Original Article

Food-Induced Anaphylaxis: Data From the European Anaphylaxis Registry

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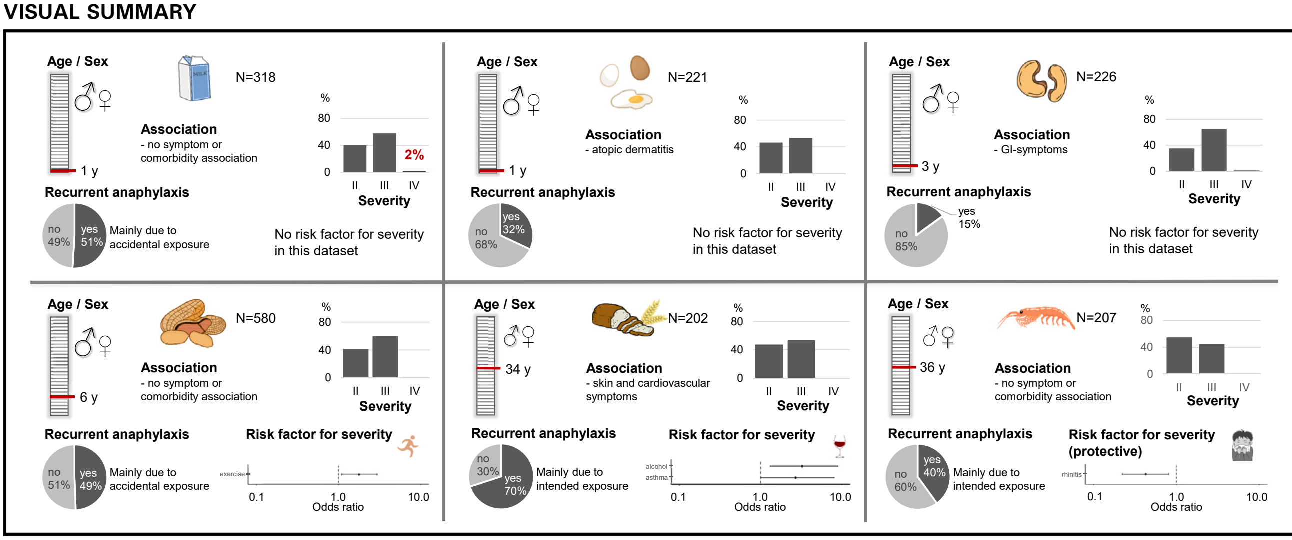
What is already known about this topic? Food is one of the most common elicitors of anaphylaxis. The five major food allergens triggering food-induced anaphylaxis (FIA) in children are peanut, cow's milk, cashew, hen's egg, and hazelnut.

What does this article add to our knowledge? Shellfish and wheat were identified as major triggers of FIA in adults. External factors can alter the outcome of a reaction. Exercise was statistically proven in peanut and alcohol intake in wheat anaphylaxis.

How does this study impact current management guidelines? A broader range of possible food triggers should be considered in adults. The severity of FIA can be enhanced by exercise and alcohol intake.

VISUAL SUMMARY



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Abbreviations used
AD- Atopic dermatitis
FIA- Food-induced anaphylaxis

BACKGROUND: Food is one of the most common elicitors of anaphylaxis, with an increasing incidence over recent years.
OBJECTIVES: To characterize elicitor-specific phenotypes and identify factors enhancing the risk or severity of food-induced anaphylaxis (FIA).
METHODS: We analyzed data from the European Anaphylaxis Registry applying an age- and sex-matched analysis of associations (Cramer's V) for single food triggers and calculated odds ratios (ORs) for severe FIA.
RESULTS: We identified 3,427 cases of confirmed FIA showing an age-dependent elicitor ranking (for children: peanut, cow's milk, cashew, and hen's egg; and for adults: wheat flour, shellfish, hazelnut, and soy). The age- and sex-matched analysis revealed defined symptom patterns for wheat and cashew. Wheat-induced anaphylaxis was more frequently associated with cardiovascular symptoms (75.7%; Cramer's V = 0.28) and cashew-induced anaphylaxis with gastrointestinal symptoms (73.9%; Cramer's V = 0.20). Furthermore, concomitant atopic dermatitis was slightly associated with anaphylaxis to hen's egg (Cramer's V = 0.19) and exercise was strongly associated with anaphylaxis to wheat (Cramer's V = 0.56). Additional factors influencing the severity were alcohol intake in wheat anaphylaxis (OR = 3.23; CI, 1.31-8.83) and exercise in peanut anaphylaxis (OR = 1.78; CI, 1.09-2.95).
CONCLUSIONS: Our data show that FIA is age-dependent. In adults, the range of elicitors inducing FIA is broader. For some

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The Anaphylaxis Registry is supported by the Network for Online Registration of Anaphylaxis NORA e.V. This work is partially supported by funds to M. Worm and S. Dölle-Bierke from the Deutsche Forschungsgemeinschaft (German Research Foundation) as part of the clinical research unit (CRU339): Food Allergy and Tolerance (FOOD@ - 428447634) and by the German Federal Ministry of Education and Research (Grants 01KU2005 and 01EA2107B). U. Jappe has projects on food allergy funded by the German Research Foundation, the Federal Ministry of Education and Science, and the Federal Ministry of Food and Agriculture. I. Maris received grant funding related to this work from the National Children's Research Centre, Dublin, Ireland.

Conflicts of interest: L.C. Lopes de Oliveira has received lecture fees from Aché, Danone, Nestlé, Sanofi, Takeda and Thermo Fisher and consultancy fees from Novartis. R. Treudler has received fees for lectures and congresses as well as study support from, or conducted clinical trials for, AbbVie, ALK-Abello, CSL-Behring, Lilly, Novartis, Pfizer, Sanofi-Genzyme, and Takeda. M. Fernandez-Rivas reports grants from Instituto de Salud Carlos III, the Spanish government, grants and personal fees from Aimmune Therapeutics, personal fees from Diater, Ediciones Mayo, GA2LEN, HAL Allergy, EPG Health, Medscape, Novartis, DBV, Reacta Healthcare, and SPRIM, outside the submitted work. K. Nemat reports personal fees from Nutricia/Danone (lecture fees) and Aimmune Therapeutics (consulting fees), outside the submitted work. C. Pföhler received honoraria (speaker honoraria or honoraria as a consultant) and travel support from Novartis, BMS, MSD, Merck Serono, MSD, Celgene, AbbVie, Sunpharma, Pierre Fabre, UCB, Nutricia Milupa, and LEO. F. Ruëff has received personal fees for lectures and/or advisory boards from ALK-Abelló Arzneimittel GmbH, Firma Allergopharma GmbH & Co. KG, Blueprint medicines (Germany) GmbH, Boehringer Ingelheim, Mylan Germany Team, Novartis, Thermo Fisher Diagnostics Austria GmbH, and UCB Pharma GmbH, outside the submitted work. D. Sabouraud-Leclerc has received personal fees for lectures and/or advisory boards from Nutricia, ALK, Stallergènes, Thermo Fisher, Novartis, and Aimmune, outside the submitted work. K. Hartmann has received research funding from Thermo Fisher and consultancy or lecture fees from Allergopharma, ALK-Abello, Blueprint, Deciphera, Leo Pharma, Menarini, Novartis, Pfizer, Takeda, and Thermo Fisher. A. Köhli received travel reimbursement from Allergopharma, and personal fees (advisory board) and speaker honoraria from Menarini outside the submitted work. N.G. Papadopoulos has received speaker/advisor fees from Abbott, Abbvie, ALK, Asit Biotech, AstraZeneca, Biomay, Boehringer Ingelheim, GSK, HAL, Faes Farma, Medscape, Menarini, MSD, Novartis, Nutricia, OM Pharma, Regeneron, Sanofi, Takeda, and Viatris. N. Wagner is or recently was a speaker and/or advisor for and/or has received research funding or is/was involved in clinical trials of/from ALK-Abelló, Novartis Pharma GmbH, Allergopharma GmbH &Co KG, Sanofi-Aventis Deutschland GmbH, Takeda, Blueprint, and Abbvie GmbH & Co KG. M. Worm declares the receipt of honoraria or consultation fees by Novartis Pharma GmbH, Sanofi-Aventis Deutschland GmbH, DBV Technologies S.A, Aimmune Therapeutics UK Limited, Regeneron Pharmaceuticals, Inc, Leo Pharma GmbH, Boehringer Ingelheim Pharma GmbH & Co KG, AstraZeneca GmbH, Worg Pharmaceutics (Hangzhou) Co, Ltd, ALK-Abelló Arzneimittel GmbH, Lilly Deutschland GmbH, Kymab Limited, Phadia GmbH, Amgen GmbH, and Viatris, outside the submitted work. The rest of the authors declare that they have no relevant conflicts of interest.
Received for publication September 14, 2022; revised February 22, 2023; accepted for publication March 12, 2023.
Available online March 27, 2023.
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2213-2198
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https://doi.org/10.1016/j.jaip.2023.03.026

elicitors, the severity of FIA seems to be related to the elicitor. These data require confirmation in future studies considering a clear differentiation between augmentation and risk factors in FIA. **© 2023 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).** **(J Allergy Clin Immunol Pract 2023;11:2069-79)**

Key words: *Food anaphylaxis; Peanut; Cashew; Hazelnut; Phenotype; Risk factors; Shellfish; Wheat*

INTRODUCTION

Besides insect venom and drugs, food is one of the most common elicitors of anaphylaxis.[1] The estimated lifetime prevalence of food-induced anaphylaxis (FIA) is 0.3%.[2] Its incidence has increased with the higher prevalence of food allergy in recent years.[3-5] Recent data from the United Kingdom showed an increase in the incidence of FIA based on the increased hospitalization rate in children aged 0 to 14 years.[6] These findings are in accordance with data from the United States and Australia and underpin the important role of food allergy in pediatric anaphylaxis.[7]

Peanut is the key trigger of FIA in children in the United States, but also many countries in Europe.[8,9] However, besides peanut, other food allergens such as tree nuts, hen's egg, cow's milk, and shellfish are common causes of severe but also fatal anaphylaxis.[7] From a clinical perspective, severe and fatal outcomes of FIA remain unpredictable and FIA irrespective of its severity affects health-related quality of life.[10] Moreover, FIA may present with heterogeneous clinical outcomes related to the allergenic sources and their physicochemical properties.

Food allergens as such are of animal or plant origin. The latter includes a wide variety of proteins (seed storage proteins, lipid transfer proteins, and pathogenesis-related proteins) or may even be carbohydrates such as galactose-1,3-alpha-galactose.[11]

Previous data from the European Anaphylaxis Registry suggested that FIA is determined by the age and type of the eliciting food.[8,12] In the current study, we investigated elicitor-specific phenotypes and identified factors enhancing the risk for or severity of FIA based on a large dataset from the European Anaphylaxis Registry.

METHODS

Data

The European Anaphylaxis Registry is a database that collects data on real-life anaphylaxis from moderate to severe anaphylactic reactions by means of a standardized online questionnaire.[13] More than 100 specialized tertiary allergy centers report anaphylaxis cases from 10 European countries (Germany, Switzerland, France, Italy, Austria, Poland, Spain, Ireland, Greece, and Bulgaria) and Brazil (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). The study centers enter severe anaphylaxis cases after obtaining written informed consent from patients. Deidentified data from patients who had experienced anaphylaxis within the past 12 months before presenting to the participating allergy centers were captured by trained health care professionals on-site through the Web interface. Data were submitted after completion of the diagnostic workup. The diagnostic certainty of the triggering food allergen sources was documented at the level of confirmed or highly suspected, based on the local allergy specialist's individual judgment.

The questionnaire includes data regarding the patient's details, including age at the time of the anaphylactic reaction, elicitor, symptoms, factors accompanying the reaction, diagnostic workup (semiquantitative: done with a positive result, done with a negative result, or not done), treatment, and prevention measures.[1,14]

The study was approved by the ethics committee at Charité—Universitätsmedizin Berlin, Germany (EA1/079/06). It was accredited by the local ethics committees in the participating centers and is registered on ClinicalTrials.gov (Identifier: NCT05210543).

Sample extraction

The registry was launched in 2007 in German-speaking countries and expanded to other countries in 2011. Figure 1, *A* shows the registered cases over time. In total, 14,474 cases were registered with approximately 1,300 cases/y since 2011.

For this analysis, 13,323 reported anaphylactic cases included between January 2007 and October 2020 met the modified criteria of the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network.[15] Finally, 4,468 FIA cases (Figure 1, *B*) were identified (34%).

Food-induced anaphylaxis was reported in children (n = 2,540; 57%; mean age, 6 ± 5 years) and adults (n = 1,928; 43%; mean age, 41 ± 15 years) (Figure 1, *C*).

Statistical analysis

For statistical analysis, we used IBM SPSS Statistics (version 27, Chicago, Ill) and R (version 4.1.2, R Core Team, Vienna, Austria). Descriptive statistics were used to describe demographic data and the frequencies of atopic history, symptoms, severity of reaction, recurrence, timing of reactions, and amount of food ingested between elicitor groups. For each food of interest, the reference food group included cases induced by food, except the food of interest. For the analysis of associations among variables, we used data matched to sex and age. Propensity score matching was carried out using the MatchIt package for R.[16] Then, Cramer's V was analyzed using the r-companion package.[17] The level of association was defined as weak (0.10 to 0.29), moderate (0.30 to 0.49), or strong association (0.50 or greater). The direction of the association was analyzed based on a comparison of the frequency distribution of the variables in both groups (food of interest vs reference food group). Nonbinary variables were transformed to binary categories (eg, severity according to Ring and Messmer).[18] They were classified as grades II, III, and IV and combined into two groups: grades II and III+IV.

We calculated odds ratios (ORs) for severe anaphylaxis because augmentation and/or a risk factor was present and evaluated the differences in ORs among all elicitors.

RESULTS

Age-dependent elicitor profile of FIA

Among 4,468 reported FIA cases, 77% (n = 3,427) were confirmed by case history and diagnostic workup performed in the local allergy center (Figure 1, *B*; see Table E2 in this article's Online Repository at www.jaci-inpractice.org). Among confirmed FIA cases, the most common elicitors are shown in Figure 2 for children and adults. In children, the most frequent elicitors were peanut, cow's milk, cashew, and hen's egg; in adults, the most frequent elicitors were wheat flour, shellfish, hazelnut, and soy. Age distribution among the single food triggers are shown in Figure E1 (in this article's Online Repository at www.jaci-inpractice.org).

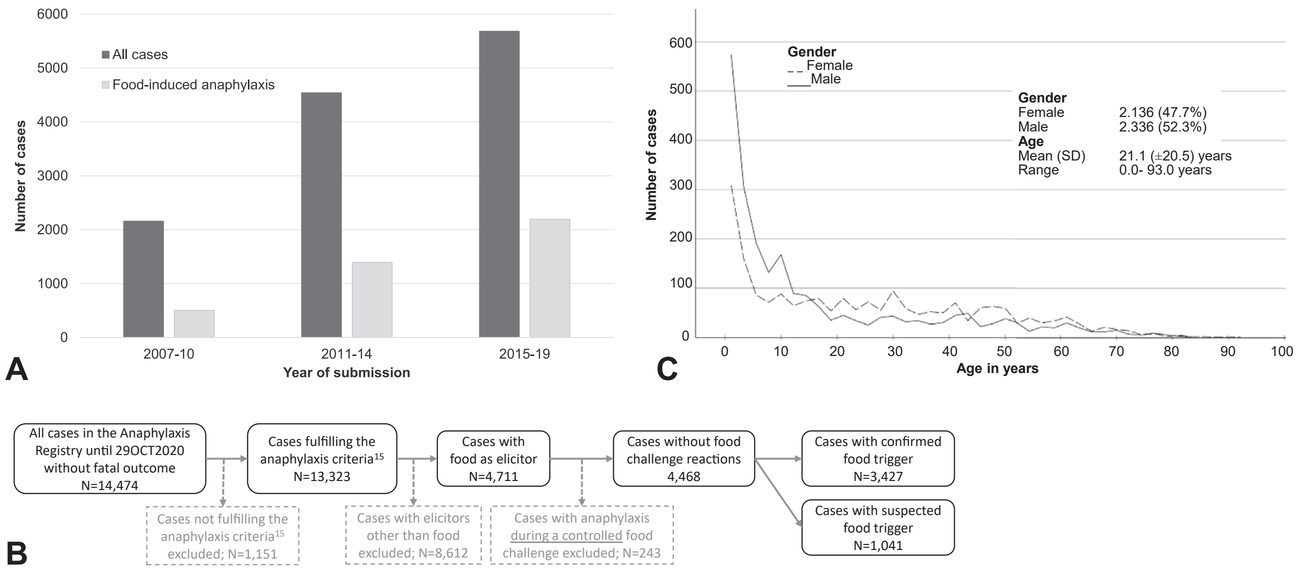

FIGURE 1. (**A**) Registered cases over time shown until December 2019. Date of data extraction was October 2020. (**B**) Flow diagram of database adjustment. (**C**) Age distribution of patients with food-triggered reactions, sorted by sex. The sex distribution was age-dependent. Males were affected in 63% of children and in 38% of adults.

Shrimp was the main food trigger in the shellfish subgroup. It was the elicitor in 152 of 207 cases (74%). Almond (45 of 196 cases), pistachio (42 of 196 cases), pine nut (37 of 196 cases), and Brazil nut (31 of 196 cases) were the main food allergen sources in the subgroup of other tree nuts. The group of seeds consisted of sesame as the leading food allergenic source (67 of 110 cases; 61%) followed by sunflower (20 of 110 cases; 18%) and pumpkin seeds (13 of 141 cases; 12%). Codfish was the most common trigger among fish-induced anaphylaxis (45 of 84 cases; 54%), followed by salmon (14 of 84 cases; 17%). In the subgroup of meat and poultry, red meat such as beef and pork accounted for 59% (47 of 79 cases).

Symptoms of FIA

Next, we analyzed whether defined food allergen sources may be associated with a pattern of organ system involvement and/or anaphylaxis severity (see Table E3 in this article's Online Repository at www.jaci-inpractice.org). No associations with a specific food, or only weak ones symptoms, were detected using an age- and sex-matched Cramer's V analysis (see Table E4 in this article's Online Repository at www.jaci-inpractice.org). We identified that cashew-induced anaphylaxis was more frequently associated with gastrointestinal symptoms (73.9%; weak association with Cramer's V = 0.20). Furthermore, patients with wheat-induced anaphylaxis presented more frequently with cardiovascular symptoms (75.7%; weak association with Cramer's V = 0.28) and less frequently with respiratory symptoms (54.5%; weak association with Cramer's V = 0.22) compared with the frequency of symptoms in an age- and sex-matched reference food group. We also detected that meat or poultry and hen's egg induced respiratory symptoms less frequently than did other foods (55.7% and 69.2%; weak association with Cramer's V = 0.29 and 0.13). The lowest percentage of gastrointestinal symptoms was observed for celery (31.2%; weak association with Cramer's V = 0.17).

Fifty percent of the total FIA cohort experienced grade III reactions and only 0.5% (n = 17) had grade IV reactions. Most of the grade IV reactions were registered for cow's milk (six of 318; 1.9%) and hazelnut (three of 237; 1.3%). Cashew-induced anaphylaxis was associated with the highest proportion of Ring and Messmer grade III cases, at 64.6% (weak association with Cramer's V = 0.12). By contrast, wheat and walnut displayed a weak association (Cramer's V = 0.12 and 0.11) with more severe reactions; however, no grade IV reaction had been registered for both food triggers. Weak associations with the severity of a reaction were determined for soy (Cramer's V = 0.11) and celery (Cramer's V = 0.17). These elicitors predominantly induced milder reactions (soy: grade II, 65.7%; grade III-IV, 34.3%; celery: grade II, 69.0%, grade III-IV, 31.0%).

Considering single symptoms (see Table E5 in this article's Online Repository at www.jaci-inpractice.org), moderate associations were found between cow's milk, cashew, other tree nuts, and vomiting. Patients with wheat and meat or poultry anaphylaxis more frequently experienced urticaria and less often angioedema (Table E5). In addition, wheat anaphylaxis was slightly associated with loss of consciousness (Cramer's V = 0.25).

Atopic comorbidities in patients with FIA

Because it was previously described[19] that certain food allergies occur more frequently in patients with atopic comorbidities, we analyzed such possible associations in more detail. In general, atopic comorbidities were present in different frequencies among the specific elicitors (Table E5).

No associations, or weak ones, were detected for asthma as a comorbidity when the food allergen of interest was compared with the food reference group (Table E4). The highest (although weak) association was detected in patients with meat- or poultry-induced anaphylaxis, who experienced it less often from asthma (Cramer's V = 0.23). We observed the presence of concomitant atopic dermatitis (AD) more frequently in patients with hen's egg

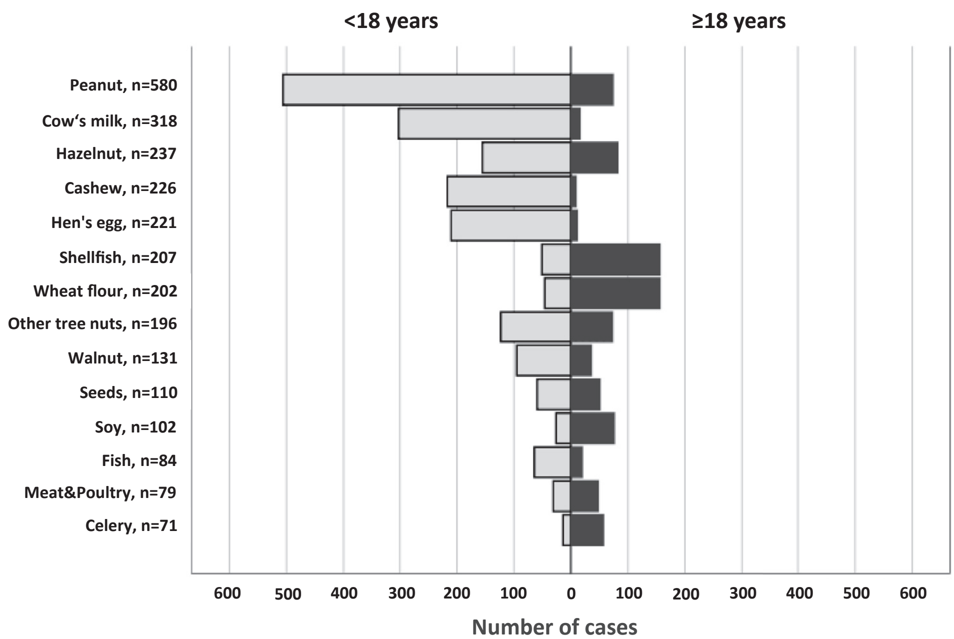

FIGURE 2. Most common elicitors of confirmed food-induced anaphylaxis by age (2,764 of 3,427 cases with confirmed food trigger).

anaphylaxis (weak association with Cramer's V 0.19), whereas patients with shellfish anaphylaxis presented less frequently with AD (weak association with Cramer's V = 0.17) (Table E4).

Patients with soy- or celery-induced anaphylaxis demonstrated associations with concomitant allergic rhinitis (moderate and weak association with Cramer's V = 0.30 and 0.24).

Risk and augmentation factors

Certain factors are known to affect the severity of an anaphylactic reaction. We identified asthma in wheat-induced anaphylaxis as a significant risk factor of severe anaphylaxis (OR = 2.68; CI, 1.01-8.01) (Figure 3). In contrast, concomitant allergic rhinitis was associated with less severe reactions in shellfish-induced (OR = 0.43; CI, 0.22-0.81) and soy-induced anaphylaxis (OR = 0.31; CI, 0.08-1.09) (data not shown). Alcohol intake, when taken together and/or within 1 hour before or after the food allergen exposure, in wheat anaphylaxis (OR = 3.23; CI, 1.31-8.83) and exercise in peanut anaphylaxis (OR = 1.78; CI, 1.09-2.95) were significant risk factors for severe reactions. Concomitant asthma had an opposite impact in fish-induced anaphylaxis (OR = 0.32; CI, 0.09-1.03) and exercise in meat- or poultry-induced anaphylaxis (OR = 0.18; CI, 0.02-0.93) (data not shown). Although the concomitant infection during anaphylaxis tended to increase the risk for more severe reactions (OR = 2.91; CI, 0.7-16.1), this observation was not statistically significant (P = .118) because of the low number of patients with concomitant infections (n = 16). We also analyzed data on menses and certain drugs as augmentation factors, but these did not reveal significant findings.

Frequency of recurrent reactions depends on food trigger

On average, 41% of reactions were recurrent reactions to the same food allergen source, but the frequency rate differed largely among food triggers (Table I). Our findings indicate a high rate

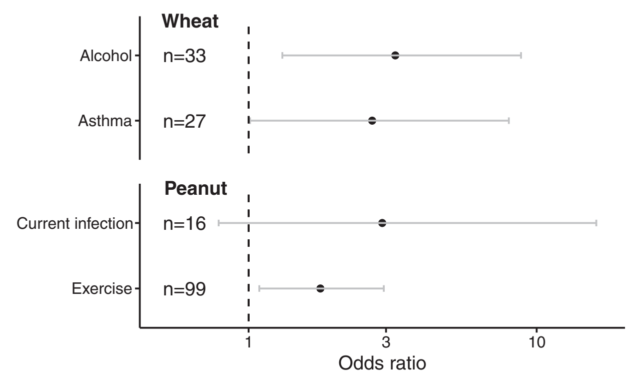

FIGURE 3. Risk and augmentation factors identified in wheat- and peanut-induced anaphylaxis.

of recurrent reactions for wheat, meat or poultry, and fish anaphylaxis. In contrast, soy- and cashew-induced anaphylaxis had the lowest rates of recurrent anaphylaxis.

Approximately 60% of patients with a recurrent reaction were aware of the food allergy at the time of the reported reaction. The remaining 40% were unaware of the allergy, especially patients with meat or poultry, wheat, and celery anaphylaxis. In contrast, the recurrent anaphylaxis reactions in patients with cow's milk, peanut, hen's egg, walnut, and hazelnut anaphylaxis were mainly triggered by accidental exposure (see Table E6 in this article's Online Repository at www.jaci-inpractice.org).

Amount of food eliciting the reaction

The eliciting dose is a relevant parameter in food allergy and an important measure for regulatory issues (eg, food allergen labeling). We considered the eliciting dose in our questionnaire. However, for practical reasons, we estimated the amount of food ingested using kitchen measurements (eg, teaspoon, tablespoon).

TABLE I. Recurrence of anaphylaxis: most common food elicitors sorted by frequency of recurrent reaction to same food allergen source

		Recurrent reaction to the same food				
Recurrency	Elicitor	n	%	Total n*	Cramer's V	CI
High rate	Wheat flour	136	70.1	194	0.36	0.26-0.45
	Meat and poultry	52	69.3	75	0.42	0.27-0.57
	Fish	53	65.4	81	0.35	0.21-0.48
Median rate	Cow's milk	158	51.3	308	0.32	0.24-0.39
	Peanut	267	49.4	540	0.06	0.01-0.12
	Hazelnut	98	43.8	224	0.07	0.01-0.16
	Shellfish	81	39.9	203	0.03	0.00-0.14
	Celery	25	37.9	66	0.01	0.00-0.20
	Seeds	35	34.3	102	0.01	0.00-0.16
	Hen's egg	70	32.4	216	0.04	0.00-0.14
	Other tree nuts	56	30.3	185	0.04	0.00-0.15
	Walnut	34	28.8	118	0.03	0.00-0.17
Low rate	Soy	17	17.5	97	0.23	0.09-0.37
	Cashew	32	14.7	218	0.19	0.10-0.28

The level of association is weak (>0.1 to 0.29), moderate (0.3-0.49), or strong (≥0.5).
*Only cases with valid data on recurrence were included (total n = 3,241).

Figure 4 shows the amount of food ingested that caused the anaphylactic reaction among the most common food elicitors. In detail, cashew (74.0%), peanut (67.6%), and walnut (65.7%) elicited reactions to 1 teaspoon or less (see Table E7 in this article's Online Repository at www.jaci-inpractice.org). For peanut, 1 teaspoon corresponds to four to five peanuts, which is approximately equivalent to 1 g peanut protein. The amount ranged in most cases from 1 teaspoon to 1 tablespoon (62.0%) for hen's egg, and from 1 tablespoon to half a cup for cow's milk. In contrast, other food allergen sources such as wheat, shellfish, meat or poultry, soy, and celery elicited reactions after the consumption of a full meal or a regular portion size of the corresponding food (one plate) in most cases.

Location of a reaction and type of food product

Most cases of FIA occurred in the country of residence (95%) and predominantly at home (49%), regardless from the food elicitor (see Table E8 in this article's Online Repository at www.jaci-inpractice.org). Outside home (eg, restaurant, cafeteria, takeaway, hotel, friend's home) (17%) and in school or kindergarten (6%) were less frequent locations of reactions.

Overall, prepackaged products were consumed in 45% of food-induced anaphylactic reactions and loose (non-prepackaged) food in 56% (Table II). For hazelnut, cashew, peanut, cow's milk, and soy, the most frequently consumed food sources were prepackaged. Loose products were mainly taken up when the registered reaction was a recurrent event to a previously known food allergen source (67.1% loose vs 34.2% prepackaged products; data not shown).

Loose products were bought primarily in a supermarket (23%) or catered (catering, 11%; and buffet, 12%). For prepackaged products, the food elicitor was listed as an ingredient in most severe allergic reactions (75%; 283 of 376 cases with available data).

Other elicitors of interest

Besides the main elicitors of FIA, 663 cases were triggered by other food allergen sources (Figure 5). The most important food group was fruit, which comprised 244 cases (see Table E9 in this article's Online Repository at www.jaci-inpractice.org).

DISCUSSION

We report on 3,427 cases of FIA registered by specialized allergy centers in Europe and Brazil. The most common reported food elicitors were peanut, cow's milk, hazelnut, cashew, and hen's egg in children, and shellfish and wheat in adults. Recently, a systematic review assessed the most common triggers for food anaphylaxis.[7] Despite significant regional differences, the authors found that peanut and tree nuts, as well as cow's milk and shellfish, are the most common food triggers that cause anaphylaxis, based on emergency department admission data, which is consistent with our data reported from allergy centers. Furthermore, cow's milk and shellfish appear to induce a high percentage of anaphylaxis when the reported prevalence of food allergy in Europe is considered.[7] In contrast to our data, wheat was a less common cause of anaphylaxis in Europe, perhaps because of the challenging and delayed diagnosis of wheat anaphylaxis.[12]

In children, 65% of FIA was triggered by five food allergen sources (peanut, cow's milk, hen's egg, cashew, and hazelnut). On the contrary, the spectrum of frequent food elicitors was broader in adults. In total, we identified up to 11 food triggers covering 65% of FIA in adults (wheat, shellfish, hazelnut, soy, peanut, other tree nuts, celery, seeds, meat and poultry, walnut, and fish).

Because of the large number of cases in this analysis, but also of participating centers and regions, we were able to identify even rare causes of FIA in this cohort, such as fenugreek (n = 4), broccoli (n = 1), the coloring agent E120 cochineal (n = 2), and prepackaged plant pollen (n = 5).

Numerous studies revealed that the prevalence of atopic diseases shows sex-related differences. Food allergy, but also AD and allergic asthma, are known to affect male infants and younger children more frequently, which reverses after puberty.[6,20-22] Sex hormones and their impact on sensitization and elicitation have been suggested as possible causes for these observations, although the exact mechanisms are still not known. Food-induced

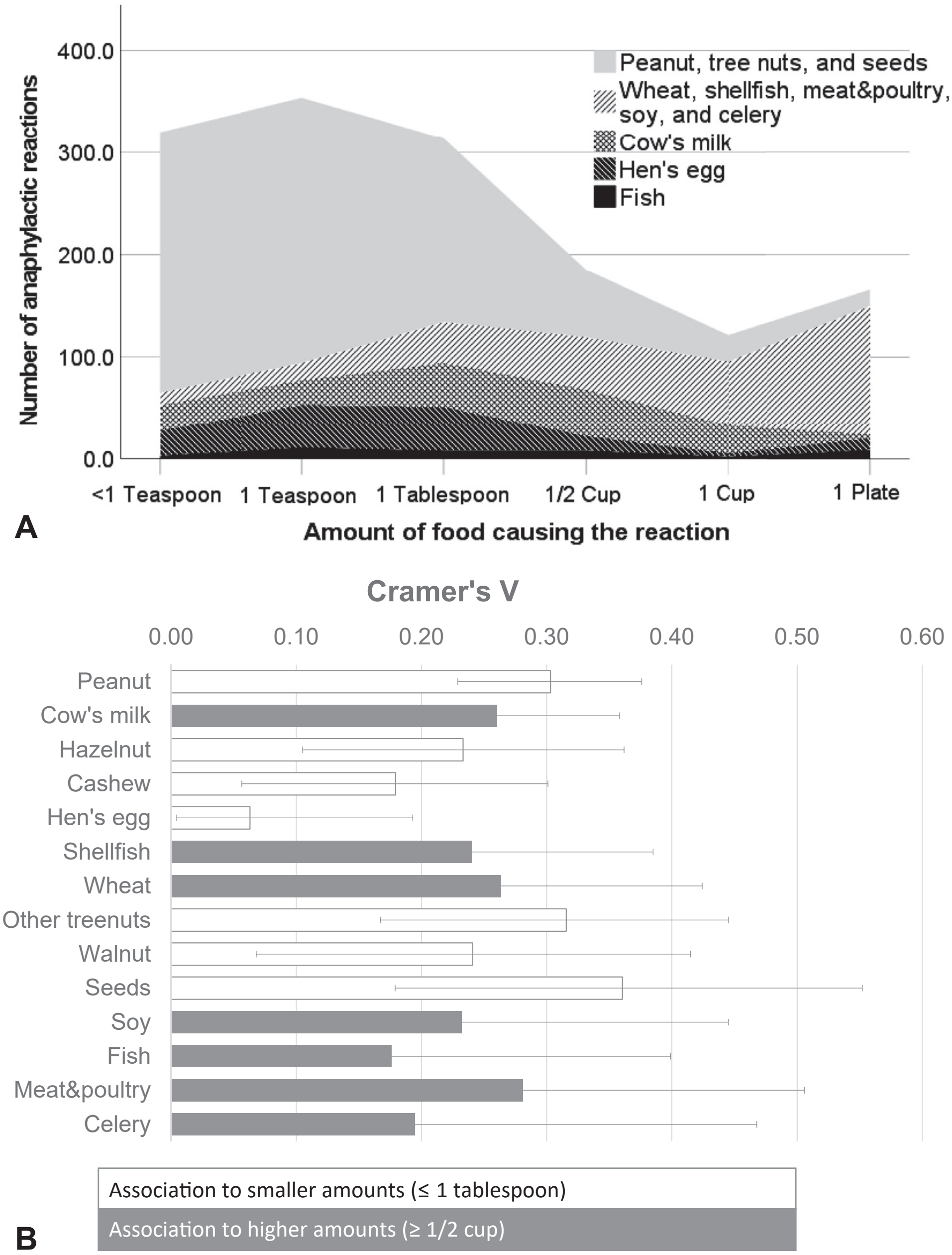

FIGURE 4. Ingested amount of food containing the food allergen and causing the reaction. (**A**) Foods grouped by similar amounts causing the reaction. (**B**) Association of food of interest with amount of food compared with reference food group. Black and white bars indicate the direction of association.

anaphylaxis registered to the European Anaphylaxis Registry covered all age groups, with an overall balanced sex distribution (Figure 1, *C*). When children and adults are considered separately, males predominate among children and females among adults, unless the triggering food is wheat or meat/poultry. Here, male patients are more often affected, although the average age is greater than 18 years.

Although the European Anaphylaxis Registry is targeted to collect information on severe allergic reactions, only 0.5% had grade IV reactions according to Ring and Messmer and approximately 6% of cases were treated in an intensive care unit. Most grade IV reactions were registered for cow's milk (six of 17 grade IV reactions). Cow's milk allergy is frequently outgrown in early childhood,[23] but recent data indicate that cow's milk is a major cause of severe and also fatal anaphylaxis.[6,7]

In addition to our group, others have reported that anaphylaxis differs in children and adults regarding the symptom profile. Upper and lower respiratory symptoms predominate in the pediatric age group, whereas cardiovascular involvement is more often reported in adults.[14,24] When performing an age- and sex-matched analysis, we exclude two important host-dependent factors. By doing this, we try to determine whether elicitor-

TABLE II. Food product packaging among food elicitors

	Not prepackaged		Prepackaged	
Elicitor	n	%	n	%
Peanut	153	36.7	267	64.0
Cow's milk	82	34.6	156	65.8
Hazelnut	72	43.6	95	57.6
Cashew	61	39.6	93	60.4
Hen's egg	131	79.4	35	21.2
Shellfish	83	90.2	10	10.9
Wheat flour	71	64.5	41	37.3
Other tree nuts	60	60.0	40	40.0
Walnut	61	77.2	19	24.1
Seed	44	57.1	33	42.9
Soy	21	33.9	41	66.1
Fish	42	89.4	5	10.6
Meat and poultry	25	89.3	3	10.7
Celery	25	75.8	9	27.3

Only cases with valid data on recurrence were included (total n = 3,241).

specific risk factors exist. Using this approach, we found a weak association of wheat-induced anaphylaxis with cardiovascular but not respiratory symptoms, as previously reported.[12] In addition, cashew-induced anaphylaxis was associated with gastrointestinal symptoms, especially vomiting. Besides, no other major associations between the food allergen and symptoms were identified. These findings may point to the observation from Slapnicar et al[25] reporting that patients experience an individual stereotypic anaphylactic symptom pattern irrespective of the cause of anaphylaxis.

Baseggio Conrado et al[7] reported that soy was not a major cause of FIA in any country according to prevalence data for soy allergy. However, our data showed that soy, but also celery, are common elicitors of FIA. Although soy and celery were associated with less severe anaphylactic reactions, one-third of patients experienced grade III reactions and one grade IV reaction was also elicited by soy. Most cases of soy- and celery-induced anaphylaxis were registered in Germany, France, and Switzerland (soy: 89% and celery: 93%; data not shown). Almost all subjects had allergic rhinitis as an atopic co-disease (soy: 99%, Cramer's V = 0.30; and celery: 97%, Cramer's V = 0.24). Therefore, we suspect that for both food allergen sources, the birch pollen-related pathogenesis-related-10 protein may be the responsible elicitor of these anaphylactic reactions. We cannot underpin this speculation with data from component-resolved diagnosis because this is not assessed in detail in the European Anaphylaxis Registry. However, a previous study using component-resolved diagnosis in anaphylactic patients registered in Berlin (Charité—Universitätsmedizin Berlin, Dermatology) revealed a high sensitization rate toward pathogenesis-related-10 protein in this local cohort.[26] Furthermore, other reports, including a retrospective multicenter study,[10,27,28] support the view that patients with pollen-associated food allergy should not generally be considered at no or low risk for severe outcomes.

In this analysis, concomitant asthma was frequently reported in patients whose reactions were elicited by peanut (43.1% compared with 35.6% in the food reference group) (Table E3). This observation is consistent with our previously published data comparing peanut-induced anaphylaxis with other FIA cases in children.[8] It is known from the literature that asthma is common in FIA patients in general.[24,29] However, our data show that asthma is not specifically associated with peanut-induced anaphylaxis when host-dependent factors such as age and sex are excluded. In addition, an asthma diagnosis *per se* does not predict a more severe reaction in peanut-induced anaphylaxis.[30,31] However, concomitant asthma has been discussed as a potential risk factor for severe anaphylaxis by different authors.[31-33] By contrast, other studies suggest that anaphylaxis with an airway impairment is related to poor control of asthma treatment, rather than identifying asthma itself as a strong independent risk factor.[10] Previous data from the European Anaphylaxis Registry showed an opposite association between the diagnosis of asthma and the severity of anaphylaxis.[34] To understand the association between asthma and anaphylaxis better, improved data quality is required considering not only the diagnosis, but also the current treatment and asthma control.

The finding that AD (as a comorbidity) was associated with anaphylaxis to hen's egg was weak in our analysis but is in line with a recent report from Grimshaw et al.[35] However, we did not find evidence that the presence of AD influences the severity of a reaction.

The important role of exercise in eliciting and/or promoting the outcome of food-dependent anaphylaxis is well-known and was reported by several groups.[31,36-39] In addition to our previous data,[12] in the current analysis we determined a high association (Cramer's V = 0.56) between exercise and wheat. In a previous study, we identified the intensity of exercise as an augmenting factor for more severe reactions in a food anaphylaxis restricted model.[34] However, we could not prove that exercise was an augmenting factor for experiencing a more severe reaction in wheat- and walnut-allergic patients. Rather, we observed that exercise, when present, triggered more severe reactions in peanut anaphylaxis. This finding is partially supported by data from Dua et al.[40] Those authors demonstrated in an oral food challenge study that exercise was associated with an overall increase in severity, although this was not significant. In particular, an increased severity of respiratory symptoms was observed compared with the no-intervention challenge.

However, it has not yet been completely determined how physical activity promotes an anaphylactic reaction. Suspected mechanisms include increased gastrointestinal permeability,[37] enhancement to mast cell activation by increasing plasma osmolarity, activating adenosine and eicosanoid,[41] alterations in tissue transglutaminase enzyme, and redistribution of blood flow away from the visceral organs to skeletal muscle.[42]

A novel finding of this analysis is that alcohol intake in proximity to allergen exposure increased the risk for a severe reaction in wheat anaphylaxis. The role of alcohol as an augmenting factor is ambiguous in the literature,[43,44] but it might have a role as an add-on factor in some patients.[45,46] Because 89% of wheat-induced anaphylaxis occurred in combination with exercise,[12] this finding supports the view that multiple factors may be necessary for the onset and outcome of a reaction.[43]

Repetitive anaphylactic reactions may occur despite allergen avoidance. Food-induced anaphylaxis has the highest recurrence rates compared with anaphylaxis induced by insect venom and drugs.[1] Moreover, the frequency of recurrence differed among various foods. An anaphylactic reaction as a recurrent event was observed in greater than 65% of patients for wheat, meat or

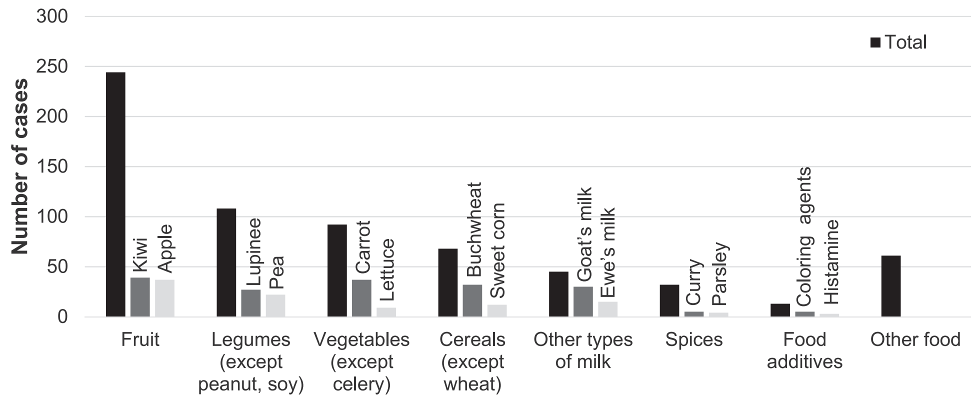

FIGURE 5. Other elicitors of interest. Single food allergen sources are listed in Table E9. The group of other food was composed of food items that did not fit one of the main food categories (fruit, vegetables, tree nuts, seeds, legumes, cereals, animal products, or additives). These included food items such as honey (n = 12) and prepackaged plant pollen as dietary supplements (n = 5).

poultry, and fish. For wheat and meat or poultry, the allergy to the specific food was known in only 29.4% or 26.9%. This suggests that such patients probably had previous reactions to similar food allergen sources without knowing the elicitor. Cow's milk- and peanut-induced anaphylaxis had a frequency of recurrence of about 50%, which is in line with previous studies.[10,47] However, those patients are aware of the allergy to a higher extent (75.3% or 73.0%). Overall, the risk for experiencing anaphylaxis owing to accidental exposure is high in food allergy.[48]

STRENGTHS AND LIMITATIONS

Strengths of the registry include the standardized manner of data acquisition by experienced health care professionals (quality) and the huge number of incidents covered. Within this large cohort, 3,427 real-world FIA cases were analyzed. The registry includes data obtained from specialized allergy centers in several countries, mainly in Europe. However, this does not provide representativeness for a specific country and/or population group. In addition, data on sensitization profiles are missing. The major strength of data analysis is that it is based on a large number of real-life anaphylaxis cases. Although the total number of FIA cases was high, the number of single elicitor groups was limited. In most cases, the association levels are weak and their relevance should not be overestimated.

CONCLUSIONS

Our data confirm peanut, cow's milk, hazelnut, cashew, hen's egg, shellfish, and wheat as the most frequent triggers of FIA in Europe and identifies wheat and shellfish as common elicitors of anaphylaxis in adulthood. The range of food-induced triggers is age-dependent and is generally broader in adults. Certain food allergens can be assigned to clinical phenotypes strongly depending on age and sex. Excluding these host-dependent aspects, specific factors were identified for single food sources such as wheat and peanut.

Acknowledgments

The authors thank all patients and parents for their support in providing data on the occurrence of anaphylaxis to the European Anaphylaxis Registry. We thank the study personnel for patient counseling and data entry: J. Grünhagen, M. Wittenberg (Berlin, Germany), K. Beyer (Berlin, Germany), A. Möser (Jena, Germany), Ugne Olendraite (Munich, Germany), B. Wedi (Hanover, Germany), H. Dickel (Bochum, Germany), A. Bauer (Dresden, Germany), E. Rietschel (Cologne, Germany), S. Aurich (Leipzig, Germany), N. Reider (Innsbruck, Austria), W. Aberer (Graz, Austria), K. Scherer, M. Mueller, S. Schmidlin, and M. Rathgeb (Basel, Switzerland), B. Bogatu (Zurich, Switzerland), F. Riffelmann (Schmallenberg, Germany), B. Kreft (Halle, Germany), T. Kinaciyan (Vienna, Austria), J. Witte (Hamburg, Germany), U. Rabe (Treuenbritzen, Germany), P. Schmid-Grendelmeier (Zurich, Switzerland), S. Nestoris (Lippe-Lemgo, Germany), T. Hawranek and R. Lang (Salzburg, Austria), S. Gernert (Bonn, Deutschland), G. Hansen (Hanover, Germany), C. Bourg and A.-C. Wagner (Homburg, Germany), Z. Szepfalusi (Vienna, Austria), P. Eng (Aarau and Lucerne, Switzerland), T. Reese (Rheine, Germany), M. Polz (Rüsselsheim, Germany), G. Stichtenoth (Lübeck, Germany), S. Thies (Schwedt, Germany), I. Yildiz (Neumünster, Germany), M. Gerstlauer (Augsburg, Germany), A. Nordwig (Dresden, Germany), P. Utz (Wangen im Allgäu, Germany), J. Klinge (Fürth, Germany), J. Fischer (previously Tübingen, Germany), A. Henschel (Berlin, Germany), S. Plank-Habibi (Alzenau, Germany), B. Schilling (Passau, Germany), A. Kleinheinz and A. Brückner (Buxtehude, Germany), K. Schäkel (Heidelberg, Germany), P.Xepapadaki and M.Kritikou (Athens, Greece), M. Kowalski (Lodz, Poland), K. Solarewicz-Madajek (Wroclaw, Poland), C. Körner-Rettberg (Bochum, Germany), J.M. Renaudin, S. Tscheiller, and all members of the Allergy Vigilance Network (France); C. Kemen (Hamburg, Germany), F. Prenzel (Leipzig, Germany), C. Ebner (Vienna, Austria), J. Seidenberg and H. Köster (Oldenburg, Germany), V. Cardona (Barcelona, Spain), S. Hämmerling (Heidelberg, Germany), N. Cabañes Higuero (Toledo, Spain), A. Vega Castro (Guadalajara, Spain), I. Poziomkowska-Gęsicka (Szczecin, Poland), S. Büsing (Osnabrück, Germany), U. Staden (Berlin, Germany), C. Virchow (Rostock, Germany), G. Christoff (Sofia, Bulgaria), A. Gülsen (Borstel, Germany), S. Müller (Freiburg, Germany), H. Straube (Darmstadt, Germany), C. Hannapp (Dresden, Germany), F. Knöpfel (Norderney, Germany), J. Hourihane (previously Cork, Ireland), B. Rogala (Silesia, Poland), T. de Vincente (Madrid,

Spain), A. Muraro (Padua, Italy), T. Buck and J. Büsselberg (Hanover-Misburg, Germany), N. Zimmermann (Potsdam, Germany), D. Hernandez (Valencia, Spain), P. Minale (Genua, Italy), S. Altrichter (Linz, Austria), A. Reissig (Gera, Germany), F. Horak (Vienna, Austria), A. Arens, R. Drägerdt, and S. Hoffmann (Hanover, Germany), R. Asero (Milan, Italy), F. Hermann and S. Zeidler (St. Augustin, Deutschland), S. Pistauer (Sylt/Westerland, Germany), Urszula Jedynak-Wąsowicz (Krakow, Poland), L. Ensina, D. Solé, P. Guerzet Ayres Bastos, F. Andrade Nunes, I. Camelo-Nunes, and R. Cocco (Sao Paulo, Brazil), A. Plaza Martin (Barcelona, Spain), J. Meister (Aue, Germany), S. Hompes (Hamburg, Germany), E. Hamelmann (Bielefeld, Germany), I. Neustädter (Nuremberg, Germany), and A. Fiocchi and S. Arasi (Rome, Italy).

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ONLINE REPOSITORY

TABLE E1. Registered cases and food-induced anaphylaxis, by country

Country	Total registered cases	Food-induced anaphylaxis
Germany	7,447	1,921
Switzerland	1,603	609
France	1,309	948
Austria	717	109
Italy	599	109
Spain	461	227
Poland	328	92
Greece	275	166
Brazil	198	67
Ireland	194	151
Bulgaria	192	69
Total	13,323	4,468

TABLE E2. Frequency of confirmed and suspected cases among the most frequent elicitors

	Confirmed		Suspected		
Elicitor	n	%	n	%	Total
Peanut	580	83.6	114	16.4	694
Cow's milk	318	92.2	27	7.8	345
Hazelnut	237	75.7	76	24.3	313
Cashew	226	89.3	27	10.7	253
Hen's egg	221	86.3	35	13.7	256
Shellfish	207	78.4	57	21.6	264
Wheat	202	68.0	95	32.0	297
Other tree nuts	196	73.4	71	26.6	267
Walnut	131	79.9	33	20.1	164
Seeds	110	77.5	32	22.5	142
Soy	102	74.5	35	25.5	137
Fish	84	63.2	49	36.8	133
Meat and poultry	79	72.5	30	27.5	109
Celery	71	68.3	33	31.7	104

TABLE E3. Frequency of severity according to Ring and Messmer and organ systems involved in anaphylactic reaction depicted for most common food allergens

	Peanut		Cow's milk		Hazelnut		Cashew		Hen's egg		Shellfish		Wheat		Other tree nuts		Walnut		Seeds		Soy		Fish		Meat and poultry		Celery	
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Total n	580	100	318	100	237	100	226	100	221	100	207	100	202	100	196	100	131	100	110	100	102	100	84	100	79	100	71	100
Age																												
Mean, y/SD	10	10	4	8	18	20	6	10	4	9	36	19	34	20	19	19	13	15	23	20	36	19	16	21	32	24	37	19
Median, y	6		1		8		3		1		36		34		12		7		15		40		6		29		36	
Range	0.25	64	0	53	1	83	0.92	80	0	64	4	90	0.5	80	1	83	0	77	1	74	1	69	1	93	1	78	2	75
Sex																												
Female	231	39.8	114	35.8	109	46.0	89	39.4	83	37.6	122	58.9	85	42.1	87	44.4	67	51.1	37	33.6	68	66.7	28	33.3	23	29.1	41	57.7
Male	349	60.2	204	64.2	128	54.0	137	60.6	138	62.4	85	41.1	117	57.9	109	55.6	64	48.9	73	66.4	34	33.3	56	66.7	56	70.9	30	42.3
Ring and Messmer severity																												
Grade II	237	40.9	128	40.3	129	54.4	79	35.0	103	46.6	113	54.6	96	47.5	107	54.6	61	46.6	48	43.6	67	65.7	42	50.0	45	57.0	49	69.0
Grade III	341	58.8	184	57.9	105	44.3	146	64.6	118	53.4	92	44.4	106	52.5	89	45.4	70	53.4	62	56.4	34	33.3	42	50.0	34	43.0	22	31.0
Grade IV	2	0.3	6	1.9	3	1.3	1	0.4	0	0.0	2	1.0	0	0.0	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
Organ systems involved																												
Skin	537	92.6	309	97.2	219	92.4	211	93.4	211	95.5	199	96.1	194	96.0	179	91.3	128	97.7	107	97.3	97	95.1	78	92.9	75	94.9	68	95.8
Gastrointestinal	367	63.3	180	56.6	116	48.9	167	73.9	129	58.4	104	50.2	78	38.6	101	51.5	66	50.4	64	58.2	59	57.8	51	60.7	42	53.2	24	33.8
Respiratory	501	86.4	256	80.5	209	88.2	179	79.2	153	69.2	151	72.9	110	54.5	161	82.1	111	84.7	83	75.5	84	82.4	72	85.7	44	55.7	61	85.9
Cardiovascular	196	33.8	90	28.3	81	34.2	80	35.4	87	39.4	100	48.3	153	75.7	60	30.6	47	35.9	46	41.8	42	41.2	31	36.9	45	57.0	33	46.5
Atopic co-disease and exercise																												
Asthma	250	43.1	80	25.2	88	37.1	51	22.6	28	12.7	57	27.5	46	22.8	72	36.7	45	34.4	46	41.8	40	39.2	27	32.1	13	16.5	26	36.6
Atopic dermatitis	248	42.8	151	47.5	89	37.6	96	42.5	144	65.2	17	8.2	45	22.3	65	33.2	46	35.1	43	39.1	19	18.6	36	42.9	9	11.4	9	12.7
Rhinitis	220	37.9	68	21.4	128	45.3	48	21.2	31	14.0	94	45.4	87	43.1	105	53.6	65	49.6	56	50.9	101	99.0	35	41.7	30	38.0	69	97.2
Exercise	99	17.1	27	8.5	35	14.8	18	8.0	17	7.7	45	21.7	136	67.3	31	15.8	34	26.0	20	18.2	16	15.7	14	16.7	13	16.5	11	15.5

TABLE E4. Associations among severity according Ring and Messmer, organ systems involved in anaphylactic reaction, atopic comorbidities, exercise, and food of interest compared with reference food group

	Peanut		Cow's milk		Hazelnut		Cashew		Hen's egg		Shellfish		Wheat	
Characteristic	**CV**	**CI**	**CV**	**CI**	**CV**	**CI**	**CV**	**CI**	**CV**	**CI**	**CV**	**CI**	**CV**	**CI**
Severity (grade III/IV)	0.08	0.03-0.14	0.00	0.00-0.09	0.01	0.00-0.11	0.14*↑	0.04-0.23	0.01	0.00-0.11	0.02	0.00-0.11	0.12*↑	0.03-0.22
Skin	0.03	0.00-0.08	0.08	0.01-0.15	0.01	0.00-0.11	0.00	0.00-0.11	0.00	0.00-0.11	0.08	0.01-0.17	0.12*↑	0.04-0.21
Gastrointestinal	0.10	0.04-0.15	0.01	0.00-0.09	0.03	0.00-0.12	0.20*↑	0.11-0.29	0.03	0.00-0.12	0.02	0.00-0.12	0.13*↓	0.04-0.23
Respiratory	0.03	0.00-0.09	0.04	0.00-0.13	0.09	0.01-0.18	0.01	0.00-0.11	0.13*↓	0.04-0.23	0.09	0.01-0.19	0.22*↓	0.12-0.32
Cardiovascular	0.01	0.00-0.07	0.06	0.01-0.15	0.05	0.00-0.14	0.02	0.00-0.11	0.12*↑	0.03-0.22	0.02	0.00-0.12	0.28*↑	0.19-0.38
Asthma	0.07	0.01-0.13	0.12*↑	0.05-0.20	0.10*↑	0.01-0.20	0.03	0.00-0.13	0.11*↓	0.01-0.21	0.08	0.01-0.18	0.15*↓	0.06-0.25
Atopic dermatitis	0.01	0.00-0.07	0.03	0.00-0.12	0.03	0.00-0.13	0.06	0.00-0.15	0.19*↑	0.10-0.29	0.17*↓	0.07-0.25	0.03	0.00-0.14
Rhinitis	0.02	0.00-0.09	0.10*↑	0.02-0.18	0.08	0.01-0.17	0.02	0.00-0.11	0.02	0.00-0.12	0.13*↓	0.02-0.23	0.20*↓	0.10-0.30
Exercise	0.05	0.00-0.11	0.01	0.00-0.09	0.04	0.00-0.15	0.06	0.00-0.15	0.01	0.00-0.11	0.03	0.00-0.13	0.56*↑	0.47-0.65

	Other tree nuts		Walnut		Seeds		Soy		Fish		Meat and poultry		Celery	
Severity (grade III/IV)	0.05	0.00-0.15	0.11*↑	0.01-0.23	0.05	0.00-0.18	0.11*↓	0.01-0.26	0.00	0.00-0.17	0.01	0.00-0.18	0.17*↓	0.02-0.33
Skin	0.03	0.00-0.13	0.06	0.00-0.17	0.09	0.00-0.20	0.00	0.00-0.16	0.02	0.00-0.18	0.10	0.00-0.23	0.16	0.01-0.30
Gastrointestinal	0.02	0.00-0.13	0.03	0.00-0.16	0.05	0.00-0.18	0.12	0.01-0.27	0.09	0.00-0.24	0.01	0.00-0.18	0.17	0.02-0.33
Respiratory	0.01	0.00-0.12	0.06	0.00-0.18	0.11	0.01-0.24	0.11	0.00-0.24	0.06	0.00-0.21	0.29*↓	0.14-0.43	0.08	0.01-0.24
Cardiovascular	0.13*↓	0.03-0.23	0.03	0.00-0.16	0.09	0.00-0.24	0.10	0.01-0.25	0.01	0.00-0.18	0.15	0.01-0.31	0.18	0.02-0.33
Asthma	0.01	0.00-0.12	0.02	0.00-0.14	0.10	0.01-0.24	0.07	0.00-0.22	0.04	0.00-0.21	0.23*↓	0.05-0.38	0.16	0.02-0.34
Atopic dermatitis	0.02	0.00-0.13	0.01	0.00-0.16	0.07	0.00-0.20	0.09	0.00-0.25	0.04	0.00-0.22	0.05	0.00-0.22	0.05	0.00-0.22
Rhinitis	0.03	0.00-0.14	0.07	0.00-0.20	0.07	0.00-0.21	0.30*↑	0.15-0.43	0.08	0.00-0.25	0.17	0.02-0.34	0.24*↑	0.07-0.40
Exercise	0.04	0.00-0.15	0.19*↑	0.07-0.31	0.02	0.00-0.16	0.01	0.00-0.16	0.06	0.00-0.22	0.04	0.00-0.19	0.04	0.00-0.20

CV, Cramér's V.

The level of association is weak (>0.1 to 0.29), moderate (0.3-0.49), or strong (≥0.5).

*Significant difference between food of interest and the reference food group. Arrows indicate the direction of the association (↑ shows higher frequency, and ↓ lower frequency).

TABLE E5. Association between symptoms and food of interest compared with reference food group, depicted as matrix

Cramér's V	Peanut	Cow's milk	Hazelnut	Cashew	Hen's egg	Shellfish	Wheat	Other tree nuts	Walnut	Seeds	Soy	Fish	Meat and poultry	Celery
Urticaria	0.03	0.05	0.08	0.10	0.03	0.06	0.24*↑	0.08	0.01	0.00	0.17*↓	0.03	0.26*↑	0.00
Angioedema	0.04	0.05	0.04	0.05	0.04	0.06	0.17*↓	0.09	0.09	0.03	0.07	0.03	0.22*↓	0.16↑
Vomiting	0.06	0.11*↑	0.05	0.22*↑	0.10	0.05	0.01	0.24*↑	0.02	0.15↓	0.00	0.19↑	0.18↓	0.18↓
Dysphagia	0.03	0.02	0.02	0.04	0.04	0.24*↓	0.21*↓	0.14	0.02	0.06	0.08	0.03	0.13↓	0.03
Dyspnea	0.00	0.12*↑	0.03	0.06	0.07	0.06	0.04	0.03	0.03	0.00	0.09	0.12	0.10	0.01
Rhinitis	0.10	0.04	0.15*↓	0.00	0.01	0.05	0.13	0.09	0.01	0.17↓	0.06	0.21*	0.13↓	0.10
Throat/chest tightness	0.00	0.01	0.07	0.19*↑	0.12↓	0.00	0.08	0.00	0.07	0.16↑	0.09	0.06	0.11↑	0.02
Cough	0.05	0.02	0.03	0.01	0.12*↓	0.04	0.01	0.05	0.10	0.03	0.13↓	0.02	0.15↑	0.10
Reduced alertness	0.11*↑	0.06	0.06	0.02	0.17↑	0.05	0.08	0.02	0.05	0.01	0.11↓	0.06	0.03	0.12↓
Dizziness	0.01	0.03	0.03	0.06	0.17↓	0.12↑	0.00	0.05	0.12↓	0.03	0.04	0.12↓	0.11↑	0.05
Hypotension	0.04	0.11↓	0.14↓	0.05	0.14↓	0.00	0.10	0.12↑	0.05	0.01	0.28*↓	0.14↑	0.12↑	0.04
Loss of consciousness	0.05	0.08	0.13	0.03	0.07	0.09	0.25*↑	0.01	0.09	0.04	0.14↓	0.19↑	0.25↑	0.16↓

The level of association is weak (>0.1 to 0.29), moderate (0.3-0.49), or strong (≥0.5).
*Significant difference between food of interest and the reference food group. Arrows indicate the direction of the association (↑ shows higher frequency, and ↓ lower frequency).

TABLE E6. Repetitive reaction to previously known elicitor

Recurrency	Elicitor	Recurrent reaction to previously known elicitor n	%	Total n*
High rate	Wheat flour	40	29.4	107
	Meat and poultry	14	26.9	44
	Fish	21	39.6	41
Median rate	Cow's milk	119	75.3	151
	Peanut	195	73.0	233
	Hazelnut	59	60.2	79
	Shellfish	25	30.9	70
	Celery	7	28.0	17
	Seeds	11	31.4	25
	Hen's egg	47	67.1	65
	Other tree nuts	21	37.5	39
	Walnut	22	64.7	33
Low rate	Soy	9	52.9	14
	Cashew	17	53.1	29

The most common food elicitors are shown, sorted by their frequency of recurrent reactions.
*Only cases with valid data on recurrence and information about previous identification of the allergen source were included in the calculation (total n = 2,913).

TABLE E7. Ingested amount of food, by elicitors

Elicitor	<1 teaspoon	1 teaspoon	1 tablespoon	1/2 cup	1 cup	1 plate	Total
Peanut	107 (34.3%)	104 (33.3%)	67 (21.5%)	22 (7.1%)	6 (1.9%)	6 (1.9%)	312
Coẃs milk	26 (15.2%)	24 (14.0%)	43 (25.1%)	46 (26.9%)	28 (16.4%)	4 (2.3%)	171
Hazelnut	30 (24.0%)	32 (25.6%)	39 (31.2%)	13 (10.4%)	9 (7.2%)	2 (1.6%)	125
Cashew	46 (35.1%)	51 (38.9%)	22 (16.8%)	7 (5.3%)	3 (2.3%)	2 (1.5%)	131
Heńs egg	24 (17.5%)	42 (30.7%)	43 (31.4%)	14 (10.2%)	3 (2.2%)	11 (8.0%)	137
Shellfish	6 (5.6%)	3 (2.8%)	17 (15.9%)	13 (12.1%)	14 (13.1%)	54 (50.5%)	107
Wheat	5 (5.7%)	4 (4.6%)	8 (9.2%)	9 (10.3%)	12 (13.8%)	49 (56.3%)	87
Other tree nuts	27 (26.0%)	38 (36.5%)	22 (21.2%)	10 (9.6%)	6 (5.8%)	1 (1.0%)	104
Walnut	31 (42.5%)	17 (23.3%)	14 (19.2%)	7 (9.6%)	1 (1.4%)	3 (4.1%)	73
Seed	16 (23.9%)	21 (31.3%)	18 (26.9%)	8 (11.9%)	2 (3.0%)	2 (3.0%)	67
Soy	1 (1.9%)	3 (5.6%)	5 (9.3%)	16 (29.6%)	28 (51.9%)	1 (1.9%)	54
Fish	2 (5.0%)	11 (27.5%)	8 (20.0%)	8 (20.0%)	2 (5.0%)	9 (22.5%)	40
Meat and poultry	0	5 (17.9%)	3 (10.7%)	4 (14.3%)	4 (14.3%)	12 (42.9%)	28
Celery	0	2 (6.5%)	7 (22.6%)	9 (29.0%)	4 (12.9%)	9 (29.0%)	31

TABLE E8. Location of anaphylactic reaction among different food elicitors

	Peanut		Cow's milk		Hazelnut		Cashew		Hen's egg		Shellfish		Wheat		Other tree nuts		Walnut		Seeds		Soy		Fish		Meat and poultry		Celery	
Location	n	%	n	%	N	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Home	255	44.0	223	70.1	118	49.8	132	58.4	157	71.0	76	36.7	59	29.2	92	46.9	57	43.5	38	34.5	37	36.3	40	47.6	42	53.2	31	43.7
Restaurant, cafeteria, takeout, hotel	47	8.1	13	4.1	12	5.1	6	2.7	12	5.4	58	28.0	17	8.4	17	8.7	11	8.4	23	20.9	22	21.6	16	19.0	10	12.7	13	18.3
Relative's or friend's home	63	10.9	9	2.8	19	8.0	28	12.4	18	8.1	9	4.3	8	4.0	18	9.2	10	7.6	9	8.2	5	4.9	2	2.4	2	2.5	5	7.0
School, kindergarten	67	11.6	21	6.6	25	10.5	7	3.1	10	4.5	3	1.4	7	3.5	4	2.0	11	8.4	5	4.5	5	4.9	9	10.7	0	0	2	2.8
Urban public place (street, movie theater, etc)	24	4.1	8	2.5	8	3.4	14	6.2	0	0	7	3.4	41	20.3	7	3.6	8	6.1	6	5.5	6	5.9	1	1.2	3	3.8	6	8.5
Garden, park, countryside, etc	18	3.1	1	0.3	6	2.5	2	0.9	3	1.4	8	3.9	26	12.9	6	3.1	7	5.3	6	5.5	0	0	1	1.2	3	3.8	1	1.4
Place of work	11	1.9	1	0.3	6	2.5	1	0.4	3	1.4	3	1.4	5	2.5	7	3.6	2	1.5	4	3.6	3	2.9	2	2.4	2	2.5	2	2.8
Public transport including airplanes	2	0.3	0	0	1	0.4	1	0.4	1	0.5	1	0.5	0	0	1	0.5	0	0	0	0	1	1.0	0	0	0	0	0	0
Other	14	2.4	5	1.6	8	3.4	3	1.3	2	0.9	8	3.9	5	2.5	4	2.0	3	2.3	8	7.3	1	1.0	1	1.2	1	1.3	2	2.8
Unknown	79	13.6	37	11.6	34	14.3	32	14.2	15	6.8	34	16.4	34	16.8	40	20.4	22	16.8	11	10.0	22	21.6	12	14.3	16	20.3	9	12.7
Total	580		318		237		226		221		207		202		196		131		110		102		84		79		71	

TABLE E9. Details about other food elicitors of interest

Food elicitior	Cases, n
Fruit	
Kiwi	39
Apple	37
Peach	28
Banana	24
Fig	12
Mango	11
Cherry	9
Citrus fruits	9
Nectarine	8
Grape	8
Pineapple	6
Melon	6
Plum	6
Pear	5
Lychee	5
Jackfruit	4
Apricot	3
Redcurrant	3
Chestnut	3
Strawberry	2
Huckleberry	2
Raspberry	2
Pomegranate	2
Goji berry	2
Passionfruit	1
Date	1
Tangerine	1
Dragon fruit	1
Khaki	1
Sea buckthorn	1
Fruit unspecified	2
Total	244
Legumes (except peanut and soy)	
Lupine	27
Pea	22
Lentil	21
Bean	9
Chickpea	4
Legumes unspecified	25
Total	108
Vegetables (except celery)	
Carrot	37
Lettuce	9
Tomato	7
Mushrooms	6
Avocado	6
Bell pepper	5
Cabbage	3
Potato	2
Chicory	1
Asparagus	1
Eggplant	1
Parsnip	1
Squash	1
Vegetables unspecified	12
Total	92
Cereals (except wheat)	
Buckwheat	32
Sweet corn	12
Spelt	4
Rye flour	4
Amaranth	3
Oat	1
Rice	1
Barley	1
Cereals unspecified	10
Total	68
Other types of milk	
Goaťs milk	30
Ewés milk	15
Total	57
Spices	
Curry	5
Parsley	4
Paprika	3
Garlic	3
Ginger	2
Cardamom	2
Caraway	2
Fennel	2
Chamomile	2
Pepper	1
Spices unspecified	6
Total	32
Food additives	
Coloring agents	5
Histamine	3
Unspecified	5
Total	13
Other food	
Honey	12
Prepackaged plant pollen	5
Quaiĺs egg	2
Animal products unspecified	10
Unspecified	32
Total	61

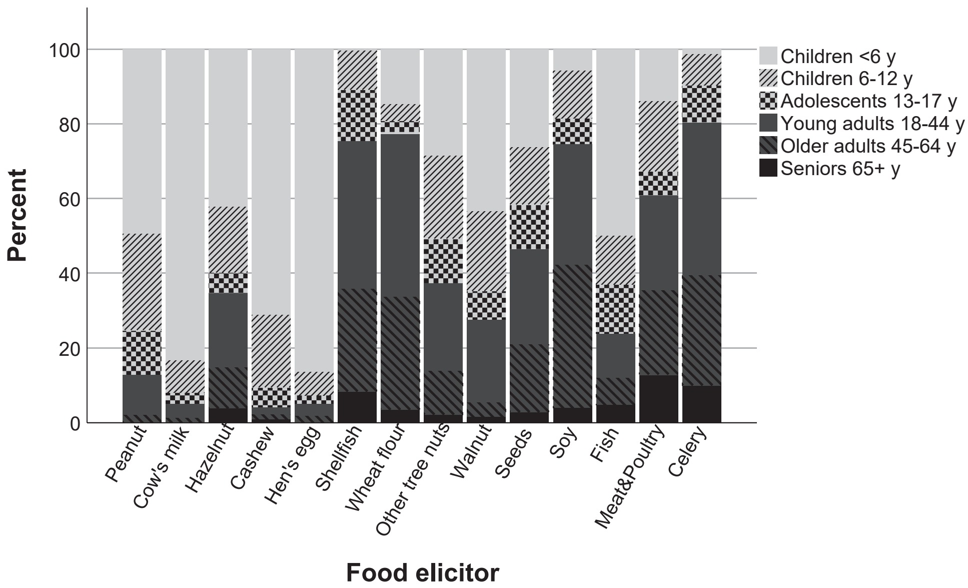

FIGURE E1. Age distribution among food elicitors.