European Journal of Clinical Nutrition (2005) 59, 399–403
 0954-3007/05 $30.00
www.nature.com/ejcn

ORIGINAL COMMUNICATION

Prevalence of self-reported food allergy and IgE antibodies to food allergens in Swedish and Estonian schoolchildren

A Sandin[1]*, T Annus[2], B Björkstén[3], L Nilsson[4], M-A Riikjärv[5], M van Hage-Hamsten[6] and L Bråbäck[7]

[1]*Department of Clinical Sciences, Division of Paediatrics, Umeå University Hospital, Umeå, Sweden;* [2]*Tartu University Children's Hospital, Tartu, Estonia;* [3]*Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden;* [4]*Department of Molecular and Clinical Medicine, Division of Paediatrics, Linköping University, Sweden;* [5]*Tallinn Children's Hospital, Tallinn, Estonia;* [6]*Department of Medicine, Clinical Immunology and Allergy Unit, Karolinska Institute and Hospital, Stockholm, Sweden; and* [7]*Department of Public Health and Research, Sundsvall Hospital, Sweden*

Objective: To compare the prevalence of self-reported food allergy and IgE antibodies to food allergens in wheezing and non-wheezing Estonian and Swedish schoolchildren, in the light of the disparities in the standard of living, food consumption and prevalence of respiratory allergies that still exist between Estonia and the Scandinavian countries.
Design and setting: As a part of the ISAAC Phase II study, children from a random sample of schools in Tallinn in Estonia and Linköping and Östersund in Sweden participated in skin prick tests to inhalant allergens and the parents replied to questionnaires. IgE antibodies against a panel of food allergens (egg white, milk, soy bean, fish, wheat and peanut) were taken from children with questionnaire-reported wheezing and a random sample of nonwheezing children.
Subjects: Children aged 10–11 y.
Results: The prevalence of self-reported food allergy was similar in Estonia and Sweden and about twice as high in wheezing children than in nonwheezing children. In Estonia, however, 3% of the children with perceived food allergy reported reactions from at least four different foods, as compared to 31% in Sweden. The prevalence of sensitisation to food allergens was similar in wheezing and nonwheezing children in Estonia (8%) while, in Swedish children, IgE antibodies to food allergens were more likely among wheezing children (Linköping 38 *vs* 11%, crude OR 5.1, 95% CI 2.2–11.6, and Östersund 24 *vs* 7%, crude OR 4.1, 95% CI 1.9–8.5).
Conclusion: Our study suggests that IgE-mediated food reactions were less likely in Estonian schoolchildren. Moreover, the perception of food allergy and thereby the meaning of self-reported food allergy appears to be different in the two countries.
Sponsorship: This study was supported by a grant from the Swedish Foundation for Health Care Sciences and Allergy Research.
European Journal of Clinical Nutrition (2005) **59,** 399–403. doi:10.1038/sj.ejcn.1602087
Published online 15 December 2004

Keywords: food allergy; children; IgE antibodies; wheezing

Introduction

A number of studies have investigated the geographical variations in respiratory allergies, but the epidemiology of food allergy has been studied less intensively. The prevalence rates for reported food allergy/intolerance range from 4.6% in Spain to 19.1% in Australia among young adults in the European Community Respiratory Health Survey (ECRHS) (Woods *et al*, 2001). As there were no objective analyses of

***Correspondence: A Sandin, Department of Clinical Sciences, Division of Paediatrics, Umeå University Hospital, SE-901 85 Umeå, Sweden.**
E-mail: annasandin@telia.com
***Guarantor*: A Sandin.**
***Contributors*: AS collected data, analysed data, wrote the manuscript and involved in the final approval of the manuscript. TA coinvestigator, collected data and involved in the final approval of the manuscript. BB involved in study design and in the final approval of the manuscript. LN coinvestigator, involved in the final approval of the manuscript. M-AR coinvestigator, involved in the final approval of the manuscript. M van H-H data analyses and involved in the final approval of the manuscript. LB coinvestigator, involved in study design, data analysis and in the final approval of the manuscript.**
The work was carried out at the Division of Paediatrics, Linköping University, the Department of Paediatrics, Östersund Hospital, and Karolinska Institutet.
Received 6 February 2004; revised 23 June 2004; accepted 27 September 2004; published online 15 December 2004

IgE antibodies for comparison, it is possible that there are cultural differences that influence the perception of 'food allergy'. A comparison between Nordic countries revealed that in Iceland, 4% of a study population of young adults were positive to one or more of the allergens in a panel of the six most common food allergens compared with 6% in Sweden (Gislason *et al*, 1999). In a cross-sectional study of 18-month-old children, however, the prevalence of adverse food reactions and sensitisation to food allergens was similar in Sweden and Iceland (Kristjansson *et al*, 1999).

Estonia is part of the Nordic region, but disparities in the standard of living and food consumption remaining from the communist era still exist between Estonia and the Scandinavian countries. We have previously demonstrated low prevalence rates for atopic disease and sensitisation to inhalant allergens in Estonia (Annus *et al*, 2001). The aim of this study, which was undertaken as part of the ISAAC Phase II study, was to compare the prevalence of self-reported food allergy and food IgE antibodies in wheezing and nonwheezing Estonian and Swedish schoolchildren.

Material and methods

The study design adhered to the ISAAC Phase II protocol (ISAAC Steering Committee, 1998). All the 10- to 11-year-old children from all 25 schools in Östersund and from a random sample of schools in Linköping ($n=15$) and in Tallinn ($n=20$) were invited during the winter of 1996/1997 to participate in the initial questionnaire and skin prick test to eight common inhalant allergens (tree mix, grass mix, mugwort, horse, dog, cat, *Dermatophagoides pteronyssinus*, *D. farinae*). Details from this part of the study have been reported previously (Annus *et al*, 2001). The response rates to the questionnaire were similar in the three towns (82–85%). The children who were invited to take part in the case–control study were those with a reported history of wheezing in the past 12 months (122, 72 and 81 children in Östersund, Linköping and Tallinn, respectively) and a random sample of nonwheezing children (244, 207 and 259 children) from the original cohorts.

Questionnaire-reported food allergy was defined as a positive response to the question: 'Is your child allergic to any food (yes/no)?'. The parents were also asked if and how their child reacted to 16 different foods, that is, milk, egg, fish, wheat, mandarin, orange, apple, peach, kiwi, avocado, banana, carrot, tomato, peanut, nut and almond. In all, 78% (63/81) of the wheezers and 86% (224/259) of the nonwheezers replied to the questionnaire in Tallinn. The corresponding participation rates in Linköping were 85% (61/72) and 69% (143/207), respectively, while they were 89% (109/122) and 70% (170/244), respectively in Östersund.

Serum samples obtained from the children were stored at -20°C until used. IgE antibodies against a panel of relevant food allergens (f × 5; egg white, milk, soya bean, fish, wheat and peanut) were analysed with the Pharmacia CAP System-Specific IgE FEIA (Pharmacia Diagnostics, Uppsala, Sweden). IgE antibody levels were measured in kU_A/l and defined as class 0 (<0.35), class 1 (0.35 to <0.7), class 2 (0.7 to <3.5), class 3 (3.5 to <17.5), class 4 (17.5 to <50), class 5 (50 to <100) and class 6 (100 and larger).

Blood samples were obtained from 47% (38/81) of the wheezers and 48% (125/259) of the nonwheezers in Tallinn, 72% (52/72) and 53% (110/207), respectively, in Linköping and 84% (103/122) and 67% (164/244), respectively, in Östersund.

Statistical analysis

All the data were coded and entered into the database module of the SPSS statistics software (SPSS Inc, Chicago, IL, USA). All subsequent analyses were performed using this package, (version 10.0). A χ^2 test or, whenever appropriate, Fisher's exact test was used to compare rates between groups. Statistical significance was set at the 5% level.

Ethical considerations

The study was approved by the Ethics Committees at Umeå University and Linköping University and the institutional review board at the Tallinn Institute of Experimental and Clinical Medicine. Written parental consent was obtained separately for each element of the study.

Results

The prevalence of self-reported food allergy was similar in Sweden and Estonia and about twice as high in wheezing children compared with nonwheezing children (Table 1). However, the number of specified foods differed between the two countries. In Estonia, 28% (16/58) of the children with reported food allergy did not specify any food allergen, as compared to 9% in Sweden (10/118). Moreover, only 3% (2/63) of the wheezing children in Estonia perceived reactions to at least four different food allergens as compared to 18% (11/60) ($P=0.008$) of the wheezing children in Linköping and 15% in Östersund (16/109) ($P=0.02$). The corresponding rates in nonwheezing children were 0/224 in Tallinn, 2% (3/143) in Linköping ($P=0.06$) and 4% (6/170) in Östersund ($P=0.006$). A positive panel of food allergens was significantly more common in Sweden but only in wheezing children. Positive skin prick tests to inhalant allergens were more common in Sweden, however, in both wheezing and nonwheezing children.

Reported reactions to nut, peanut, apple, peach, kiwi and carrot were more likely in the Swedish children (Table 2). The prevalence of self-reported reactions to apple in wheezing children was 2% (1/63) in Tallinn (reference group), 13% (8/61) in Linköping ($P=0.02$) and 10% (11/109) in Östersund ($P=0.06$). The corresponding prevalence rates for self-reported allergy to kiwi were 3% (2/63), 21% (13/61) ($P=0.002$) and 15% (16/109) ($P=0.02$), respectively.

The prevalence of circulating IgE antibodies to food allergens was similar in wheezing and nonwheezing children in Estonia (8%, Table 1), while in Swedish children, IgE

Table 1 Questionnaire-reported food allergy, positive skin test to pollen and IgE antibodies to a panel of food allergens in wheezing and nonwheezing children in Tallinn, Linköping and Östersund

	Tallinn	*Linköping*		*Östersund*	
	Wheezers (n = *81*)	*Wheezers* (n = *72*)	*OR (95% CI)*[a]	*Wheezers* (n = *122*)	*OR (95% CI)*[a]
Questionnaire-reported food allergy	21/63 (33%)	23/61 (38%)	1.2 (0.6–2.5)	47/109 (43%)	1.5 (0.8–2.9)
Positive skin test to pollen	4/54 (7%)	24/61 (39%)	8.1 (2.6–25.4)	32/100 (32%)	5.9 (2.0–17.7)
Positive IgE to food allergens	3/38 (7.9%)	20/52 (38.5%)	7.3 (2.0–26.9)	25/103 (24.3%)	3.7 (1.1–13.2)
Class 1–2	2/38 (5.3%)	12/52 (23.1%)		13/103 (12.6%)	
Class 3 or more	1/38 (2.6%)	8/52 (15.4%)		12/103 (11.7%)	
	Nonwheezers (n = *259*)	*Nonwheezers* (n = *207*)	*OR (95% CI)*[b]	*Nonwheezers* (n = *244*)	*OR (95% CI)*[b]
Questionnaire-reported food allergy	37/224 (17%)	24/143 (17%)	1.0 (0.6–1.8)	24/170 (14%)	0.8 (0.5–1.5)
Positive skin test to pollen	5/150 (3%)	24/187 (13%)	4.3 (1.6–11.5)	37/200 (19%)	6.6 (2.5–17.2)
Positive IgE to food allergens	10/125 (8.0%)[c]	12/110 (10.9%)	1.4 (0.6–3.4)	12/164 (7.3%)[d]	0.9 (0.4–2.2)
Class 1–2	10/125 (8.0%)	8/110 (7.3%)		11/164 (6.7%)	
Class 3 or more	0	4/110 (3.6%)		1/164 (0.6%)	

[a]Crude odds ratios (OR) with 95% confidence intervals (CI) and wheezing children in Tallinn as the reference group.
[b]Crude odds ratios (OR) with 95% confidence intervals (CI) and nonwheezing children in Tallinn as the reference group.
[c]Three wheezers and two nonwheezers in Estonia did not answer the food questionnaire (one of the wheezers was IgE positive).
[d]One child in Sweden with negative IgE did not answer the food questionnaire.

Table 2 Questionnaire-reported reactions to specific food allergens among wheezing and nonwheezing schoolchildren in Tallinn, Linköping and Östersund (Tallinn reference area)

	Tallinn	*Linköping*		*Östersund*	
	Wheezers (n = *81*)	*Wheezers* (n = *72*)	P-*value*	*Wheezers* (n = *122*)	P-*value*
Apple, peach, kiwi or carrot	3/63 (5%)	16/61 (26%)	0.001	22/109 (20%)	0.006
Nut or peanut	4/63 (6%)	10/61 (16%)	ns	25/109 (23%)	0.005
Orange, mandarin or tomato	8/63 (13%)	7/61 (11%)	ns	22/109 (20%)	ns
Milk, egg, fish or wheat	5/63 (8%)	10/61 (16%)	ns	9/109 (8%)	ns
	Nonwheezers (n = *259*)	*Nonwheezers* (n = *207*)	P-*value*	*Nonwheezers* (n = *244*)	P-*value*
Apple, peach, kiwi or carrot	9/224 (4%)	9/143 (6%)	ns	15/170 (9%)	0.06
Nut or peanut	1/224 (0%)	10/142 (7%)	0.000	9/170 (5%)	0.003
Orange, mandarin or tomato	19/224 (8%)	2/143 (1%)	0.005	7/170 (4%)	ns
Milk, egg, fish or wheat	5/224 (2%)	5/143 (3%)	ns	4/170 (2%)	ns

ns: nonsignificant.

antibodies to food allergens were more likely among wheezing children (Linköping, 38 *vs* 11%, crude OR 5.1, 95% CI 2.2–11.6, and Östersund, 24 *vs* 7%, crude OR 4.1, 95% CI 1.9–8.5).

The rate of self-reported food allergy in Sweden was 20% (70/359) in children with a negative panel of food allergens, 36% in children with food allergen class 1 or 2 (16/44) and 84% (21/25) in children with class 3 or more. The percentage of children with self-reported food allergy in Estonia was 18% (26/146) in children with a negative panel of food allergens. Food allergen class 1 or 2 was detected in 11 Estonian children and two of them had self-reported allergy. Only one child in Estonia had food allergen class 3 and this child had self-reported food allergy. A total of 12 children (all of them from Sweden) had food allergen class 4 or more and all of them had self-reported food allergy.

Positive skin prick tests to inhalant allergens were more common in children with food allergen class 3 or more. In all, 21 of 22 children with class 3 or more had at least one positive skin test and 16 of 22 children were skin positive to pollen allergens. The prevalence of self-reported food allergy did not differ between participants and nonparticipants in the serum screening. However, in Swedish children, positive skin prick tests to inhalant allergens were significantly more common in children who had provided blood samples.

Discussion

The main finding in this study was the low prevalence of IgE antibodies to food allergens in Estonia, particularly in wheezing children. In contrast, wheezing children in Sweden were often sensitised to food allergens. The main limitation

was the fairly low number of serum samples that were obtained in Estonia. However, we have no indication that the drop-outs have biased our results. Self-reported food allergy and positive skin tests to inhalant allergens were similar in those children who underwent serum IgE determination and those declining it. Furthermore, the low prevalence of IgE serum antibodies to food allergens is in agreement with the very low prevalence of positive skin tests to inhalant allergens previously reported in Estonia (Annus *et al*, 2001).

The recent European multicentre study (ECHRS) revealed large differences in the prevalence of food allergies among adults, with a high prevalence in Scandinavian countries and Germany and the lowest in Southern European countries (Woods *et al*, 2001). It was suggested that differences in food allergies were related to differences in birch pollen allergy and dietary habits, for example. It is equally (or even more) possible that the perception of food allergy, and thereby the prevalence of perceived food allergy, may vary in different cultures.

Our study was based on self-reported adverse food reactions and a serum screening test for IgE antibodies to food allergens. Questionnaires most probably overestimate the real occurrence of food allergy (Brugman *et al*, 1998; Woods *et al*, 2002). Self-reported food allergy was common in our study, with similar prevalence rates in the two countries. However, a quarter of the children with perceived food allergy in Estonia did not report any reaction to a specified food, whereas one-third of the children with perceived food allergy in Sweden reported reactions to at least three different foods. These findings underline the fact that the concept of food allergy is diffuse and the meaning of food allergy may differ between different countries.

The prevalence of food allergy based on a determination of allergen-specific IgE antibodies was much lower than the prevalence rates based on self-reported symptoms, both in Estonia and in Sweden. This is consistent with other studies from the Nordic countries, in infants (Kristjansson *et al*, 1999), and university students, as well as adults (Gislason *et al*, 1999; Mattila *et al*, 2003). A specific diagnosis of food allergy would require a double-blind provocation test, but this is not feasible in epidemiological studies, as it is difficult to carry out practically, even in clinical settings.

The prevalence of self-reported food allergy was about 20% in children who were negative to a panel of food allergens and the agreement between self-reported food allergy and a positive screening test was poor in children with low levels of IgE antibodies. This suggests that many children with self-reported food allergy did not have an IgE-mediated allergy. High IgE titres were associated with reported food allergy, while a low IgE was not useful for predicting clinical symptoms.

Ongoing birth cohort studies have demonstrated that allergic IgE-mediated reactions to food allergens are common in both Estonian and Swedish infants during the first two years of life (Julge *et al*, 1997). However, the incidence of atopy in 5-y-old Estonian children is low and indicates a downregulation of allergic manifestations after 2 y of age (Julge *et al*, 2001). Our study demonstrates that IgE antibodies to food allergens, as previously shown for inhalant allergens, were uncommon in 10- to 11-y-old schoolchildren in Estonia.

The higher rates of IgE antibodies to food allergens and self-reported allergies to apple, nut, peanut, kiwi and other similar food allergens in Sweden could be consistent with the high prevalence of pollen allergy in the Swedish children, as there is a well-known crossreactivity (Vieths *et al*, 2002). It could be argued that differences in food consumption between the two countries may explain some of the differences in sensitivity to food allergens. Sweden has adopted the Western lifestyle and more imported foodstuffs and a variety of ingredients in Swedish cooking might be of importance. It is reasonable to believe that a low consumption of kiwi may contribute to the low prevalence of self-reported allergy to kiwi in Estonia. However, it is less likely that the low prevalence of food allergy to apple and nuts in Estonia could be explained by less exposure to these allergens.

The rise of allergies in westernised countries has been associated with changes in the composition of the intestinal bacterial flora. Dietary habits and handling of food affect the gut flora. The contribution of lactobacilli in the diet was reduced when deep-freezing replaced lactic acid fermentation as a method of food preservation (Bråbäck, 1999). Dietary supplementation with lactobacilli may possibly prevent atopy (Kalliomäki *et al*, 2003). The diet in Estonia is still based on locally produced food, and consumption of lactic acid-fermented vegetables is not uncommon. The intestinal microbiota in Estonian children comprises more lactic acid-producing microorganisms than in Swedish children (Sepp *et al*, 1997), and similar differences have also been detected between nonatopic and atopic children (Böttcher *et al*, 2000).

In conclusion, our study suggests that IgE-mediated food reactions were less likely among wheezing schoolchildren in Estonia. These findings are in agreement with the low prevalence of sensitisation to inhalant allergens in Estonia. Moreover, the perception of food allergy, and thereby the meaning of self-reported food allergy, appears to be different in the two countries. Differences in perception may confound international comparative studies based on questionnaires.

Acknowledgements
We wish to thank Ing-Marie Sandberg, Lena Lindell, Lena Spets, Kristina Fluur-Hedman and Karin Helgesson for performing the SPTs and the blood samples. This work was supported by a grant from the Swedish Foundation for Health Care Sciences and Allergy Research.

References

Annus T, Björkstén B, Mai XM, Nilsson L, Riikjärv MA, Sandin A & Bråbäck L (2001): Wheezing in relation to atopy and environmental factors in Estonian and Swedish schoolchildren. *Clin. Exp. Allergy* **31**, 1846–1853.

Böttcher MF, Nordin EK, Sandin A, Midtvedt T & Björkstén B (2000): Microflora-associated characteristics in faeces from allergic and nonallergic infants. *Clin. Exp. Allergy* **30**, 1590–1596.

Bråbäck L (1999): Do infections protect against atopic diseases? *Acta Paediatr.* **88**, 705–708.

Brugman E, Meulmeester JF, Spee-van der Wekke A, Beuker RJ, Radder JJ & Verloove-Vanhorick SP (1998): Prevalence of self-reported food hypersensitivity among school children in The Netherlands. *Eur. J. Clin. Nutr.* **52**, 577–581.

Gislason D, Björnsson E, Gislason T, Janson C, Sjöberg O, Elfman L & Boman G (1999): Sensitization to airborne and food allergens in Reykjavik (Iceland) and Uppsala (Sweden)—a comparative study. *Allergy* **54**, 1160–1167.

ISAAC Steering Committee (1998): Phase II Modules of The International Study of Asthma and Allergies in Childhood (ISSAC). Münster: Institute of Epidemiology and Social Medicine, University of Münster.

Julge K, Vasar M & Björkstén B (1997): The development of atopic sensitization in Estonian infants. *Acta Paediatr.* **86**, 1188–1194.

Julge K, Vasar M & Björkstén B (2001): Development of allergy and IgE antibodies during the first five years of life in Estonian children. *Clin. Exp. Allergy* **31**, 1854–1861.

Kalliomäki M, Salminen S, Poussa T, Arvilommi H & Isolauri E (2003): Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial. *Lancet* **361**, 1869–1871.

Kristjansson I, Ardal B, Jonsson JS, Sigurdsson JA, Foldevi M & Björkstén B (1999): Adverse reactions to food and food allergy in young children in Iceland and Sweden. *Scand. J. Prim. Health Care* **17**, 30–34.

Mattila L, Kilpeläinen M, Terho E, Koskenvuo M, Helenius H & Kalimo K (2003): Food hypersensitivity among Finnish university students: association with atopic diseases. *Clin. Exp. Allergy* **33**, 600–606.

Sepp E, Julge K, Vasar M, Naaber P, Björkstén B & Mikelsaar M (1997): Intestinal microflora of Estonian and Swedish infants. *Acta Paediatr.* **86**, 956–961.

Vieths S, Scheurer S & Ballmer-Weber B (2002): Current understanding of cross-reactivity of food allergens and pollen. *Ann. N.Y. Acad. Sci.* **964**, 47–68.

Woods RK, Abramson M, Bailey M & Walters EH (2001): International prevalences of reported food allergies and intolerances. Comparisons arising from the European Community Respiratory Health Survey (ECRHS) 1991–1994. *Eur. J. Clin. Nutr.* **55**, 298–304.

Woods RK, Stoney RM, Raven J, Walters EH, Abramson M & Thien FC (2002): Reported adverse food reactions overestimate true food allergy in the community. *Eur. J. Clin. Nutr.* **56**, 31–36.