

Accidental allergic reactions in food allergy: Causes related to products and patient's management

To the Editor,

Whilst European labelling regulations require food manufacturers and providers to list 14 common allergens in prepackaged and non-prepackaged foods (eg, food service), products may contain undeclared allergens. Allergens can accidentally end up in food during the production process as a result of cross-contamination.¹ The unintentional presence of allergens in food is a serious concern for people with food allergies. Cross-contamination is not covered by labelling regulations, although food producers often use precautionary statements. Despite all measures, ingestion resulting in accidental reactions still occurs and can be severe and even fatal.² Therefore, we evaluated frequency, causes, severity and consequences in terms of medical treatment of accidental allergic reactions in adults with a physician-diagnosed food allergy confirmed by convincing history and sensitization.

A prospective study with 1-year follow-up was carried out in adults ($n = 157$) with a mean of 3.5 (SD 2.1) confirmed food allergies. Response rate was 65%. Most patients had a combination of primary and pollen-related food allergy (Table 1). All patients received dietary advice per food allergen by the physician or dietician based on the patient's history and observations during oral food challenges. Patients were asked to report all accidental reactions online to obtain data about causes, severity, medical treatment and sick leave. Reactions with local oral allergy symptoms were classified as being mild, reactions with symptoms from skin and mucous membranes and/or gastrointestinal tract were classified as moderate, and reactions with respiratory symptoms and/or cardiovascular symptoms were classified as being severe. Each reaction and submitted label were reviewed within 1 week by the multidisciplinary research team to determine whether the reaction was compatible with a food allergic reaction and the food allergy of the patient. (see Data S1-method section in detail).

A total of 153 reactions were reported by 73 of 157 patients (46%), whereas 84 (54%) of the patients did not report any accidental reaction in the 1-year follow-up. From the patients that reacted, 41 (26%) reported 1 reaction and 32 (20%) ≥ 2 reactions (range 2-11). Of those who reacted, the mean number of accidental reactions was 2.10 (SD 2.0) per person per year. Patients who reported reactions were significantly more often women, had a significantly longer duration of food allergy and had significantly more often a

confirmed allergy for peanut, sesame and vegetables compared with patients who did not report reactions.

Of the reactions, 62 (41%) were due to prepackaged foods, 37 (24%) were during a meal outside the home, 30 (20%) were due to fresh products, 13 (9%) were due to products or meals in a foreign country, and 11 (7%) occurred whilst having a meal at home. A total of 52 labels of prepackaged products or composite meals were received. Related to the specific food allergy profile of individual patients, in 19 of these 52 reactions (37%), the suspected allergen(s) were not mentioned as ingredient or warning on the label. Patients read the label in $n = 36$ (69%). Reasons for not reading the label were as follows: label was illegible ($n = 3$), consumed the food before ($n = 3$) and other reasons such as "I didn't expect allergens in the product"/"thought that it was safe" ($n = 10$).

Thirty-seven reactions (24%) were caused by composite meals outside the home: 68% in restaurants, followed by 22% at friends' or relative's home and 11% at other places (eg, camp and exhibition). Patients had called the restaurant before visiting or informed the cook, chef or waiter in 26 reactions (70%) or carefully checked the menu in 5 reactions (14%) or assumed it was safe in 6 reactions (16%). A wide range of food products were responsible for causing accidental reactions. Products could have up to four culprit allergens present that were not mentioned on the label or were undeclared in non-prepackaged foods.³

Severity of accidental reactions was mild in 33 (22%), moderate in 77 (50%) and severe in 43 (28%), of which 9 with cardiovascular involvement. In 103 (67%) reactions, patients used medication for treatment of the reaction; number and types of medication use increased with severity of the reaction. No medication was used in 19 (58%) of the mild reaction, 25 (32%) of the moderate reactions and 6 (14%) of severe reactions. In eight reactions, medical care was sought. (Table 2).

We showed that the mean number of accidental reactions was approximately 1 per person per year. Other studies have also reported frequencies of accidental reactions, but comparability is limited due to difference in age group (children vs adults), time frame and food allergens. For example, Anibarro et al⁴ reported 1.98 (range 1-10) reactions over a 5-year period. Kanny et al⁵ reported a mean of 4.7 (SD 5.6), 53% had 2 or more reactions, but the time frame within which these reactions occurred was not further specified, and

TABLE 1 Demographic and illness-related data

Demographic and illness-related data	Total n = 157	Patients who reported allergic reactions (n = 73)	Patients who did not report allergic reactions (n = 84)
Gender			
Female	116 (74%)	60/73 (82%)	56/84 (67%)*
Age			
Mean age, in years (SD, min-max)	35.3 (SD 12.7; range 18-70)	35.5 (12.2)	35.1 (13.4)
Education			
Primary education	10 (7%)	3 (4%)	7 (8%)
Secondary and intermediate vocational education	63 (41%)	27 (38%)	36 (43%)
Higher vocational or academic education	78 (50%)	40 (56%)	38 (46%)
Other (not specified)	4 (3%)	2 (3%)	2 (2%)
Missing n = 2		1	1
Food allergy for			
Hazelnut	87 (55%)	41 (56%)	46 (55%)
≥1 other nuts	75 (48%)	37 (51%)	38 (45%)
Almond	39 (25%)	20 (27%)	19 (23%)
Walnut	49 (31%)	21 (29%)	28 (33%)
Cashew nuts	19 (12%)	9 (12%)	10 (12%)
Pecan	7 (5%)	2 (3%)	5 (6%)
Macadamia nuts	1 (1%)	7 (1%)	0
Pistachios	7 (5%)	5 (7%)	2 (2%)
Brazil nuts	1 (1%)	1 (1%)	0
Peanut	73 (47%)	40 (55%)	33 (39%)*
Milk	29 (19%)	16 (22%)	13 (16%)
Egg	25 (16%)	14 (19%)	11 (13%)
Soya bean	17 (11%)	9 (12%)	8 (10%)
Sesame	12 (8%)	9 (12%)	3 (4%)*
Celery	12 (8%)	6 (8%)	6 (7%)
Crustaceans	6 (4%)	3 (4%)	3 (4%)
Fish	5 (3%)	2 (3%)	3 (4%)
Lupin	4 (3%)	2 (3%)	2 (2%)
Mollusc	2 (1%)	0	2 (2%)
Mustard	0	0	0
Other allergens, not belonging to the major allergens^a			
Fruit	96 (61%)	46 (63%)	50 (60%)
Vegetables	50 (32%)	29 (40%)	21 (25%)*
Other food allergies	11 (7%)	4 (6%)	7 (8%)
Type of food allergies			
Food allergy with primary sensitization only	26 (17%)	14 (19%)	12 (14%)
Pollen-related food allergy in combination with a food allergy with primary sensitization/due to LTP or storage protein	95 (61%)	45 (62%)	50 (60%)
Pollen-related food allergy only	16 (10%)	4 (6%)	12 (14%)
Pollen-related food allergy and uncertain cosensitization with or without LTP/storage protein	20 (13%)	10 (14%)	10 (12%)
Number of allergens			
Mean number of confirmed food allergies (fruit, vegetables, other food allergy each considered as 1). ^a	3.5 (SD 2.1; range 1-10)	3.8 (2.3)	3.2 (1.9)

(Continues)

TABLE 1 (Continued)

Demographic and illness-related data	Total n = 157	Patients who reported allergic reactions (n = 73)	Patients who did not report allergic reactions (n = 84)
Mean number of self-reported and confirmed allergens	4.9 (SD 3.1; range 1-17)	5.7 (3.3)	4.3 (2.8)
Years of having food allergy	n = 154		
Years of having food allergy (SD, min-max)	15.1 (12.7, 0-54)	17.5 (SD 12.7)	13.0 (12.4)*
Missing n = 3			
Historical severity			
Mild	7 (5%)	4 (6%)	3 (3%)
Moderate	36 (23%)	13 (18%)	23 (27%)
Severe	114 (73%)	56 (77%)	58 (69%)
Prescribed medication to treat the accidental reaction (more answers possible) in case of accidental reactions			
Oral antihistamines	149 (95%)	70 (96%)	79 (94%)
Adrenaline autoinjector	110 (70%)	50 (69%)	60 (71%)
Oral corticosteroids	89 (57%)	41 (56%)	48 (57%)
Inhaler	33 (21%)	22 (30%)	11 (13%)
No emergency medication	4 (3%)	2 (3%)	2 (2%)
Atopic comorbidities			
Atopic dermatitis	92 (59%)	49 (67%)	43 (51%)
Asthma	84 (54%)	44 (60%)	40 (48%)
Self-reported pollinosis	120 (76%)	60 (82%)	60 (71%)
Dietary management at baseline			
Reading labels			
Always read label	78 (50%)	42 (58%)	36 (43%)
Sometimes read label	63 (40%)	27 (37%)	36 (43%)
Never read label	16 (10%)	4 (6%)	12 (14%)
Which part of the label is read (n = 141)			
Ingredients	23 (16%)	11 (15%)	12 (14%)
Allergy information	9 (6%)	5 (7%)	4 (5%)
Both ingredients and allergy information	109 (77%)	53 (73%)	56 (67%)
Asking for presence of allergens in fresh products			
Always	99 (63%)	47 (64%)	53 (63%)
Sometimes	6 (4%)	3 (4%)	3 (4%)
Never	52 (33%)	23 (32%)	29 (35%)
Informing chef/personnel by eating out			
Always	123 (78%)	59 (80%)	64 (76%)
Sometimes	2 (1%)	0	2 (2%)
Never	32 (20%)	14 (19%)	18 (21%)

^aNumber of allergens includes primary food allergies but also pollen-related food allergies, confirmed by convincing history and sensitization and/or food challenges. Number of self-reported allergies are only self-reported and not confirmed by diagnostic tests. The number of food allergies for one or more fruit(s) and one or more vegetables is counted as one to correct for the large number of food allergies due to cross-reactivity. One or more other allergens than those of the major groups were also taken as 1.

*Significant difference between patients who reported accidental reactions and those who did not $P < 0.05$.

there was a possibility of overreporting, due to the food allergy being self-reported and not physician-diagnosed. Some studies were carried out in children; Fleischer's et al⁶ reported a mean of 0.81 reactions per year. Nguyen-Luu⁷ reported an annual incidence rate of 12.5% in children with peanut allergy. We showed that half of the food allergic patients reported no accidental allergic reactions in

the 1-year follow-up. However, patients with a wider range of food allergies had a higher risk of unexpected reactions. These patients have to examine the ingredients for multiple allergens, and it also requires vigilance for cross-contamination. Although all patients received dietary advice and information about labelling and going out for dinner, we found that not all patients always had checked

TABLE 2 Causal products of accidental reactions, medication use, medical care and sick leave

	Total number of reactions (n = 153)	Mild allergic reaction ^a (n = 33)	Moderate allergic reaction ^a (n = 77)	Severe allergic reaction ^a (n = 43)
Prepackaged product	62 (41%)	18 (55%)	32 (42%)	12 (28%)
Composite meals outside the home	37 (24%)	3 (9%)	22 (29%)	12 (28%)
Fresh product	30 (20%)	7 (21%)	11 (14%)	12 (28%)
In foreign country	13 (8%)	3 (9%)	5 (6%)	5 (12%)
Composite meals at home	11 (7%)	2 (6%)	7 (9%)	2 (5%)
Total	153 (100%)	33 (100%)	77 (100%)	43 (101%)
No medication	50 (33%)	19 (58%)	25 (32%)	6 (14%)
Antihistamines only	70 (46%)	13 (39%)	41 (53%)	16 (37%)
Inhaler	1 (0.7%)	0	0	1 (2%)
Antihistamines and inhaler	9 (6%)	0	2 (3%)	7 (16%)
Antihistamines and prednisone	17 (11%)	1 (3%)	9 (12%)	7 (16%)
Antihistamines and prednisone and inhaler	4 (3%)	0	0	4 (9%)
Antihistamines and prednisone and inhaler and adrenaline	2 (1%)	0	0	2 (5%)
Total	153 (100%)	33 (100%)	77 (100%)	43 (100%)
Medical help (n = 108)				
By a general practitioner	2 (2%)	0	1 (2%)	1 (3%)
By a hospital (hospitalization)	6 (6%) (1 [1%])	1 (6%) 0	1 (2%) 0	4 (11%) (1, [3%])
None/no professional help	100 (93%)	15 (94%)	53 (96%)	32 (86%)
Total	108 (100%)	16 (100%)	55 (100%)	37 (100%)

^aMild: local symptoms; moderate: skin and mucosa and/or gastrointestinal symptoms; severe: respiratory and/or cardiovascular symptoms.

the label or had informed the waiter when eating out, even in case of a history of severe reactions. According to patients, total avoidance of PAL is impossible and they suppose that it is mostly used by producers to avoid litigation.⁸ The response of the patients to their accidental reactions was far from adequate. Although the majority took some medication, this was insufficient according to current guidelines,⁹ despite correct advice, most clearly illustrated by the fact that even in case of severe reactions adrenaline was used only by a small number of patients. This is in line with Le et al¹⁰ who reported that more than half of the patients with severe allergic reactions to food did not seek medical help. This emphasizes the need for improved and repeated patient education, regarding risks of accidental reactions, label reading, instructions on when and how to use emergency medication and the importance of communicating with others about their food allergies.

All patients were recruited in a tertiary allergy centre, had multiple food allergies, and 73% had a history of severe reactions. This might explain the relatively high number of accidental reactions. Additionally, due to our recruitment strategy the group consisted of a relatively high number of patients with an allergy to tree nuts, peanut, egg and milk. These allergens are most common in Europe,¹¹ frequently mentioned as cause of accidental reactions² and are often used in food production,¹² which could have led to an overestimation of the frequency of accidental reactions.

This prospective study in adult patients with a wide range of food allergies shows that almost half of them reported accidental allergic reactions. Of those who suffered reactions, accidental allergic

reactions to food occurred on average 2 times per year. Prepackaged foods were the main causal products. Despite a significant number of moderate and severe reactions, only a small number of patients sought medical treatment and/or used the adrenaline autoinjector. This study emphasizes the need for improved patient education, even for patients who have lived with food allergy for years, regarding risks of accidental reactions and the importance of reading labels and communicating with others about their food allergies. Labelling issues, including precautionary allergen labelling, are still a major matter of concern, despite labelling regulations for food industry and food services.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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REFERENCES

- Remington BC, Baumert JL, Blom WM, Houben GF, Taylor SL, Kruizinga AG. Unintended allergens in precautionary labelled and unlabelled products pose significant risks to UK allergic consumers. *Allergy*. 2015;70:813-819.
- Versluis A, Knulst AC, Kruizinga AG, et al. Frequency, severity and causes of unexpected allergic reactions to food: a systematic literature review. *Clin Exp Allergy*. 2015;45:347-367.
- Blom WM, Michelsen-Huisman AD, van Os-Medendorp H, van Duijn G, de Zeeuw-Brouwer ML, Versluis A, Castenmiller JJM, Noteborn HPJM, Kruizinga AG, Knulst AC, Houben GF. Accidental food allergy reactions: products and undeclared ingredients. *J Allergy Clin Immunol*. 2018 Jun 14. pii: S0091-6749(18)30853-4. <https://doi.org/10.1016/j.jaci.2018.04.041>. [Epub ahead of print]
- Anibarro B, Seoane FJ, Mugica MV. Involvement of hidden allergens in food allergic reactions. *J Investig Allergol Clin Immunol*. 2007;17:168-172.
- Kanny G, Moneret-Vautrin DA, Flabbee J, Beaudouin E, Morisset M, Thevenin F. Population study of food allergy in France. *J Allergy Clin Immunol*. 2001;108:133-140.
- Fleischer DM, Perry TT, Atkins D, et al. Allergic reactions to foods in preschool-aged children in a prospective observational food allergy study. *Pediatrics*. 2012;130:e25-32.
- Nguyen-Luu NU, Ben-Shoshan M, Alizadehfar R, et al. Inadvertent exposures in children with peanut allergy. *Pediatr Allergy Immunol*. 2012;23:133-139.
- Padua I, Moreira A, Moreira P, Barros R. Food allergy: practical approach on education and accidental exposure prevention. *Eur Ann Allergy Clin Immunol*. 2016;48:174-181.
- Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy*. 2014;69:1008-1025.
- Le TM, van Hoffen E, Pasmans SG, Bruijnzeel-Koomen CA, Knulst AC. Suboptimal management of acute food-allergic reactions by patients, emergency departments and general practitioners. *Allergy*. 2009;64:1227-1228.
- Nwaru BI, Hickstein L, Panesar SS, et al. Prevalence of common food allergies in Europe: a systematic review and meta-analysis. *Allergy*. 2014;69:992-1007.
- Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol*. 2010;125(2 suppl 2):S116-S125.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Control of Allergic Rhinitis and Asthma Test with 1-week recall: Validation of paper and electronic version

To the Editor,

Both asthma and allergic rhinitis (AR) are high prevalence diseases that frequently occur simultaneously.^{1,2} The Allergic Rhinitis and its Impact on Asthma initiative (ARIA) recognizes the need for a concomitant evaluation and treatment of asthma and AR.^{1,2} The Control of Allergic Rhinitis and Asthma Test (CARAT)³⁻⁵ measures control of both asthma and AR with a 4-week recall period. In a time where the use of mobile devices has grown, a new modality to monitor patients is at our disposal. An electronic CARAT questionnaire allows clinicians to gain more

insight into the period between visits and therefore could be a convenient and reliable alternative to the use of the current paper version of the CARAT. The main purpose of this study was to investigate the psychometric properties of the CARAT with 1-week recall period as paper version (CARATp1) and as electronic version (CARATe1).

This is a diagnostic study with repeated measurements in four consecutive weeks. The study population consisted of consecutive Dutch primary care asthma patients who were referred by their general practitioner to the asthma/COPD service.⁶ Inclusion criteria were