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Article type : Letter to the Editor

Eliciting Allergens and Treatment of Anaphylaxis: Report of the Finnish National Anaphylaxis Registry

Anaphylaxis is the most severe form of an allergic reaction. The Finnish National Anaphylaxis Registry has been collecting data of severe allergic reactions since year 2000 (1). Here we summarize a total of 1442 reported anaphylactic cases between 2000 and 2017 and identify and report changes in provoking agents as well as characterize the symptoms and treatments over the full Registry period.

The data is based on voluntary reports of systemic allergic reactions filed by hospital personnel and covering the Finnish population of 5.5 million people. A questionnaire or an online electronic form were used for reporting. Children (<16y) represented 663 (46%) cases (Table 1) with the highest frequency of reports (336 cases, 23%) accumulating from small children under school age (<6y)(Suppl. Figure 1). Males accounted the majority (61%) of anaphylactic reports in children, whereas females dominated among adults (64%) (Suppl. Figure 1).

The most frequently reported provoking allergens were foods (811 cases, 56%), drugs (365 cases, 25%) and insect venoms (90 cases, 6%) in concordance with earlier reports of anaphylactic elicitors (2,3). However, the Finnish Anaphylaxis Registry revealed significantly less reported cases due to insect stings both in children and adults compared to the European Anaphylaxis Registry (Fig 1A) (2). Furthermore, severe allergic reactions due to immunotherapy were reported in 121 (8%) cases. Other causative agents were involved in 48 (3%) patient cases, and without knowledge of a potential triggering allergen anaphylaxis affected 21 (1.5%) patients.

Food triggered 502 (76%) anaphylaxis in children, of which the six most frequent elicitors remained the same over the Registry period (i.e. milk, wheat, eggs, nuts, fruits and fish). Intriguingly, the amount of anaphylaxis due to nuts significantly increased during the past five years, mostly due to increase in reported cases with peanut and cashew nut (Supplemental Figure 2A and B). The increase in nut exposure and in particularly cashew could be explained by increase in importation and simultaneous decrease in retail price (4). Furthermore, cashew has become a substituting nut for more expensive nuts or seeds in many foods, hence, providing cause for accidental exposures. Nonetheless, no increase in nut provoked anaphylaxis in adults was observed.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/all.13858

134 (27%) cases of food-triggered anaphylaxis in children were due to accidental exposure to a known allergen. To that end, we analyzed the places of accidental food exposures and noticed decrease in events in daycare centers or schools and increase at home and leisure time (Supplemental Figure 2C). Overall, the food-triggered anaphylaxis among pediatric patients occurred mostly at private homes (47%), daycare centers and schools (16%), and leisure time (14%). These data indicate slightly higher frequency of anaphylaxis in daycare centers and schools compared to earlier European reports (5). Most likely the differences in warm meal catering services for children between European countries play a significant role in the observation.

In adults the most common causes of anaphylaxis were foods (39%) and drugs (39%) (Table 1). Nuts, fruits and wheat were the most reported food elicitors, and antibiotics, contrast media and analgesics the most frequent drug elicitors (Table 1). No significant changes in eliciting allergens, location of anaphylaxis events or symptoms were observed among adult patients during the Registry period.

Insect venom caused 38 (6%) anaphylaxis in children and 53 cases (7%) in adults. Anaphylaxis due to bee sting was rare (0% in children and 0,5% in adults). The lower frequency of hymenoptera anaphylaxis compared to European reports (5) may be due to shorter summers or differences in the colliding habitats of the insects and humans in countries with low population density. A recent registry-based report on anaphylaxis associated deaths in Finland, however, identified hymenoptera venoms as major cause of fatal cases (6). Only one report of fatal hymenoptera anaphylaxis was collected to the Registry, indicating a significant lack of reports from the fatal cases.

Therapeutic allergen products comprised 8% of the reported cases in the Registry. Immunotherapy (IT) to birch pollen was better tolerated than timothy (Table 1). Only 2 cases of anaphylaxis due to hymenoptera IT were reported. No reports of Sublingual IT were received.

Symptoms in skin and in respiratory system were involved in most cases (87% and 79%, respectively). Most frequent allergic symptoms in skin were urticaria (59%), angioedema (48%) and pruritus (47%). Most common respiratory symptoms were difficulty to breath (65%), wheezing (28%), swelling of upper airways (24%), cough (21%) and hoarse voice (19%). Gastrointestinal system was affected in 45% of patients and 43% had cardiovascular symptoms.

The use of adrenalin in Finnish health care has been frequent throughout the Registry period (75%) and exceptionally high compared to the average of European countries (Fig. 1B) (2,7). Similarly, corticosteroids and antihistamines were also used more often than in the other European countries (Figure 1B). To further asses the self-usage of an adrenalin injector, we asked the presence of prescription for and usage of an auto-injector. In year 2017 27% of the cases had a prescription for an auto-injector but only 28% of those patients had self-injected adrenalin.

The Finnish Anaphylaxis Registry and the present study also have some limitations. The level of information filled into the questionnaires showed variation and not all the factors or cofactors were always reported in desired detail. The data received by voluntary reports represents only an unknown percentage of the actual cases of anaphylaxis over period when hospitalizations due to anaphylactic reactions in general have increased (8). Overall, the volunteer based reporting of

anaphylaxis deaths has been incomplete. In addition, seasonal trends, such as publicity of an allergen, may influence on the number of reports.

In conclusion, during the 18-year registry period increase in nut caused anaphylaxis was observed as a new arising trend in children. Importantly, the cases of accidental food allergen exposures at daycare centers and schools decreased during the past ten years, overlapping with the period of Finnish Allergy Program (2008-2018) that aimed at endorsing knowledge and treatment of severe allergies and adaptating a new attitude to allergy by suggesting the avoidance of low risk cross-reactive allergens is only mandatory (9).

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The authors declare no conflict of interest to disclose.

Table 1.

Most frequent provoking allergens

	Children, <16 y		Adults		All	
Eliciting allergen	n	%♦	n	%♦♦	n	%
	663	46.0 (of total)	779	54.0 (of total)	1442	100.0
Food	502	75.7	309	39.7	811	56.2
Nuts	136	20.5	58	7.4	194	13.5
Milk	114	17.2	13	1.7	127	8.8
Egg	73	11.0	4	0.5	77	5.3
Wheat	72	10.9	33	4.2	105	7.3
Fruits	32	4.8	35	4.5	67	4.6
Cereals (not wheat)*	16	2.4	23	3.0	39	2.7
Fish	13	2.0	11	1.4	24	1.7
Seeds	10	1.5	17	2.2	27	1.9
Soya	8	1.2	13	1.7	21	1.5
Crustaceans	3	0.5	16	2.1	19	1.3
Drugs	59	8.9	306	39.3	365	25.3
Antibiotic	24	3.6	79	10.1	103	7.1
Contrast media	3	0.5	59	7.6	62	4.3
Analgesics	16	2.4	46	5.9	62	4.3
Muscle relactant	1	0.2	34	4.4	35	2.4
Local anesthetic	2	0.3	14	1.8	16	1.1
Insect Venoms	38	5.7	53	6.8	91	6.3
Wasps	34	5.1	44	5.6	78	5.4
Bee	0	0.0	4	0.5	4	0.3
Immunotherapy	44	6.6	77	9.9	121	8.4
Birch	12	1.8	26	3.3	38	2.6
Timothy	32	4.8	54	6.9	86	6.0

*) Other cereals include: oat, rye, barley, corn, rice, buckwheat and millet

♦) % of children cases

♦♦) % of adult cases

Details of rare eliciting allergens not included

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Figure legends

Figure 1. Major elicitors and treatments of anaphylaxis in Finland. A) Percentages of reported severe allergic reactions elicited by drug, insect venom and food allergens in Finnish Anaphylaxis Registry compared to the European Anaphylaxis Registry. B) Frequency of reported adrenaline, antihistamine and corticosteroid treatments for severe allergic reactions in Finland compared to the European Anaphylaxis Registry.

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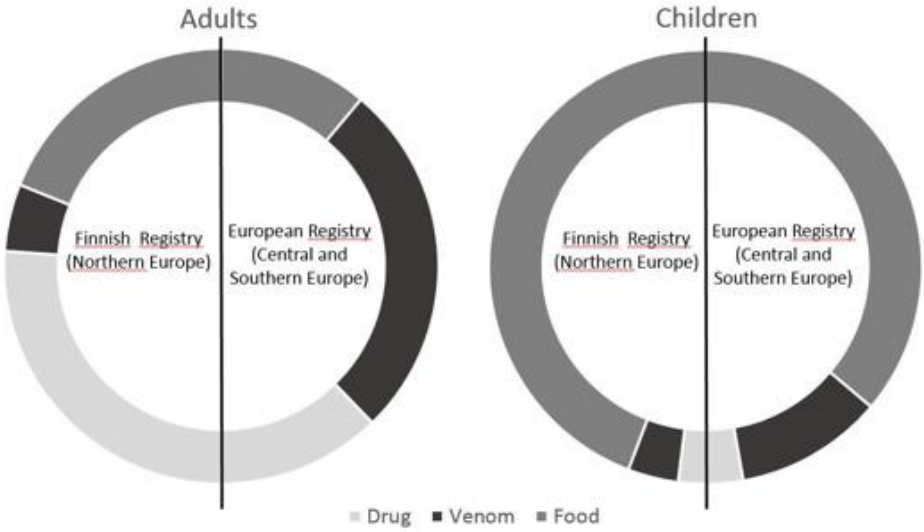

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