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## Age-related differences in the clinical presentation of food-induced anaphylaxis

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### Abstract

Food-induced anaphylaxis may be more difficult to recognize in younger children. We describe age-related patterns in the clinical presentation of children with anaphylaxis, which may facilitate the early recognition and treatment of this potentially life-threatening condition.

### Keywords

food allergy; anaphylaxis; emergency department; infant; child; adolescent

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Food allergies are the most common trigger for anaphylaxis in children<sup>1,2</sup> and recent reports indicate that the prevalence of food allergies among U.S. children is rising.<sup>3</sup> The diagnosis of anaphylaxis is complicated for several reasons, including the wide variety of clinical presentations and the delay in establishing widely-accepted diagnostic criteria.<sup>4</sup> Anaphylaxis may be even more difficult to diagnose in younger children due to inherent differences in their ability to communicate their symptoms.<sup>5</sup> Because delays in the recognition and treatment of anaphylaxis has been consistently associated with poor outcomes,<sup>6</sup> we sought to describe age-related patterns in the clinical presentation of food-induced anaphylaxis in children.

### Methods

We used ICD-9 diagnostic codes to identify all children presenting to the emergency department (ED) at either Massachusetts General Hospital or Children's Hospital Boston, between 1/1/01 and 12/31/06, with a food-related acute allergic reaction.<sup>3,7</sup> These codes included 995.60 (anaphylactic shock due to unspecified food), 995.61-995.69 (anaphylactic shock due to specified food), 995.0 (other anaphylactic shock), 693.1 (dermatitis due to

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food), 995.7 (adverse food reaction, not otherwise classified), 558.3 (allergic gastroenteritis), and 692.5 (contact dermatitis due to food). In addition, we randomly sampled patients with codes 995.3 (allergy, unspecified), 995.1 (angioedema) and 708.X (urticaria) to identify cases of food-related acute allergic reactions within these non-specific allergy codes.

A food-related acute allergic reaction was defined as an acute episode of symptoms suggestive of an IgE-mediated reaction in which the onset was immediately related to a known or suspected food allergen exposure. Based on current diagnostic criteria, anaphylaxis was defined as an acute allergic reaction involving 2+ organ systems or hypotension alone.<sup>4</sup> Hypotension was defined as a systolic blood pressure less than (70 mmHg + [age multiplied by 2]) for children <10 years old and less than 90 mmHg for children 10-17 years.<sup>4</sup>

For ED visits determined to due to a food-related acute allergic reaction within any diagnosis code, a structured chart review was performed to collect the following data: patient demographics, medical history, presentation and clinical course. The charts were reviewed by two physicians, including a pediatric allergist. We used a stratified sampling method to reflect the population of patients within the partly reviewed ICD-9 codes (708.X, 995.1 and 995.3). Using the survey module in STATA 10.0 (StataCorp, College Station, Texas), sample weights were assigned to account for unequal probabilities of selection, over-sampling, and non-response. Anaphylaxis patients were divided into four age groups: infants (<2 years), pre-school (2-5 years), school-aged (6-11 years) and adolescents (12-18). Data are expressed as mean  $\pm$  standard error (SE) and proportion (95% confidence interval [CI]). Comparisons between age groups were evaluated using Chi-square tests. A two-sided  $P < 0.05$  was considered statistically significant.

## Results

Within the six-year period, we reviewed medical records for 605 children who presented to the ED with a food-related acute allergic reaction. With appropriate statistical weighting, this represented a study cohort of 1255 patients. Approximately half (52%; 95% CI, 48-57%) of these cases met criteria for anaphylaxis. The largest proportion of anaphylaxis patients were less than 2 years old (Table I). Patients were predominantly male in younger age groups; however, females represented approximately half (52%) of the adolescents. There were no significant differences in race/ethnicity across the four age groups. At the time of their ED presentation, infants less frequently had a history of known allergy to the offending food or other allergic disorder. Infants also less frequently owned an epinephrine auto-injector prior to their ED presentation.

Peanuts and milk were more common food triggers in infants, whereas adolescents more frequently reported reactions to tree nuts, fruits, and vegetables (Table II). Infants with anaphylaxis more often presented with hives and vomiting, and wheezing and stridor were more commonly observed in pre-school aged children. Subjective symptoms such as “trouble swallowing” and “difficulty breathing” were more frequently documented in adolescents. Adolescents were also more frequently noted to have cardiovascular signs or symptoms. Among all children, 3% had documented hypotension and this finding was consistent across the age groups. However, the youngest children were least likely to have their blood pressure measured during their ED stay (age <2: 60%; age 2-5: 79%; age 6-11: 95%; age 12-18: 99%;  $P < 0.001$ ). Overall, 14% of patients who met criteria for anaphylaxis were assigned an ED discharge diagnosis that included the term “anaphylaxis”. This percentage was significantly smaller in infants (6%).

## Discussion

The diagnosis of anaphylaxis is challenging for several reasons, including the wide variety of possible clinical presentations. Some data exist on the different patterns of anaphylaxis presentation in children vs. adults.<sup>2</sup> However, to our knowledge; this is the first paper to directly examine anaphylaxis presentation among children of different ages. Several patterns were observed, including that hives and vomiting were more commonly documented in infants, and certain respiratory findings were more frequently observed in pre-school aged children. Our data also support the notion that many of the signs or symptoms of anaphylaxis are potentially more difficult to interpret in infants.<sup>5</sup> Specifically, many subjective symptoms that could be noted in infants with careful observation, such as itching (scratching) and difficulty swallowing (drooling), were less frequently documented in this age group. Additionally, we found that cardiovascular symptoms were rarely reported in younger children. Although this could represent an age-related clinical pattern, the finding is complicated by less frequent measurement of blood pressures in younger children. This observation supports a previous assertion that hypotension often goes unnoticed in infants<sup>5</sup> and highlights a specific area requiring improvement in the diagnosis of anaphylaxis in younger children.

Anaphylaxis can progress rapidly, even when the initial symptoms are mild. Therefore, its prompt recognition is essential for optimal treatment.<sup>6</sup> Our study supports other recent reports that anaphylaxis is often under-recognized.<sup>8,9</sup> Furthermore, in our ED population, infants were least frequently diagnosed with anaphylaxis when there are suggestive findings. Although the retrospective nature of our study allows for the possibility of inaccurate/incomplete documentation, this finding may point towards the need for age-specific diagnostic guidelines for anaphylaxis.

In summary, food-related anaphylaxis is a potentially life-threatening medical condition that commonly affects children of all ages. We describe age-related patterns in the clinical presentation of children with anaphylaxis, which may facilitate its early recognition and treatment. Our data suggest that food-induced anaphylaxis may be more difficult to recognize in infants, highlighting the need for improved awareness and education.

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## Abbreviations

<b>CI</b>	confidence interval
<b>ED</b>	emergency department

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Table 1

Demographic characteristics and medical history of children presenting to the Emergency Department with a food-related anaphylaxis.\*

	Infants (ages <2) (n=191) % (95%CI)	Pre-school (ages 2-5) (n=171) % (95%CI)	School-aged (ages 6-11) (n=150) % (95%CI)	Adolescents (12-18) (n=145) % (95%CI)	P value
<i>Demographic characteristics</i>					
Male	69 (58 – 80)	57 (45 – 69)	71 (60 – 82)	48 (35 – 61)	0.03
White race/ethnicity	53 (41 – 65)	49 (37 – 61)	40 (26 – 54)	44 (31 – 57)	0.53
<i>Medical history<sup>‡</sup></i>					
Known allergy to offending food allergen	27 (15 – 38)	48 (37 – 60)	57 (43 – 71)	51 (37 – 64)	0.004
Other known allergic problems	63 (51 – 74)	84 (77 – 91)	86 (78 – 93)	80 (71 – 90)	0.001
Prior allergic reactions to other sources	50 (35 – 66)	68 (56 – 79)	65 (50 – 79)	74 (62 – 87)	0.12
Asthma	22 (9 – 35)	42 (29 – 55)	73 (58 – 87)	54 (39 – 70)	<0.001
Hayfever	NC**	24 (13 – 35)	36 (21 – 51)	27 (14 – 40)	0.001
Eczema	56 (40 – 71)	41 (29 – 54)	NC**	NC	--
Hives	0	NC**	NC**	0	--
Angioedema	0	0	0	0	--
Patient owns epinephrine auto-injector	21 (10 – 32)	67 (56 – 78)	67 (52 – 81)	46 (32 – 60)	<0.001

Abbreviations: CI, confidence interval; ED, emergency department.

\* Anaphylaxis defined as allergic reaction involving 2+ organ systems or hypotension. Hypotension is defined as systolic blood pressure less than (70 + (age multiplied by 2)) for children age <10 years and systolic blood pressure less than 90 mmHg for children age 10-18 years.

\*\* NC, non-calculable. When the number of observations was <30, robust estimates could not be produced.

<sup>‡</sup> Medical history based on patient report at the time of ED presentation.

Table 2

Clinical presentation of children presenting to the Emergency Department with a food-related anaphylaxis.\*

	Infants (ages <2) (n=191) % (95%CI)	Pre-school (ages 2-5) (n=171) % (95%CI)	School-aged (ages 6-11) (n=150) % (95%CI)	Adolescents (12-18) (n=145) % (95%CI)	P value
<i>Presentation and clinical course</i>					
Arrive to ED by ambulance	43 (32 – 55)	46 (35 – 58)	39 (27 – 51)	40 (28 – 53)	0.83
Time since exposure					0.42
< 1 hour	7 (6 – 28)	15 (6 – 24)	15 (7 – 23)	22 (9 – 35)	
1-3 hours	67 (55 – 79)	63 (51 – 75)	76 (66 – 85)	57 (43 – 72)	
> 3 hours	16 (8 – 24)	22 (12 – 33)	NC**	21 (9 – 32)	
Location of exposure					<0.001
Home	89 (81 – 97)	65 (53 – 76)	58 (43 – 73)	58 (44 – 72)	
School/daycare	9 (0 – 17)	11 (3 – 18)	9 (2 – 15)	12 (5 – 19)	
Restaurant	NC**	17 (6 – 27)	NC**	17 (6 – 28)	
Other	NC**	8 (3 – 13)	22 (8 – 36)	13 (5 – 21)	
<i>Specific food trigger causing reaction<sup>‡</sup></i>					
Peanuts	31 (20 – 43)	26 (17 – 36)	22 (13 – 32)	10 (7 – 13)	0.01
Tree nuts	9 (4 – 14)	28 (18 – 38)	21 (9 – 33)	20 (12 – 28)	0.02
Seeds	0	NC**	NC**	NC**	--
Fruits and vegetables	4 (0 – 9)	7 (0 – 13)	6 (0 – 11)	19 (7 – 32)	0.01
Shellfish	NC**	NC**	NC**	22 (10 – 35)	--
Fish	NC**	NC**	NC**	NC**	--
Food additives	NC**	0	0	NC**	--
Milk products	40 (28 – 51)	16 (7 – 26)	13 (4 – 21)	NC**	<0.001
Eggs	9 (3 – 16)	NC**	NC**	NC**	--
Wheat	NC**	NC**	0	0	--
Other food <sup>†</sup>	13 (5 – 22)	22 (11 – 24)	28 (14 – 42)	20 (10 – 31)	0.29
<i>Signs and symptoms</i>					
Hives	88 (79 – 97)	78 (69 – 88)	64 (51 – 77)	59 (46 – 72)	0.002

	Infants (ages <2) (n=191) % (95%CI)	Pre-school (ages 2-5) (n=171) % (95%CI)	School-aged (ages 6-11) (n=150) % (95%CI)	Adolescents (12-18) (n=145) % (95%CI)	P value
Itching	19 (10 – 29)	29 (18 – 40)	54 (40 – 67)	36 (24 – 48)	0.001
Swelling	53 (41 – 65)	56 (45 – 68)	44 (30 – 57)	36 (24 – 48)	0.09
Angioedema	NC**	NC**	NC**	NC**	--
Trouble swallowing	NC**	18 (8 – 29)	41 (27 – 55)	48 (35 – 61)	<0.001
Trouble breathing/shortness of breath	37 (26 – 48)	34 (23 – 45)	39 (27 – 52)	57 (44 – 70)	0.051
Wheezing	29 (20 – 39)	55 (43 – 66)	42 (29 – 56)	23 (13 – 32)	<0.001
Hoarse voice	NC**	12 (4 – 19)	NC**	13 (3 – 22)	0.80
Stridor	5 (3 – 7)	10 (2 – 18)	NC**	NC**	0.02
Nausea/vomiting	53 (41 – 65)	34 (24 – 45)	29 (17 – 42)	17 (9 – 26)	<0.001
Abdominal pain/cramps	0	NC**	12 (3 – 21)	NC**	--
Diarrhea	NC**	0	0	NC**	--
Dizziness/fainting	0	0	NC**	12 (4 – 20)	--
Altered mental status	NC**	NC**	NC**	0	--
Organ system involvement					
Respiratory	59 (47 – 71)	81 (72 – 89)	70 (56 – 83)	71 (58 – 83)	0.07
Cutaneous	98 (94 – 100)	95 (90 – 99)	92 (87 – 98)	87 (78 – 96)	0.11
Gastrointestinal	56 (44 – 67)	50 (38 – 61)	59 (45 – 72)	59 (46 – 72)	0.71
Cardiovascular	NC**	NC**	NC**	12 (4 – 20)	0.006
ED discharge diagnosis included term "anaphylaxis" (%)	6 (3 – 9)	25 (14 – 37)	13 (7 – 19)	13 (1 – 24)	0.02

Abbreviation: CI, confidence interval; ED, emergency department.

\* Anaphylaxis defined as allergic reaction involving 2+ organ systems or hypotension. Hypotension is defined as systolic blood pressure less than (70 + (age multiplied by 2)) for children age <10 years and systolic blood pressure less than 90 mmHg for children age 10-18 years.

\*\* NC, non-calculable. When the number of observations was <30, robust estimates could not be produced.

‡ All potential food allergen triggers reported by the patient were documented by reviewer.

† Other foods include less frequently reported food allergens (e.g., soy, barley) and foods with multiple potential allergens (e.g., cookies, pizza).