

Allergen-specific sensitization in asthma and allergic diseases in children: the study on farmers' and non-farmers' children

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Summary

Background Farmers' children are less frequently sensitized to common allergens than the non-farmers' children, but less is known about their sensitization to other allergens and its association with clinical diseases.

Objective To examine the association of farm environment with atopic sensitization, allergic diseases, expression of allergen-induced symptoms, and the importance of specific sensitization against 'common' (timothy, dog, cat, birch, *Dermatophagoides pteronyssinus*, mugwort) and 'other' (cockroach, horse, *Lepidoglyphus destructor*, cow) allergens for asthma and allergic diseases in children.

Methods A cross-sectional study including 344 farmers' and 366 non-farmers' children aged 6–13 years in eastern Finland, using a self-administered written questionnaire and skin prick tests against the above-mentioned allergens.

Results Farmers' children had less asthma and allergic diseases and were less often sensitized against common allergens than the non-farmers' children. However, little difference was observed in sensitization against the other allergens between the farmers' (17.2%) and non-farmers (14.5%) children [adjusted odds ratios (aOR) 1.11 (0.71–1.72)]. Being sensitized against only other allergens, without sensitization against common allergens, was unrelated to asthma or allergic diseases. Among the single allergens, sensitization against pets or pollen, or against horse or cow, had the strongest association with asthma, hayfever, and atopic eczema; no such association was seen in *D. pteronyssinus*, mugwort, cockroach, or *L. destructor*. Farmers' children had significantly less often symptoms of allergic rhinitis in contact with dog (aOR 0.32%, 95% confidence interval (CI) 0.15–0.67), cat (aOR 0.45, 0.22–0.88), or pollen (aOR 0.58%, 95% CI 0.37–0.90) than the non-farmers' children.

Conclusion Farm environment reduces the occurrence of asthma, allergic diseases, and atopic sensitization in children, and also the occurrence of allergen-induced rhinitis. Remarkable differences were observed between single allergens in their association with allergic disease, stressing the importance of allergen selection when defining atopy in epidemiological studies.

Keywords allergen, asthma, atopy, children, cockroach, epidemiology, farm, pets, sensitization, skin prick test

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Introduction

A number of studies have recently reported an inverse association between farming environment and both allergic diseases [1, 2] and atopic sensitization [1, 3] in children. This inverse association has, for the most part, been attributed to the microbial environment of the farm on developing immune system. Recent studies suggest that the differentiation of the immune system is influenced by a complex interplay between allergens [4] and various microbial products [5]. The comparison of children living or not living on the farm has

been shown to offer a fruitful platform to study the complex association of allergic sensitization and atopic diseases in real life [1].

Although childhood asthma and allergic diseases have a strong association with allergic sensitization, there are (especially asthma) cases in which sensitization may not be important [6]. It has also been suggested that sensitization against some allergens may not be associated with asthma or allergic disease [7]. Including such allergens in the definition of atopy may reduce the likelihood of detecting clinically relevant associations between atopy and environmental exposures. In epidemiological studies, atopy is often considered as a marker of genetic predisposition towards allergy; for such purposes, the use of allergens common in the study area may be preferred. Finally, the increased prevalence and

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public awareness of childhood asthma and allergy [8] has increased allergy testing, revealing not only important information on sensitization among the symptomatic patients but also harmless sensitization not associated with allergic diseases even among the non-symptomatic children.

The objective of our study was to examine the importance of allergen-specific sensitization for asthma and allergic diseases in children, whether the risk of allergic diseases and atopic sensitization is reduced by farming environment, and whether living on a farm influences the expression of allergen-induced symptoms, when sensitization has been taken into account. These issues were studied in a cross-sectional sample of 344 farmers' and 366 non-farmers' children in Eastern Finland.

Methods

Sampling of the study population

The detailed description of the study design has recently been published [9]. Briefly, all children aged 6–13 years whose father was a farmer and who were living in the 17 communities around Kuopio town were drawn from the population register. An equal number of randomly selected children living in the same communities, whose fathers were not farmers, were drawn. Urban areas of the Kuopio town were excluded. Only one child per family, and only the children for whom maternal name was available, were included. The final number of children invited to the study was 924 (462 farmers' and 462 non-farmers' children). The mothers of these 924 children were mailed the invitation letter and the written questionnaire between January and March 2001. The study area consists of mostly rural areas with a few small towns in the Province of Eastern Finland.

Written questionnaire

The mothers of the children were asked to fill in a written questionnaire on respiratory and allergic symptoms and diagnoses of the child, including the International Study of Asthma and Allergies in Children (ISAAC) core questions [10]. The questionnaire also included questions on farming and potential confounding factors, as listed below.

Definitions

Farming. The children whose mothers answered 'yes' to the question 'Is your family involved in farming?' were defined as farmers' children.

Asthma. If a child had ever had doctor-diagnosed asthma.

Wheezing. Wheezing or whistling in the chest during the preceding 12 months [10].

Dry cough at night. Dry cough at night, not associated with cold or respiratory infection, during the preceding 12 months.

Hayfever. If a child had ever had doctor-diagnosed hayfever.

Rhinoconjunctivitis. Sneezing, or a runny, or a blocked nose apart from infections accompanied by itchy–watery eyes, during the preceding 12 months [10].

Allergic rhinitis (AR) in association with the allergen contact. Sneezing, or a runny, or a blocked nose apart from

infections, associated with the specified allergen contact, during the preceding 12 months.

Atopic eczema. If a child had ever had doctor-diagnosed atopic eczema.

Flexural dermatitis. Itchy rash coming and going for at least 6 months, affecting the folds of the elbows or knees, being present in front of the ankles, under the buttocks, or around the neck, ears, or eyes, during the preceding 12 months [10].

Skin prick tests

Skin prick tests (SPTs) were performed in the local elementary schools between January and March 2001. The testing was carried out in winter (i.e. with snow on ground) to avoid the influence of pollen season. The ALK (Allergologiska Laboratorium, Copenhagen, Denmark) allergen solutions were used. The allergens tested were birch, timothy grass and mugwort pollen, cat, dog, cow, and horse epithelial danders, cockroach (*Blatella germanica*), house dust mite (HDM) (*Dermatophagoides pteronyssinus*), and storage mite (*Lepidoglyphus destructor*). The concentration of the seven standardized extracts was 10 histamine equivalent prick (HEP); the concentrations of the three non-standardized extracts were 100 biological units (BU) (storage mite) and 1 : 100 weight/volume (cow epithelial dander and cockroach). Histamine dihydrochloride (10 mg/mL) and glycerol (50%) were used as positive and negative controls, respectively. The same batch of each solution was used throughout the study.

The tests were performed according to the ISAAC protocol by the same trained study nurse (see <http://isaac.auckland.ac.nz>). The test was regarded positive if the average diameter of the weal was at least 3 mm. The reaction produced by the positive control had to be at least 3 mm and no larger than 1 mm reactions were allowed in negative controls.

Statistical analyses

The data were analysed using STATA [11]. For categorical variables, the Pearson χ^2 test was used. Multivariate linear and logistic regression models were fitted to examine the association of SPT sensitization with asthma and allergic diseases, and the association of farming with asthma, allergic diseases, and SPT sensitization, while adjusting for potential confounders [12, 13]. Potential confounding factors that were adjusted for when reporting the odds ratios (aOR), if not mentioned otherwise, included child's gender, age, parental history of hayfever, day care attendance (> 1 month) during the first year of life, the number of older siblings (0, 1, 2, ≥ 3), and parental education (≤ 10 , 10–15, ≥ 15 years). In addition, most models were adjusted for current farming (see above for definition); inclusion of current farming has been notified in the footnotes. A two-sided α level of 5% was considered significant. The κ statistic was used for assessing cross-reactivity between sensitivity against cockroach and the other allergens [13].

Ethics

The research nurse asked an informed written consent of the mother and child during the school visit. The study was

approved by the Joint Ethical Committee for Human Research at the University of Kuopio and the Kuopio University Hospital, Kuopio, Finland.

Results

The written questionnaire was available from 765 children (82.8%), of whom 714 participated in skin prick testing (overall proportion participating 77.3%). There were more participants among the children of the farmer fathers (82.9%, $N = 383$) than among the other children (71.7%, $N = 331$) ($P < 0.001$). The age of the non-participating children (mean age 8.7 years, SD 2.3) did not differ from those who participated (mean age 9.0 years, SD 2.3) ($P = 0.11$). Among the 714 children who participated in the skin prick testing, four children were excluded because of > 1 mm reactions in the negative control. The remaining 710 children form the material of the present study. The baseline characteristics of the farmers' and non-farmers' children have recently been published [9].

Farmers' children had significantly less often dry cough at night and symptoms of rhinoconjunctivitis during the preceding 12 months (Table 1). Farmers' children also tended to have less asthma, hayfever, and wheezing, and more atopic eczema ever, although these differences did not reach statistical significance (Table 1). The farmers' children tended to be less often sensitized against most of the common

allergens when compared with the non-farmers' children. Largest differences were observed in sensitization against dog (13.9% vs. 20.9%, respectively). No significant differences were observed in sensitization against most of the other allergens; only cow sensitization tended to be more common among the farmers' children (5.2% vs. 2.6%, respectively) (Table 1). sensitization against any of the tested allergens was significantly less common among the farmers' than the non-farmers' children (Table 1).

We analysed the results on atopic sensitization in Table 1 also using the ratio of a weal of allergen vs. weal of histamine ≥ 0.5 for the definition of a positive SPT response [14]. By this definition, the prevalences of positive allergen-specific SPT reactions, and the differences between the groups, did not significantly change. If any, the prevalences tended to be slightly smaller by this definition in both farmers' and non-farmers' children (not shown). We also compared the prevalences of sensitization according to the farming status of the family during the first year of the index child, instead of the current farming status. The results remained almost identical, the differences being only slightly smaller than in the current farming (not shown).

The number of positive SPT reactions against common allergens was significantly higher among the non-farmers' than the farmers' children; the proportion of children with one positive reaction in the two groups was 13.4% and 10.1%, with two positive reactions 12.8% and 6.0%, and three or more positive reactions, 13.4% and 11.8%, respectively

Table 1. Asthma, allergic diseases, and atopic sensitization of the children, by current farming status of the family

	No farming ($N = 344$)		Yes farming ($N = 366$)		Farmers vs. non-farmers aOR (95% CI)†
	%	N	%	N	
Symptom or disease					
Asthma ever	6.7	23	5.5	20	0.73 (0.38–1.41)
Wheezing <12 months	14.5	50	10.7	39	0.69 (0.43–1.12)
Dry cough at night, not associated with infection <12 months	19.5	67	10.9	40	0.48 (0.31–0.77)**
Hay fever ever	12.8	44	9.6	35	0.61 (0.37–1.02)
Rhinoconjunctivitis <12 months	22.7	77	15.7	56	0.54 (0.35–0.82)**
Atopic eczema ever	23.2	79	24.7	90	1.31 (0.90–1.90)
Flexural dermatitis <12 months	21.9	75	21.2	77	1.02 (0.69–1.50)
Atopic sensitization					
Common allergens					
Timothy grass	20.9	72	16.1	59	0.69 (0.46–1.04)
Dog	20.9	72	13.9	51	0.68 (0.45–1.04)
Cat	18.0	62	13.7	50	0.78 (0.50–1.20)
Birch	16.3	56	11.5	42	0.70 (0.44–1.10)
<i>Dermatophagoides pteronyssinus</i>	8.1	28	6.3	23	0.60 (0.32–1.14)
Mugwort	2.0	7	3.3	12	1.91 (0.67–5.48)
Other allergens					
Cockroach	7.0	24	8.5	31	1.16 (0.63–2.15)
Horse	6.4	22	4.4	16	0.57 (0.28–1.18)
<i>Lepidoglyphus destructor</i>	4.4	15	4.4	16	0.90 (0.39–2.08)
Cow	2.6	9	5.2	19	2.10 (0.88–5.01)
Any common	39.5	136	27.9	102	0.60 (0.43–0.84)**
Any other	14.5	50	17.2	63	1.11 (0.71–1.72)
Total any positive	43.0	148	34.4	126	0.67 (0.48–0.93)*

* $P < 0.05$; ** $P < 0.01$.

†Adjusted for age, gender, parental hayfever, day care attendance during the first year of life, the number of older siblings, and parental education.

aOR, adjusted odds ratio; CI, confidence interval.

($P = 0.002$; Pearson's χ^2 ; $df = 3$). A similar trend was seen in the number of positive reactions against any allergens ($P = 0.025$). In contrast, no difference was seen in the other allergens (not shown).

Being sensitized against only other allergens, without concomitant sensitization to the common allergens, was unrelated to asthma or allergic diseases (Table 2). Those children with sensitivity against both common and other allergens had, as expected, the highest frequency of symptomatic allergy (Table 2). When looking separately at each specific allergen, there were significant differences between single allergens in association of sensitization with asthma, hayfever, or atopic eczema (Table 3). All of the three allergic diseases had a strong association with sensitization against pets, pollen, horse, and cow (Table 3), whereas sensitization against HDM, mugwort, storage mite, or cockroach was unrelated to allergic disease (Table 3). Sensitization against common allergens was present among 50–79% of the children with asthma, hayfever, or atopic eczema. Among the children with asthma, hayfever, or eczema, sensitization against common allergens identified 'atopic' cases very well; only 1–4 new cases (1.3–2.4%) would have been identified if the other allergens were included in the definition of 'atopy' (Table 3).

The prevalence of sensitization against cockroach was similar in both farmers' and non-farmers' children (7.0–8.5%) (Table 1). Of the 55 children sensitized to cockroach, 26 (47.3%) were also sensitized to at least one of the common allergens. Sensitization to cockroach was not, however, associated with diagnosed asthma, hayfever, or atopic eczema (Table 3), or wheezing, rhinoconjunctivitis, or flexural dermatitis (not shown). Actually, there were no children with asthma sensitized against cockroach. In spite of the relatively high percentage of cockroach sensitivity in our study population, the report of having seen cockroach in the surroundings of the child's home was extremely rare. Only five families (0.7%), all of which were living on a farm, reported having seen cockroach in the proximity of the house

during the last 10 years. Only three of these five families had seen cockroach during the last year. The correlation of sensitivity against cockroach with the other allergens was low: dog (κ 0.069, $P = 0.021$), cow (κ 0.021, $P = 0.27$), horse (κ 0.07, $P = 0.028$), *D. pteronyssinus* (κ 0.14, $P < 0.001$), and *L. destructor* (κ 0.24, $P < 0.001$).

The symptoms of AR induced by contact with pollen, dog- or cat were less common among the farmers' than the non-farmers' children (Table 4). The reduction of dog, and cat-induced symptoms remained significant when the models were adjusted for current dog- and cat ownership, respectively (Table 4). Further adjustment of the models by SPT sensitivity against dog or cat did not change the results (aOR (95% confidence interval) for farmers' vs. non-farmers'; dog, 0.34 (0.16–0.71); cat, 0.44 (0.22–0.89)). Likewise, the difference in pollen-induced rhinitis between the farmers' and non-farmers' children remained of borderline significance after further adjustment for sensitivity against pollen (aOR: 0.64 (0.39–1.04)). No difference was found in symptoms of rhinitis in contact with cow or horse between the farmers' and non-farmers', although the small number of children (1–3%) reporting these symptoms made proper analysis difficult (not shown).

Discussion

The main finding of our study was that there were allergens against which sensitization had no association with asthma, AR, or atopic eczema. Sensitization against common aero-allergens seemed to have the most clinical relevance. sensitization against other allergens alone (in the absence of sensitization against the common allergens) was unrelated to symptomatic allergy, but the low number of such children limits the interpretation of these findings. Another important finding was that farming environment seems to modify the

Table 2. Prevalence of asthma and allergic diseases in all the 710 children, according to the sensitivity to common and/or other allergens

Symptom or disease	% (N) aOR (95% CI)†			
	Common – other – (N = 436)‡	Common + other – (N = 161)	Common – other + (N = 36)	Common + other + (N = 77)
Asthma ever	3.7 (16)	8.1 (13)	2.8 (1)	16.9 (13)
	1.0	1.78 (0.81–3.93)	0.61 (0.08–4.95)	3.97 (1.70–9.27)**
Wheezing < 12 months	10.6 (46)	15.0 (24)	8.3 (3)	20.8 (16)
	1.0	1.09 (0.61–1.95)	0.57 (0.13–2.58)	1.80 (0.90–3.57)
Dry cough at night, not associated with infection < 12 months	12.6 (55)	17.4 (28)	11.1 (4)	26.0 (20)
	1.0	1.21 (0.70–2.08)	1.25 (0.40–3.87)	2.43 (1.28–4.63)**
Hayfever ever	3.7 (16)	24.4 (39)	2.8 (1)	30.3 (23)
	1.0	7.23 (3.73–14.0)***	0.69 (0.09–5.50)	9.89 (4.64–21.0)***
Rhinoconjunctivitis < 12 months	8.5 (36)	38.8 (62)	5.6 (2)	42.9 (33)
	1.0	7.36 (4.34–12.4)***	0.78 (0.17–3.56)	7.71 (4.05–14.7)***
Atopic eczema ever	18.7 (81)	31.5 (50)	11.1 (4)	44.2 (34)
	1.0	1.91 (1.22–2.98)**	0.44 (0.13–1.50)	3.75 (2.16–6.49)***
Flexural dermatitis < 12 months	24.5 (106)	37.3 (60)	16.7 (6)	44.2 (34)
	1.0	1.61 (1.01–2.55)*	0.76 (0.28–2.09)	2.89 (1.64–5.09)***

** $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ vs. reference group.

†Adjusted for age, gender, parental hayfever, day care attendance during the first year of life, the number of older siblings, parental education, and current farming. aOR, adjusted odds ratio; CI, confidence interval.

‡Reference group.

Table 3. Association of asthma, hayfever, and atopic eczema with specific allergen sensitization

Sensitization	% sensitized (n) aOR (95% CI)†		
	Asthma (N = 43)	Hayfever (N = 79)	Atopic eczema (N = 169)
<i>Common allergens:</i>			
Timothy grass (N = 131)	37.2 (16) 2.33 (1.17–4.67)*	60.8 (48) 8.63 (4.98–15.0)***	28.4 (48) 2.11 (1.36–3.27)**
Dog (N = 123)	48.8 (21) 4.79 (2.42–9.46)***	46.8 (37) 5.29 (3.06–9.16)***	33.7 (57) 3.97 (2.54–6.20)***
Cat (N = 112)	34.9 (15) 2.30 (1.12–4.71)*	40.5 (32) 3.75 (2.16–6.53)***	29.6 (50) 3.35 (2.11–5.31)***
Birch (N = 98)	27.9 (12) 2.38 (1.13–5.00)*	39.2 (31) 5.79 (3.27–10.3)***	29.0 (49) 3.97 (2.48–6.36)***
<i>Dermatophagoides pteronyssinus</i> (N = 50)	14.0 (6) 2.14 (0.81–5.70)	11.4 (9) 1.40 (0.57–3.45)	7.7 (13) 1.36 (0.67–2.73)
Mugwort (N = 19)	7.0 (3) 1.34 (0.28–6.49)	3.8 (3) 1.33 (0.34–5.13)	3.6 (6) 1.64 (0.59–4.60)
<i>Other allergens</i>			
Cockroach (N = 55)	0 (0) —	5.1 (4) 0.37 (0.11–1.27)	6.5 (11) 0.69 (0.32–1.49)
Horse (N = 38)	23.3 (10) 5.79 (2.35–14.3)***	21.5 (17) 9.16 (4.13–20.3)***	11.8 (20) 4.90 (2.40–10.0)***
<i>Lepidoglyphus destructor</i> (N = 31)	11.6 (5) 2.97 (0.91–9.67)	8.9 (7) 2.90 (1.06–7.92)*	6.5 (11) 2.04 (0.87–4.79)
Cow (N = 28)	16.3 (7) 6.56 (2.33–18.5)***	13.9 (11) 6.66 (2.69–16.5)***	10.1 (17) 5.33 (2.36–12.0)***
Any common (N = 237)	60.5 (26) 2.51 (1.29–4.91)**	78.5 (62) 8.30 (4.54–15.2)***	49.7 (84) 2.52 (1.72–3.70)***
Any other (N = 113)	32.6 (14) 2.24 (1.07–4.68)*	30.4 (24) 2.47 (1.38–4.43)**	22.5 (38) 1.88 (1.18–3.01)**
Total any positive (N = 273)	62.8 (27) 2.17 (1.10–4.27)*	79.8 (63) 6.84 (3.71–12.6)***	52.1 (88) 2.05 (1.40–2.98)***

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

†Adjusted for age, gender, parental hayfever, day care attendance during the first year of life, the number of older siblings, parental education, and current farming. aOR, adjusted odds ratio; CI, confidence interval.

Table 4. AR in contact with various allergens among the farmers' and non-farmers' children

AR induced by	No farming (N = 344)	Yes farming (N = 366)		Farmers' vs. non-farmers'	
	Rhinitis % (N)	Rhinitis % (N)	P	aOR (95% CI)*	P
Dog	8.7 (30)	3.8 (14)	0.007	0.32 (0.15–0.67)†	0.003
Cat	10.2 (35)	5.5 (20)	0.020	0.45 (0.22–0.88)‡	0.021
Pollen§	19.8 (68)	13.4 (49)	0.023	0.58 (0.37–0.90)¶	0.016

*All models were adjusted for age, gender, parental hayfever, day care attendance during the first year of life, the number of older siblings, and parental education.

†Adjusted for current dog ownership (further adjustment for dog sensitivity; see text).

‡Adjusted for current cat ownership (further adjustment for cat sensitivity; see text).

§Symptoms in association with pollen from flowers, hay, or trees.

¶Further adjustment for pollen (timothy grass, birch, mugwort) sensitivity; see text.

aOR, adjusted odds ratio; CI, confidence interval; AR, allergic rhinitis.

occurrence of allergen-induced symptoms and the level and development of atopic sensitization.

Large differences of sensitization against the common aeroallergens (typically including pollen, pets, and HDM) between the farmers' and non-farmers' children have been observed in a number of recent studies [9, 15–18]. On the other hand, it could be argued that the allergens important in the microenvironment of a specific child might be different in the farming and non-farming environment. In that case, ignoring the allergens typical for the farming environment

might overestimate the true difference in sensitization rates between the farmers' and non-farmers' children. However, when also including the 'farm'-related allergens into the allergen panel, such as storage mite and farm animals, the differences still exist both in the previous studies [1, 7, 19] as well as in the present study. These findings imply that the observed difference in sensitization between the farmers' and non-farmers' children is true, and is not explained by the lack of a representative allergen panel for each group of children. The lower degree of atopic sensitization among the farmers'

children, as estimated by the number of positive SPT results in our study, further support this proposal.

Although the allergen panel needs to be representative of a particular environment, the allergens should also be clinically relevant. Ernst and Carmier [7] speculated that since there was no difference in the prevalence of sensitization against farm allergens between the farmers and non-farmers, farm allergens may be less relevant to asthma. Unfortunately, Ernst et al. did not present the data on symptoms in relation with sensitization against farm allergens. In our study, sensitization against cow or horse was clearly associated with asthma, hayfever, and atopic eczema, whereas no such association was seen in sensitization against cockroach or storage mite. On the other hand, only four out of 28 cow-sensitized children reported rhinitis in association with cow contact, all four being concomitantly sensitized against common allergens. It is therefore probable that the most sensitive children have a capability for becoming sensitized against most allergens around. We also found that sensitization against other allergens alone (including farm allergens) had no association with asthma or allergic disease, suggesting that including these allergens may not give additional value when screening for atopy in epidemiological studies.

What is then the feasible selection of 'common' allergens for epidemiological studies? Such allergens clearly depend on the geographical area of the study. Our *a priori* definition of 'common' allergens included allergens (*D. pteronyssinus*, mugwort) that, albeit being of major importance in many parts of Europe and thus are hard to ignore, may have less importance in our area. Mugwort season is short and the pollen counts are relatively low in eastern Finland [20], probably explaining the low prevalence of mugwort sensitivity in our study. Likewise, HDM levels are very low in homes in eastern Finland [21], and we found only a weak association of HDM sensitization and clinical allergy. Therefore, HDM appears not to be a clinically important allergen in our area. On the other hand, some allergens, although associated with clinical allergy, may not be feasible for atopy screening since sensitization depends on the level of personal exposure (e.g. horse, cow). In such cases, sensitization may be more a marker of exposure than a marker of genetic predisposition. Therefore, when defining atopy with the aim to identify subjects with genetic predisposition to develop IgE antibodies, epidemiological surveys should use allergens that all subjects of the study population are exposed to.

To our knowledge, our study is the first one comparing the prevalence of sensitization between the farmers' and non-farmers' children in Scandinavia. Another recent study from Turku, Finland involved subjects aged 18–25 years [22]. The pattern of sensitization between the farmers' and non-farmers' children was somewhat different in our study when compared with that [22]. The most striking differences were observed in sensitization to dog. In our study, sensitization to dog was significantly less common in the farmers' children (13.9%) than in the non-farmers' children (20.9%); the figures from Turku [22] were the opposite (22.8% and 13.7%, respectively). Another striking difference was seen in sensitization against *D. pteronyssinus*, which was surprisingly common (22.0%) in subjects who grew up in the farm in childhood in the Turku study [22]. The differences in age, definition of the farm exposure, and the study area may partly

explain these findings; the study from Turku involved older subjects, considered only early childhood farm exposure, and was carried out in coastal area in South-Western Finland.

The relatively high prevalence of cockroach sensitivity in our study, 7.0–8.5%, is similar to the prevalences of 7.2% and 7.3% reported in adult populations of North-Karelia, Finland, and the Republic of Karelia, Russia, respectively [23]. An almost identical prevalence, 7.5%, was recently reported from Norway [24]. Allergen cross-reactivity seems not to be a likely explanation for these findings, since the correlation of sensitivity against cockroach and other allergens was low in our and in the Norwegian study [24]. However, the importance of cockroach sensitivity in our area remains unknown, since we found no association between cockroach sensitivity and clinical allergy in our study.

The finding of the current study on the decreased risk of AR in contact with dog, cat, or pollen among the farmers' children is in accordance with the recent study in adults [25]. These results suggest that the farming environment not only reduces the risk of sensitization against pets and pollen but also reduces the risk of symptoms in association with these allergens, of which reduction cannot be explained by differences in pet ownership or specific sensitization against these allergens. The mechanism behind this phenomena remains to be elucidated.

We included all families involved in farming in our main exposure variable, since an inverse association between farming and atopy may be seen irrespective of the farming type [9]. In addition, we used current farming instead of exposure to farming during infancy, since the effect of current exposure was stronger [9]. Moreover, there is a growing body of evidence about the importance of exposure not only in early life but also later in life [19]. Two different outcome measures were used: allergic sensitization, measured by SPT, and allergic diseases, measured by the questions from the standardized and validated ISAAC questionnaire [10]. To avoid the influence of pollen season on symptom reporting, our study was carried out in winter [26]. It is important to assess both symptomatic allergic diseases and markers of atopic sensitization as an outcome measure, since the association of the two is complex. For example, our results suggest that not all types of allergic sensitization are of importance for symptomatic allergy, and only part of the sensitized children have allergic symptoms. Finally, the finding of no statistically significant differences between farmers' and non-farmers' children with respect to asthma, hayfever, and wheezing may be explained by a relatively low number of children with these diseases.

The prevalence of asthma and wheezing symptoms [27], and of atopic eczema and AR [26] was similar in our study than previously reported from eastern Finland, with an exception of hayfever ever, whose prevalence was lower in our study than in the previous study [26]. Younger age of the children in the current study may explain this difference. In general, the figures were similar, implying that the potential for selection bias because of over-representation of the children with symptomatic allergy is probably small. Selection bias because of over-representation of farmers, or the 'healthy-farmer effect', seems unlikely as well, as discussed earlier [9].

In conclusion, sensitization to other allergens (including those typical for the farming environment) without sensitiza-

tion to common allergens may not be associated with allergic diseases in children. There are differences between various allergens in the association of sensitization with allergic disease. These findings stress the importance of allergen selection when defining atopy in epidemiological studies. Finally, farming seems to modify the association of sensitization with allergic diseases.

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