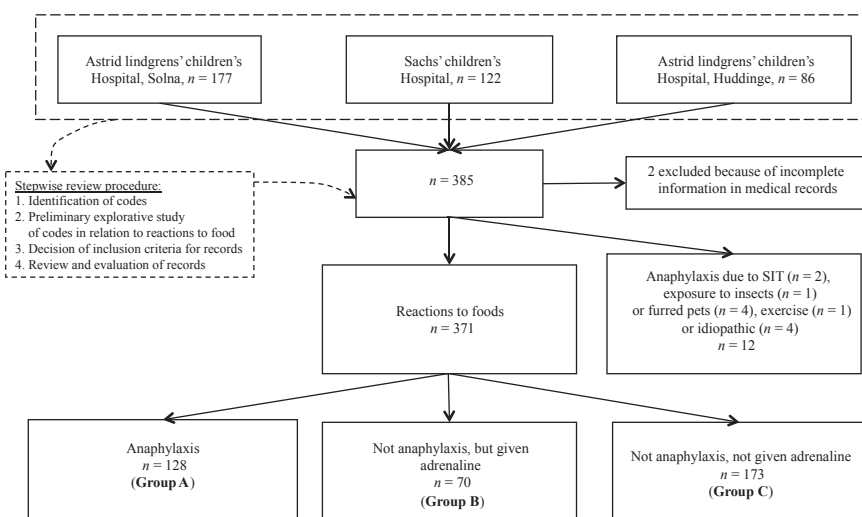


Fig. 1. Description of the review procedure of clinical records from emergency department visits at any of the three paediatric hospitals in Stockholm, Sweden, 1 Jan–31 Dec 2007 and final allocation into three groups of food reactions (A–C).

Table 2. Anthropometric data, co-morbidity and contact with health care among 371 children prior to visits due to reactions to foods to the emergency department at any of the three paediatric hospitals in Stockholm, Sweden, during 2007

	Anaphylaxis A N = 128 n (%)	No anaphylaxis		P-values	
		Adrenaline administered*	No adrenaline administered		
		B N = 70 n (%)	C N = 173 n (%)	A vs. B	A vs. C
Girls n = 176 (47%)	57 (45)	31 (44)	88 (51)	0.97	0.28
Age in years (mean/median, min–max), 6/4 (0–17)	6/6 (0–17)	7/6 (0–17)	5/2 (0–17)	0.21	<0.01
Any allergic disease co-morbidity, n = 270 (73%)	103 (80)	56 (80)	111 (64)	0.96	<0.01
Asthma, n=109 (29%)	47 (37)	26 (37)	36 (21)	0.95	<0.01
Eczema, n=94 (25%)	39 (31)	18 (26)	37 (21)	0.48	0.07
Urticaria, n=10 (3%)	4 (3)	2 (3)	4 (2)	1.00	0.73
Allergy to inhalant allergens, n=107 (29%)	46 (36)	28 (40)	33 (19)	0.57	<0.01
Previously known food allergy, n=222 (60%)	87 (68)	52 (74)	83 (48)	0.30	<0.01
No previously known allergic disease, n=101 (27%)	25 (20)	14 (20)	62 (36)	0.96	<0.01
Current contact with doctor due to any allergic disease prior to ED visit, n = 164 (44%)	62 (48)	35 (50)	67 (39)	0.83	0.09
Adrenaline auto-injector prescribed before ED visit, n = 77 (21%)	38 (30)	25 (36)	14 (8)	0.69	<0.01

*Adrenaline given at home before admission, during ambulance transport or at hospital despite absence of anaphylaxis according to our definition.

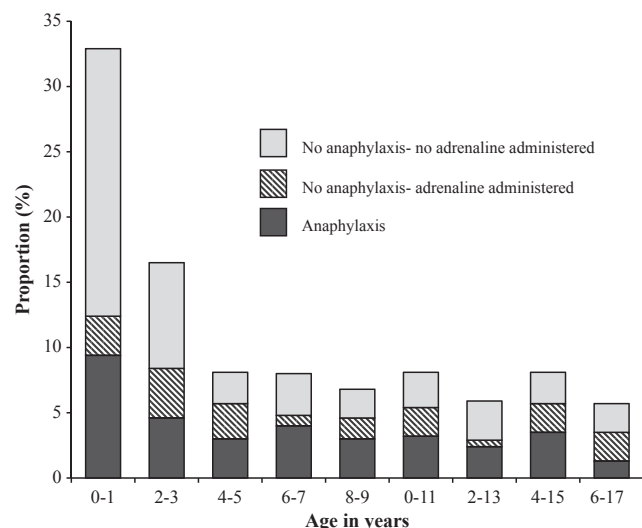


Fig. 2. Age distribution in relation to severity of reactions to foods among 371 children with 381 ED visits in Stockholm, Sweden, during 2007.

4 years and older ($P < 0.001$). At admission, a majority of the children had a history of allergic disease (73%) and 60% a history of known food allergy. Among the coexisting allergy-related diseases, asthma and allergy to inhalant allergens were most common (both 29%) in the whole group of 371 children. No significant differences in age, sex or co-morbidity between group A (anaphylactic children) and B (no anaphylaxis, adrenaline administered) were seen. However, children in group C (no anaphylaxis, no adrenaline administered)

were significantly younger, were less likely to have allergic diseases such as asthma and food allergy and had been prescribed adrenalin in an auto-injector significantly less frequently (all $P < 0.01$) compared with group A (Table 2).

Eliciting foods

Table 3 presents the foods that were considered to be associated with anaphylaxis. Peanut and tree nuts were the most common triggers (39%). Specified tree nuts accounted for 15% of the reactions; reaction to cashew nut was most prevalent. Peanut accounted for 14% of the reactions. In 26% of the children, no specific trigger food could be identified, as the ingested meal had contained several food items (i.e. 'mixed foods', Table 3). Reactions to milk and egg were common in infants (0-2 years), but became uncommon or even non-existing in teenage. This is to be compared with reactions to peanut and tree nuts, which could be observed already in the age group between 0 and 2 years and showed an increasing prevalence with increase of age (Fig. 3). However, it is noteworthy that reactions to peanuts or tree nuts were just as common as reactions to milk or egg in the age group 0-2 years ($P = 0.38$).

Among children with reported allergy to pollen, admission due to anaphylaxis tended to be more common during the deciduous tree pollen season March-May compared with the rest of the year, $P = 0.015$ (Fig. 4). Reactions to the five most

Table 3. Eliciting foods among 371 children with 381 emergency department visits* at any of the three paediatric hospital in Stockholm, Sweden, during 2007. Only eliciting foods associated with anaphylaxis in at least one child are presented

	No anaphylaxis			<i>P</i> -values	
	Anaphylaxis	Adrenaline administered [†]	No adrenaline administered		
	A <i>N</i> = 129 <i>n</i> (%)	B <i>N</i> = 73 <i>n</i> (%)	C <i>N</i> = 179 <i>n</i> (%)	A vs. B	A vs. C
Tree nuts and/or peanut, <i>n</i> = 148 (39%)	62 (48)	29 (40)	57 (32)	0.25	<0.01
Tree nuts, <i>n</i> =58 (15%)	24 (19)	12 (16)	22 (12)	0.70	0.13
Cashew nut, <i>n</i> =19 (5%)	10 (8)	3 (4)	6 (3)	0.38	0.09
Hazelnut, <i>n</i> =11 (3%)	3 (2)	1 (1)	7 (4)	1.00	0.53
Almond, <i>n</i> =8 (2%)	3 (2)	3 (4)	2 (1)	0.67	0.65
Walnut, <i>n</i> =7 (2%)	2 (2)	1 (1)	4 (2)	1.00	1.00
Pistachio, <i>n</i> =6 (2%)	3 (2)	1 (1)	2 (1)	1.00	0.65
Pecan nut, <i>n</i> =2 (0.5%)	1 (0.8)	1 (1)	0 (0)	1.00	0.42
Brazil nut, <i>n</i> =2 (0.5%)	1 (0.8)	0 (0)	1 (0.6)	1.00	1.00
Coconut, <i>n</i> =1 (0.3%)	1 (0.8)	0 (0)	0 (0)	1.00	0.42
Peanut, <i>n</i> =53 (14%)	24 (19)	9 (12)	20 (11)	0.25	0.07
Nuts un-specified, <i>n</i> =37 (10%)	14 (11)	8 (11)	15 (8)	0.98	0.46
Egg, <i>n</i> = 43 (11%)	15 (12)	10 (14)	18 (10)	0.67	0.66
Milk, <i>n</i> = 34 (9%)	8 (6)	4 (6)	22 (12)	1.00	0.08
Fish, <i>n</i> = 12 (3%)	1 (0.8)	3 (4)	8 (5)	0.14	0.09
Seeds [‡] , <i>n</i> = 7 (2%)	3 (2)	0 (0)	4 (2)	0.56	1.00
Sesame seeds, <i>n</i> =5 (1%)	3 (2)	0 (0)	2 (1)	0.56	0.65
Wheat, <i>n</i> = 6 (2%)	3 (2)	1 (1)	2 (1)	1.00	0.65
Shellfish, <i>n</i> = 6 (2%)	1 (0.8)	3 (4)	2 (1)	0.14	1.00
Apple, <i>n</i> = 6 (2%)	2 (2)	0 (0)	4 (2)	0.54	1.00
Kiwi fruit, <i>n</i> = 4 (1%)	1 (0.8)	1 (1)	2 (1)	1.00	1.00
Banana, <i>n</i> = 1 (0.3%)	1 (0.8)	0 (0)	0 (0)	1.00	0.42
Cucumber, <i>n</i> = 1 (0.3%)	1 (0.8)	0 (0)	0 (0)	1.00	0.42
Mixed foods [§] , <i>n</i> = 99 (26%)	30 (23)	20 (27)	49 (27)	0.51	0.41

*Only children with unique reactions to a certain food are included. If repeated emergency department visits were due to reactions to the same food, only the first emergency department visit was included.

[†]Adrenaline given at home before admission, during ambulance transport or at hospital despite absence of anaphylaxis according to our definition.

[‡]Seeds denote Sesame seeds (5 = 1%), Poppy seeds (1 = 0.3%) and Sunflower seeds (1 = 0.3%).

[§]Intake of several foods at the same time.

Other foods involved in reactions but not causing anaphylaxis: fish roe, legumes/beans, human milk, macadamia nut, pine nut, watermelon, mango, honey, avocado, jackfruit, blueberries, sunflower seed, poppy seeds.

common specific foods were unrelated to sex (data not shown).

Clinical symptoms

Symptoms and signs are presented in Table 4. Cutaneous manifestations were most common and occurred in 74% of all cases, irrespective of severity of reaction, followed by symptoms from the oral cavity (34%), gastrointestinal tract (29%) and lower airways (28%). Cardiovascular and neurological symptoms occurred in 4% and 7%, respectively. There were no clinical records of children who suffered confusion, cardiac arrest or fatal course during the study period. Of the nine children with tachycardia, two were noted with

tachycardia after administration of adrenaline. Older children more often had reactions in the oral cavity, on the skin and in the lower airways, but these clinical symptoms did not differ in relation to sex (data not shown).

Treatment and management

Therapeutic interventions and management are reported in Table 5. Of the children with anaphylaxis (group A), 71% were administered adrenaline either before arrival at the hospital or at the ED. Sixteen percent of those in group A were given repeated doses. Among children with anaphylaxis and with previous prescription of adrenaline in an auto-injector, all of whom had

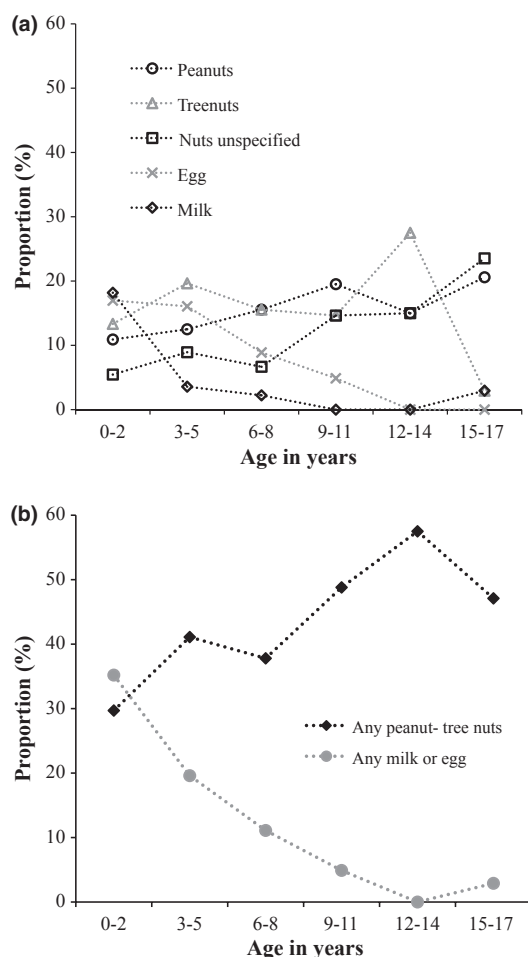


Fig. 3. Eliciting foods in relation to age among 371 children with 381 ED visits due to acute reactions to foods in Stockholm, Sweden, during 2007. In (a) the five most common eliciting food items are displayed and in (b) the proportions of reactions to peanuts, specified and unspecified nuts are summated as well as the proportions of reactions to milk and egg.

previously known food allergy, only 45% had used their injector prior to the ED visit. Concerning the association between acute wheeze and reactions to food, wheeze was elicited in 15 (18%) of the 82 children with anaphylaxis but without underlying asthma compared with 18 (38%) of the 47 children with underlying asthma ($P = 0.01$). When all lower airway symptoms listed in Table 4 were grouped as one entity, the corresponding proportions were 49% and 72% ($P = 0.03$).

Discussion

We examined all patients admitted in 2007 for anaphylaxis or acute food-related reactions to any of the three paediatric hospitals in Stockholm, Sweden, serving the total catchment area of Stockholm County. We studied eliciting foods, clinical symptoms and management at the ED, but also the incidence of anaphylaxis.

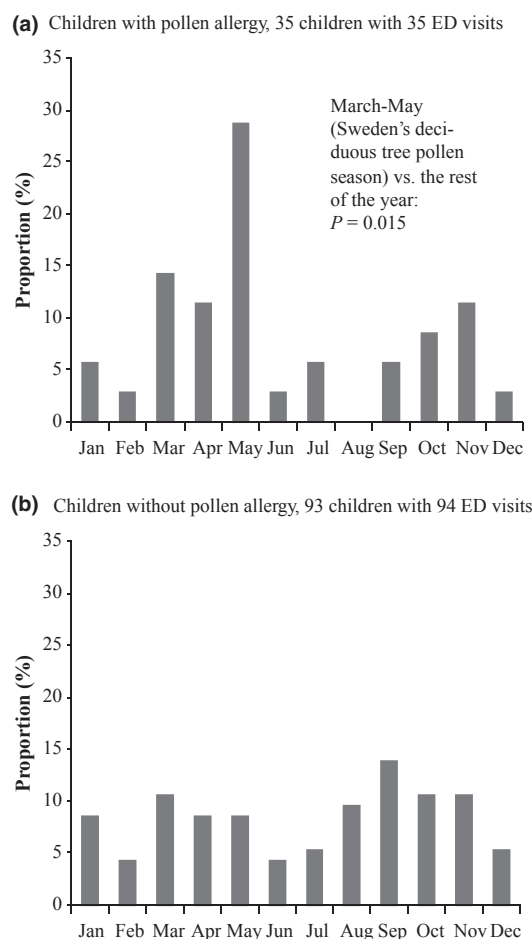


Fig. 4. Proportion of ED visits in relation to month of admittance among 128 children with 129 ED visits due to anaphylaxis to food at any of the three paediatric hospitals in Stockholm, Sweden, during 2007, in relation to underlying pollen allergy.

The incidence of anaphylaxis was 32 per 100 000 person years which is higher than the incidence estimated by Bohlke et al. [19] of 10.5 episodes per 100 000 person years, but lower than reported by Decker et al. [9] in the age group 0–19 years. However, differences in study design as well as inconsistencies in the criteria for diagnosis of anaphylaxis make comparison of results difficult. Even though our study is large and population based within a defined catchment area, we cannot exclude underestimation of the true incidence of anaphylaxis, in particular milder forms. First, adrenaline given outside the hospital prior to admission will prevent deterioration. Second, some anaphylactic episodes might have been treated by local healthcare providers and not referred. Third, mild episodes of anaphylaxis may resolve spontaneously. Using ICD codes for tracing patients has its limitations since symptoms and signs may not be correctly coded. Overall, this may also lead to an underestimation of the incidence of anaphylaxis. According to the EAACI Task Force Anaphylaxis paper, abdominal pain should be persistent and

Table 4. Clinical symptoms of acute reactions to foods among 371 children with 381 emergency department visits* at any of the three paediatric hospitals in Stockholm, Sweden, during 2007

	No anaphylaxis				
	Anaphylaxis A N = 129 n (%)	Adrenaline administered [†] B N = 73 n (%)	No adrenaline administered C N = 179 n (%)	<i>P</i> -values	
				A vs.	A vs.
				B	C
Skin, n = 282 (74%)	120 (93)	47 (64)	115 (64)	<0.001	<0.001
Urticaria, n=167 (44%)	85 (66)	28 (38)	54 (30)	<0.001	<0.001
Generalized, n=137 (36%)	75 (58)	26 (36)	36 (20)	<0.01	<0.001
Facial swelling, n=154 (40%)	66 (51)	30 (41)	58 (32)	0.17	<0.01
Generalized flush, n=43 (11%)	28 (22)	3 (4)	12 (7)	<0.01	<0.001
Rash unspecified, n=30 (8%)	7 (5)	3 (4)	20 (11)	1.00	0.08
Generalized itch, n=18 (5%)	10 (8)	1 (1)	7 (4)	0.10	0.15
Eczema, n=2 (0.5%)	0 (0)	0 (0)	2 (1)	n.a.	0.51
Oral cavity, n = 131 (34%)	46 (36)	39 (53)	46 (26)	0.01	0.06
Itch in oral cavity or throat, n=92 (24%)	26 (20)	32 (44)	34 (19)	<0.001	0.80
Feeling of tightness in oral cavity or throat, n=60 (16%)	29 (23)	13 (18)	18 (10)	0.43	<0.01
Oral ‘tingling’, n=3 (0.8%)	0 (0)	1 (1)	2 (1)	0.36	0.51
Gastrointestinal, n = 112(29%)	81 (63)	10 (14)	21 (12)	<0.001	<0.001
Vomiting, n=86 (23%)	64 (50)	5 (7)	17 (10)	<0.001	<0.001
Abdominal pain, n=33 (9%)	28 (22)	1 (1)	4 (2)	<0.001	<0.001
Diarrhoea, n=7 (2%)	6 (5)	1 (1)	0 (0)	0.43	<0.01
Nausea, n=6 (2%)	1 (0.8)	4 (6)	1 (0.6)	0.06	1.00
Loss of bowel control, n=1 (0.3%)	1 (0.8)	0 (0)	0 (0)	1.00	0.42
Upper airways, n = 39 (10%)	26 (20)	4 (6)	9 (5)	<0.01	<0.001
Conjunctivitis, n=20 (5%)	11 (9)	2 (3)	7 (4)	0.14	0.09
Hoarseness, n=11 (3%)	9 (7)	0 (0)	2 (1)	0.03	0.01
Nasal congestion or rhinorrhoea, n=9 (2%)	6 (5)	1 (1)	2 (1)	0.43	0.07
Feeling of lumpiness in throat, n=4 (1%)	1 (0.8)	2 (3)	1 (0.6)	0.30	1.00
Swallowing difficulties, n=3 (0.8%)	2 (2)	1 (1)	0 (0)	1.00	0.18
Lower airways, n = 106 (28%)	80 (62)	12 (16)	14 (8)	<0.001	<0.001
Dyspnoea, n=40 (11%)	25 (19)	5 (7)	10 (6)	0.02	<0.001
Wheeze, n=38 (10%)	33 (26)	4 (6)	1 (0.6)	<0.001	<0.001
Affected breathing pattern, n=13 (3%)	12 (9)	1 (1)	0 (0)	0.03	<0.001
Cough, n=13 (3%)	12 (9)	1 (1)	0 (0)	0.03	<0.001
SpO2<92%, n=13 (3%)	12 (9)	1 (1)	0 (0)	0.03	<0.001
Stridor, n=8 (2%)	6 (5)	1 (1)	1 (0.6)	0.43	0.02
Increased production of phlegm, n=5 (1%)	1 (0.8)	2 (3)	2 (1)	0.30	1.00
Muffled voice, n=3 (0.8%)	2 (2)	0 (0)	1 (0.6)	0.54	0.57
Cyanosis, n=3 (0.8%)	3 (2)	0 (0)	0 (0)	0.56	0.07
Chest tightness, n=1 (0.3%)	0 (0)	1 (1)	0 (0)	0.36	n.a.
Speaking difficulties, n=1 (0.3)	0 (0)	1 (1)	0 (0)	0.36	n.a.
Respiratory arrest, n=1 (0.3%)	1 (0.8)	0 (0)	0 (0)	1.00	0.42
Neurological, n = 25 (7%)	16 (12)	2 (3)	7 (4)	0.02	<0.01
Tiredness, n=15 (4%)	9 (7)	1 (1)	5 (3)	0.10	0.08
Anxiety, n=5 (1%)	5 (4)	0 (0)	0 (0)	0.16	0.01
Somnolence, n=4 (1%)	2 (2)	0 (0)	2 (1)	0.54	1.00
Unconsciousness, n=3 (0.8%)	3 (2)	0 (0)	0 (0)	0.56	0.07
Increased activity level, n=2 (0.5%)	1 (0.8)	1 (1)	0 (0)	1.00	0.42
Dizziness, n=1 (0.3%)	0 (0)	0 (0)	1 (0.6)	n.a.	1.00
Cardiovascular, n = 14 (4%)	14 (11)	0 (0)	0 (0)	<0.01	<0.001
Tachycardia [‡] , n=9 (2%)	9 (7)	0 (0)	0 (0)	0.03	<0.001

(continued)

Table 4 (continued)

	Anaphylaxis A N = 129 n (%)	No anaphylaxis		<i>P</i> -values	
		Adrenaline administered [†] B N = 73 n (%)	No adrenaline administered C N = 179 n (%)		
Hypotension, <i>n</i> =6 (2%)	6 (5)	n.a.	n.a.	n.a. [§]	n.a. [§]
Bradycardia, <i>n</i> =1 (0.3%)	1 (0.8)	0 (0)	0 (0)	1.00	0.42

*Only children with unique reactions to a certain food are included. If repeated ED visits were due to reactions to the same food, only the first ED visit was included.

[†]Adrenaline given at home before admission, during ambulance transport or at hospital despite no anaphylaxis.

[‡]Two of these nine children were registered with tachycardia after adrenaline had been administered.

[§]Not applicable because of the definition of anaphylaxis.

n.a., not applicable; ED, emergency department.

Table 5. Therapy administered to 371 children with 381 emergency department visits* to any of the three paediatric hospitals in Stockholm, Sweden, during 2007 due to acute reactions to foods

		No anaphylaxis			
	Anaphylaxis	Adrenaline administered [†]	No adrenaline administered		
	A	B	C	<i>P</i> -values	
	<i>N</i> = 129	<i>N</i> = 73	<i>N</i> = 179		
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	A vs. B	A vs. C
Adrenaline, <i>n</i> = 164 (43%)	91 (71)	73 (100)	n.a.	<0.001	–
At home, <i>n</i> =32 (8%)	17 (13)	15 (21)	n.a.	0.17	–
In ambulance, <i>n</i> =11 (3%)	5 (4)	6 (8)	n.a.	0.21	–
At hospital, <i>n</i> =135 (35%)	79 (61)	56 (77)	n.a.	0.03	–
Repeated doses, <i>n</i> =30 (8%)	20 (16)	10 (14)	n.a.	0.73	–
Inhaled β-2 agonist, <i>n</i> = 86 (23%)	51 (40)	12 (16)	23 (13)	<0.01	<0.001
At home, <i>n</i> =27 (7%)	13 (10)	2 (3)	12 (7)	0.06	0.29
In ambulance, <i>n</i> =34 (9%)	18 (14)	8 (11)	8 (5)	0.54	<0.01
At hospital, <i>n</i> =48 (13%)	38 (30)	5 (7)	5 (3)	<0.001	<0.001
Intensive care therapy, <i>n</i> = 4 (1%)	2 (2)	2 (3)	0 (0)	0.62	0.18
Observation at hospital ≥ 6 h, <i>n</i> = 80 (21%)	54 (42)	18 (25)	8 (5)	0.01	<0.001
Auto-injector with adrenaline not used when prescribed, <i>n</i> = 49/81 (60%)	21/38 (55)	12/27 (44)	16/16 (100)	0.39	n.a.
Follow-up arranged, <i>n</i> = 271 (71%)	97 (75) [‡]	51 (70) [‡]	123 (69) [‡]	0.41	0.21

*Only children with unique reactions to a certain food are included. If repeated ED visits due to reactions to the same food, only the first ED visit was included in this analysis.

[†]Adrenaline given at home before admittance, at ambulance transport or at hospital despite no anaphylaxis at admittance.

[‡]Of the 110 (29%) children who received no follow-up, 21 (16%) of the children in group A, 13 (18%) of the children in group B and 32 (18%) of the children in group C had ongoing contact with a doctor due to allergic disease before admission.

n.a., not applicable; ED, emergency department.

crampy to be considered a subcriterion for anaphylaxis [17]. This hampered our retrospective classification of anaphylaxis since the extent of abdominal pain could seldom be retrieved from the medical records [16]. Hence, we considered abdominal pain regardless of severity as a subcriterion for anaphylaxis, which may have led to an overestimate of the incidence.

In agreement with others [6, 8], we found that acute food-related reactions were significantly more common among children 0–3 years of age. Our finding that

severe reactions are less common among younger children has also recently been reported by Rudders et al. [15].

Food was the underlying cause of anaphylaxis in 92% of the cases. To our knowledge, such a high proportion has not been described before [6–8, 10, 11, 20]. Among foods causing reactions, peanut and tree nuts were the dominating eliciting food types, followed by milk and egg. Peanut and tree nuts were also frequently involved in anaphylactic reactions. These findings

confirm those of others [6, 7, 10, 15, 20]. Interestingly, reactions to peanut or tree nuts were just as common as reactions to milk or egg in the age group 0–2 years. Since tree nuts and peanuts are now recognized as potent allergens by the general public, parents of children with suspected reactions to tree nuts or peanuts may be more prone to seek medical attention than parents whose children have reacted to other foods. This might lead to a higher proportion of patients seen in the ED with peanut/tree nut allergy than in society at large. A new and emerging allergenic food seems to be cashew, most likely due to increased exposure in the population during the last 10 years [21], which also has been reported by others [22].

In several cases, a meal containing multiple food items had been ingested shortly prior to the reaction and in 26% of the cases, no specific eliciting food could be identified, a finding that echoes what has been reported by others [7]. This is likely to create a problem since lack of knowledge about what to avoid may result in an increased risk of recurrence compared with that in children for whom the eliciting food can be determined. Quality of life may also be severely affected.

Aggravating factors in relation to allergic reactions to foods are of particular interest. In the Stockholm area, the deciduous tree pollen season starts in February–March and peaks in May [23]. Our study suggests an associated risk for anaphylaxis during leaf tree pollen season among 35 pollen-allergic individuals. Thus, it seems that concomitant allergen exposure facilitates the risk of reactions to other allergens. This is on the other hand well known in the context of specific immunotherapy and a recent study showed fatal anaphylaxis to be more prevalent during spring and summer [24].

During the study year of 2007 there was no fatal case of anaphylaxis among children in our study region. As in previous reports [7, 8, 14, 15] cutaneous manifestations were the most commonly reported clinical feature. In the group of children with food-induced anaphylaxis, gastrointestinal symptoms were as common as symptoms from the lower airways. The high prevalence of gastrointestinal manifestations in our study is in contrast to the findings of previous studies [6, 7, 20] and could be attributed to a considerable variation in the criteria for anaphylaxis used by the different authors.

Some previous studies have stated that children with asthma have a higher risk of severe allergic reactions to food [25, 26], which is in line with our results. However, it is noteworthy that among children with anaphylaxis, but without underlying asthma, almost 50% presented with lower airway symptoms.

In the group of children with anaphylaxis 30% had been prescribed adrenaline in an auto-injector prior to

admission, but less than half of them used the drug when an emergency situation occurred. This finding is in line with others' [27]. However, it was not possible to determine whether the patients had the auto-injector available at the critical timepoint. Nevertheless, this indicates a need of research on how to change the attitudes towards using self-injectable adrenaline.

The primary limitation of this study is its retrospective design and our reliance on precise and complete documentation in clinical records. There are also limitations in our ability to confirm the aetiologies of the reactions in particular when a whole meal was ingested and the specific eliciting food was unknown. However, we do not see any possibilities of performing such a study in a prospective way. The criteria used to define anaphylaxis will affect the results. In this study, we used the criteria presented in EAACI Task Force Anaphylaxis paper by Muraro et al. but modified by us [16, 17]. However, since these criteria correspond to the criteria for anaphylaxis recently suggested by the World Allergy Organization [28], our results would not have been altered if the latter criteria had been used instead.

A considerable strength of this study is the use of a large number of diagnostic codes specific for food allergy, as well as more general allergy codes, combined with chart review. According to these codes, more than 500 emergency visits could be identified, but with manual review of all of these our database could be restricted to 371 children with 381 visits. This type of approach is likely to provide the most complete and representative group of patients, as demonstrated by Clark et al. [29]. Another strength is that we had access not only to the child's ED record but also to ambulance reports, referral letters at discharge and the complete medical record of each child on a regional level, both before and after the ED visit, helping to ensure that missing data on co-morbidity and so on in the ED record could be retrieved elsewhere.

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