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Fewer allergic respiratory disorders among farmers′ children in a closed birth cohort from Sweden

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Fewer allergic respiratory disorders among farmers' children in a closed birth cohort from Sweden. B. Klintberg, N. Berglund, G. Lilja, M. Wickman, M. van Hage-Hamsten. ©ERS Journals Ltd 2001.

ABSTRACT: The aim of this study was to investigate the prevalence of respiratory allergy, eczema and atopic sensitization in a closed birth cohort of Swedish schoolchildren, 7–8 yrs of age (n = 707), of farmers and nonfarmers on the island of Gotland, in the Baltic Sea. All children were born and raised on the island.

The survey comprised a questionnaire on atopic diseases and lifestyle factors. Atopic sensitization was assessed by the skin-prick test (SPT) with 15 standardized allergens.

The risk ratio (RR) for ever having asthma and/or allergic rhinoconjunctivitis was significantly lower among children of farmers compared to children of nonfarmers (RR = 0.38, confidence interval (CI) 95% 0.19–0.77). SPTs (test rate 92%) showed that 32% of the children had at least one positive test. Although the number of positive SPTs did not differ between the groups, there was a reduced risk among children of farmers for having both respiratory symptoms and sensitization to any International Study on Asthma and Allergy in Childhood allergen (RR = 0.28, CI 95% 0.09–0.88).

The present indicate that living in a farming population seems to protect against development of respiratory allergic disorders but not against allergic sensitization.

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Increases in the prevalence of respiratory allergy and atopic sensitization in children have been reported from Western industrialized countries during the last decade. The reasons for this increase remains to be elucidated. Even though the influence of indoor and outdoor allergens and pollutants has been in focus, many studies support lifestyle factors as a major causative determinant in the development of atopic diseases among children. Studies from countries in Eastern Europe and around the Baltic Sea, such as Poland and Estonia, have reported a high prevalence of nonallergic respiratory diseases and a low rate of atopic sensitization despite highly polluted environments [1, 2]. Data from Germany have demonstrated an increasing prevalence of atopy in former East Germany [3]. Furthermore, children raised in cities are more prone to develop atopic disease than children from the countryside [4–5]. Recent publications indicate that living in certain environments, such as farming and anthroposophic communities, seems to protect against the development of atopic disorders [6–11]. These studies of farming have used different study cohorts and different study designs to test the hypothesis that children living on a farm have a lower prevalence of different atopic diseases compared to other children.

This study attempted to determine whether this hypothesis also pertains to a closed birth cohort in a stable island population. Therefore, the prevalence of respiratory allergic manifestations and of atopic sensitization (positive skin-prick tests (SPTs)) in a closed birth cohort, including children of farmers and nonfarmers raised on the island of Gotland in the Baltic Sea was investigated.

Methods

Study region

Gotland, with an area of 3,140 km^2, is located in the middle of the Baltic Sea and is the largest island in this arm of the Atlantic Ocean (fig. 1). The climate is maritime, even though days with rain are few compared to the rest of Sweden. There is no heavy industry on the island and the traffic is light. The population is ~60,000 and the setting is rural to semirural. About 35% of the people on Gotland are directly or indirectly involved in farming. Farms are usually of medium size (50–100 ha) compared to other Swedish farms and are run by the members of the family and only occasionally by farm workers. Eighty-five per cent of farmers on Gotland have livestock or poultry.

Study cohort

In 1996, all schoolchildren born in the year 1989 and living on Gotland (n = 855; mean age 7 yrs and 4 months (range 7–8 yrs)) were asked to participate in the study. A total of 805 children (94%) answered the study questionnaire. From data acquired in the questionnaire and information obtained from the regional birth register, 62 children were identified as not having been born on Gotland and having lived outside the island during their first year of life. All these were excluded from the cohort in order to avoid misclassification of exposure. Children who were not living in a farming environment at the time of the questionnaire, but who had previously lived in such an environment (n = 36) were analysed separately. Thus, the final population of this closed birth cohort of 707 children born in 1989 (356 boys and 351 girls) was divided into two groups of exposures, all either living in a farming environment or never having lived in such an environment.

To exclude differences in vaccination status in the birth cohort, data was obtained from the regional public health centre of Gotland. None of the children had received Bacille Calmette-Guerin (BCG)-vaccination. Conversely, nearly all children had been immunized against polio and tetanus (99.4%) as well as against measles, mumps and rubella (95.2%).

Fig. 1. – Map of Sweden and neighbouring countries with Gotland Island circled.

Questionnaire and skin-prick test

Questionnaire. A self-administered questionnaire was distributed between December 1996 and March 1997 to all families with a child born in 1989, and was answered by the parents. The questions used were identical to those in the International Study of Asthma and Allergies in Childhood (ISAAC) for children 6–7 yrs of age and they have been validated in many international studies [12]. The questionnaire contained 80 questions of which 21 were ISAAC questions on symptoms of atopic diseases. Parents were also asked questions on farming such as past and/or present farming, keeping of livestock and horses, and distance from the family houses to stable/cowshed. Further questions on breast feeding, housing conditions and family structure, household pets (past and present), horseback riding within the family (past and present), smoking habits in the families (during pregnancy, first year of life and current smoking) and manifestation of allergic disease in other family members were also included.

Classification of disease. The definitions of disease were based on answers to questions or combinations of these in the questionnaire. "Asthma ever" was defined from the questions: "ever had asthma" or "ever had doctor diagnosis of asthma". "Asthma during the last 12 months" was defined by the question: "wheezing in the previous year without upper respiratory infection". "Allergic rhinoconjunctivitis (hay fever) ever or during the last 12 months" was defined from the questions: "ever had hay fever" or "in the last 12 months, has your child had problems with sneezing or a runny or blocked nose and without a cold or a flu, accompanied by itchy-watery eyes". "Skin rash and itchiness ever or during the last 12 months" was defined by the questions; "skin rash and itchiness ever during a period of at least 6 months" or "skin rash and itchiness during the last 12 months" and "eczema ever and during the last 12 months" was defined by the questions: "ever had eczema" and "skin rash and itchiness during the last 12 months in specified skin areas". Respiratory allergic disease was defined as a combination of "asthma and/or allergic rhinoconjunctivitis (hay fever) ever or during the last 12 months".

Skin-prick tests. Between September 1997 and December 1997, three experienced nurses performed SPTs according to the instructions of the European Academy of Allergy and Clinical Immunology [13]. The quality of the SPT scoring by each nurse was measured before and after the study according to the instructions in the ISAAC protocol [14]. The coefficient of variation was 3–7% for all the nurses. To keep variability between observers to a minimum, the results of all the tests were read by the same paediatrician.

The skin reactivity to 15 standardized allergen extracts (SoluPrick SQ, ALK, Hørsholm, Denmark) was evaluated on the left and right volar aspects of the forearm, using a lancet (ALK). On the right forearm, the SPTs were done singly and consisted of pollen (birch, timothy, mugwort), animal dander (cat, dog, horse), *Alternaria alternata* and food allergens (egg, hazelnut, peanut). On the left forearm, SPTs against house dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*) and storage mites (*Lepidoglyphus destructor*, *Tyrophagus putrescentiae* and *Acarus siro*) were performed in duplicate. The potency of the allergen extracts were 10 histamine equivalent prick (HEP) for birch, timothy, mugwort, house dust mites, cat, dog and horse, 1:20 weight/volume (w/v) for Alternaria and peanut, 1:100 w/v for egg and hazelnut and 10,000 $BU \cdot mL^{-1}$ for storage mites. Histamine dihydrochloride (10 $mg \cdot mL^{-1}$) (ALK) and the diluent (glycerol 0.5 mL, sodium chloride 2.5 mg, sodium bicarbonate 1.25 mg) (ALK) served as positive and negative control, respectively. An SPT was considered positive if the weal was half the size of the positive controls or $\geqslant 3$ mm in mean diameter. Only the largest weal from the duplicate tests was registered.

Statistical analysis

Comparisons between various lifestyle factors for children exposed to farming and nonfarming environments were calculated for dichotomous variables with the Chi-squared test for difference in proportions, and for continuous variables with paired t-tests for difference of the mean. Differences in proportions and means are presented with 95% confidence intervals (95% CIs) and p-values. Comparisons between the two groups on weal size and number of positive SPTs are performed with the Kruskal-Wallis test for equality of populations and presented as p-values. Adjusted risk ratios (RR), computed as the ratio of prevalence rates for the exposed and unexposed groups, were weighted with Mantel-Haentzel weights for the adjustment factors (sex and heredity). Logistic regression was used to test different combinations of potential confounders. A statistically significant result is defined as $p < 0.05$. All statistical calculations were performed using the statistical package STATA® (College Station, TX, USA) [15].

Ethical considerations

The Ethics Committee of Karolinska Institute, Stockholm, approved the study and all families gave informed consent before entering the study.

Results

Social and demographic data

One-hundred and thirty-six children (19.2%) were found to live on a farm and the remaining 571 had never lived on a farm. The sex distribution was similar in the two groups, 49.6% young males in the farming group and 50.7% in the nonfarming group.

There was no difference in atopic heredity between farmer and nonfarmer groups. However, the smoking frequency among the mothers (current as well as former) was lower among farmers compared to nonfarmers (table 1). In the farming population, the living area in the houses was larger, but there were also more people living in the household compared to the families of nonfarmers. Thus, crowding ($m^2 \cdot person^{-1}$) was fairly similar in farming and nonfarming households (30.6 m^2 and 28.6 m^2, respectively). Use of wood-burning boilers to supply heat and hot water, having houses with passive ventilation only, and living close to cowsheds and stables was more common among the farming families (table 1).

Data concerning keeping pets and horseback riding at any time in the past are presented in table 1. Current keeping of at least one furred pet was reported by 89% of the farmers and 65% of the nonfarmers. All types of pets including rodents were more common among families of farmers. Also, current horseback riding by at least one family member was more common among the farming population (52% *versus* 27%).

Respiratory symptoms and allergic disorders

Asthma, allergic rhinoconjunctivitis and eczema had a lower prevalence among children of farmers compared to children of nonfarmers after adjustment for sex and heredity (table 2). The risk of having had asthma and/or allergic rhinoconjunctivitis and of having had eczema during the last 12 months was significantly lower among children of farmers. This was also true for asthma and allergic rhinoconjunctivitis at any time in the past. A combination outcome of asthma and/or allergic rhinoconjunctivitis also showed decreased risk for the farming children compared to those of nonfarmers (RR = 0.38; 95% CI = 0.19–0.77).

When the children of farmers were classified into groups according to whether or not they kept livestock on the farm, 90 of the 136 children had cattle on the farm and 38 did not keep cattle (for eight children there was no information on this variable). Also, the children of nonfarmers were classified into groups according to whether or not they had lived closed to stables/cow houses. A total of 188 of the 571 children had lived close to stables/cow houses, although the parents were not involved in farming or cattle rearing. Interestingly, a comparison between cattle farmers and nonfarmers without contact with a stable showed that the former had a lower risk of having asthma and/or allergic rhinoconjunctivitis ever (RR = 0.27; 95% CI 0.10–0.73).

Table 1. – Distribution of exposure factors for children living in farming and nonfarming environments in a population cohort of 7–8 yr old children on Gotland

	Farmers PE	Nonfarmers PE	Difference	95% CI	*p*-value
Subjects n	136	571			
Heredity					
Any %	38.2	36.7	1.5	(-7.5 – 10.6)	0.734
Single %	31.6	32.1	-0.5	(-9.1 – 8.2)	0.913
Double %	6.6	4.6	2.0	(-2.5 – 6.6)	0.321
Breeding					
Exclusive breast feeding months	4.33	4.40	-0.07	(-0.62 – 0.48)	0.806
Birth weight g	3512	3498	14	(-96 – 126)	0.801
Duration of pregnancy weeks	39.1	39.3	-0.2	(-0.7 – 0.2)	0.312
Smoking (mother)					
Current %	15.5	28.5	-13.0	(-20.3 – 5.7)	0.002
During pregnancy and/or the child's 1st year of life %	20.3	36.2	-15.9	(-23.9 – 7.8)	0.001
Residency					
Humid/moldy conditions (ever) %	20.5	24.2	-3.7	(-11.4 – 4.0)	0.364
Wood burning (ever) %	85.9	61.8	24.1	(17.0 – 31.3)	<0.001
Close to stable/cow house (ever) %	89.0	30.4	58.6	(52.0 – 65.1)	<0.001
Living area m^2	148.4	120.0	28.8	(18.7 – 40.0)	<0.001
Number of persons in household	5.0	4.4	0.6	(0.43 – 0.87)	<0.001
Animal exposure					
Cat (ever) %	85.2	63.3	21.9	(14.7 – 29.1)	<0.001
Dog (ever) %	58.6	34.7	23.9	(14.7 – 33.2)	<0.001
Horseback riding (ever) %	47.8	26.8	21.0	(11.7 – 30.1)	<0.001
Male children %	27.5	14.7	12.8	(1.5 – 24.2)	0.012
Famale children %	69.2	38.9	30.3	(17.7 – 42.9)	<0.001
Other family member (ever) %	55.0	24.4	30.6	(21.4 – 39.8)	<0.001
Family ever owned horses %	52.3	12.0	40.3	(31.3 – 49.3)	<0.001

PE: point estimates, proportion exposed for dichotomous exposure and mean for continuous exposure; 95% CI: 95% confidence interval of difference.

Corresponding comparisons that included not just cattle farmers but all farmers, showed higher risk estimates. Thus, for all farmers compared to nonfarmers who did not have contact with a stable, the RR was 0.36 (95% CI 0.18 – 0.73), and for all farmers compared to all nonfarmers the RR was 0.38 (95% CI 0.19 – 0.77).

Among those who had lived in a farming environment during their first year of life, but not at the time of the study, the prevalence of asthma and/or rhinoconjunctivitis ever was intermediate between the corresponding prevalence among children of farmers and nonfarmers (10.7% *versus* 6.1% and 15.8%, respectively). Note, however, that the group

Table 2. – Risk estimates for respiratory and skin symptoms in children exposed to a farming environment in a population cohort of 7–8-yr old children on Gotland

	Farming population			Nonfarming population				
	N	n	%	N	n	%	RR	(95% CI)
Symptoms last 12 months								
Asthma*	136	11	8.1	571	74	13.0	0.62	(0.34 – 1.14)
Hay fever[#]	136	5	3.7	570	52	9.1	0.40	(0.16 – 0.99)
Eczema[¶]	135	22	16.3	571	144	25.2	0.65	(0.43 – 0.97)
Rash and itchiness[+]	136	24	17.6	571	152	26.6	0.66	(0.45 – 0.98)
Asthma and/or hay fever	136	13	9.6	570	108	18.9	0.50	(0.29 – 0.87)
Symptoms ever[§]								
Asthma	134	3	2.2	570	49	8.6	0.26	(0.08 – 0.82)
Hay fever	131	5	3.8	534	52	9.7	0.39	(0.16 – 0.96)
Eczema	136	39	28.7	570	188	33.0	0.87	(0.65 – 1.16)
Rash and itchiness	136	36	26.5	571	178	31.2	0.85	(0.63 – 1.15)
Asthma and/or hay fever	132	8	6.1	538	85	15.8	0.38	(0.19 – 0.77)

N: number of children in farming or nonfarming populations included in analysis; n: number of children having a given ailment; RR: relative risk, weighted for sex and heredity. *: wheezing in the previous year without upper respiratory infection. [#]: sneezing or a runny or blocked nose and without a cold or a flu, accompanied by itchy-watery eyes, in the last 12 months. [¶]: skin rash and itchiness for at least 6 months, in specific skin areas, in the last 12 months. [+]: skin rash and itchiness in the previous year during a period of at least 6 months. [§]: questions 'ever had asthma or ever had had doctor diagnosis of asthma′, 'ever had hay fever′, 'ever had eczema′, 'ever had rash and itchiness during a period of at least 6 months′.

is very small and the RR comparing exfarmers with nonfarmers is not significant, due to a wide confidence interval, RR = 0.68 (95% CI 0.23 – 2.01).

Potential confounders such as heredity, sex, duration of pregnancy, mother's smoking during pregnancy and/or during the child's first year of life, living and housing conditions, fur exposure, horseback riding in the family and ever having lived close to stable/cow house were identified. Logistic regression models using different combinations of these exposure variables showed that they had no or almost no effect on the clinical outcome variables when comparing children of farmers and those of nonfarmers (data not shown). Although weak, the strongest confounding factor was heredity, which is why this factor was used for adjustment along with sex.

Atopic sensitization

A complete SPT panel was obtained from 650 children (92%), 127 in the farming group and 523 in the nonfarming group. The overall prevalence of at least one positive SPT among the six usual standard ISAAC allergen (pollens from birch and timothy, dander of cat, *A. alternata*, *D. pteronyssinus* and *D. farinae*) for children of farmers and nonfarmers was 30.7% and 32.7%, respectively. The prevalence of sensitization to different allergens is shown in table 3. For some allergens, children of farmers showed a reduced risk estimate for sensitization, but this was not true for other allergens. Neither the reduced nor the increased risk estimates were statistically significant, although the reduced risk for timothy and cat sensitization among children of farmers were close to significant (table 3).

The most prevalent sensitizing allergens (birch, timothy and cat) elicited an SPT reaction with an average weal diameter that was significantly smaller among farmers' compared to nonfarmers' children. The average weal sizes among farmers' and nonfarmers' children were: for birch 3.5 mm *versus* 4.6 mm (p = 0.010), for timothy 4.0 mm *versus* 5.6 mm (p = 0.043), and for cat 3.2 mm *versus* 4.6 mm (p = 0.034). On average, the farmers' children who were sensitized to any of the allergens used in SPT exhibited fewer positive SPTs (2.3 compared to 2.9 among nonfarmers' children with any sensitization, not significant).

There was a reduced risk of having both respiratory symptoms and sensitization to any ISAAC allergen in SPT for children of farmers compared to children of nonfarmers. For ever having had respiratory symptoms and any sensitization to ISAAC allergen the RR was 0.29 (95% CI 0.09 – 0.93) and for the last 12 months the RR was 0.28 (95% CI 0.09 – 0.88).

If the cut-off value for a positive SPT was raised to $\geqslant$4 mm in mean weal diameter, the farmers' children yielded reduced risk estimates for all allergens, but significance was only reached for sensitization to the ISAAC panel (RR = 0.49, 95% CI 0.28 – 0.86). Looking at having asthma and/or rhinoconjunctivitis during the last 12 months in combination with sensitization with a higher cut-off level, farmers' children compared to nonfarmers' children had a reduced risk of having current respiratory symptoms and being sensitized to any of the 15 allergens tested (RR = 0.37, 95% CI 0.13 – 0.99) (data not shown).

Exposure to furred animals and sensitization

In the whole cohort of farmers' and nonfarmers' children together, exposure to cat during the first year of life compared to no exposure was associated with a somewhat decreased risk of sensitization to cat, RR = 0.75 (95% CI 0.55 – 1.03). The relationship between early dog exposure (1 yr) and sensitization

Table 3. – Risk estimates for sensitization in children exposed to a farming environment on a population cohort of 7 – 8-yr-old children on Gotland

	Farming population		Non farming population			
	n	%	n	%	RR	(95% CI)
Subjects n	127		523			
ISAAC panel*	39	30.7	171	32.7	0.94	(0.70 – 1.25)
Birch	17	13.4	60	11.5	1.17	(0.71 – 1.93)
Timothy	11	8.7	80	15.3	0.57	(0.31 – 1.03)
Mugwort	7	5.5	37	7.1	0.78	(0.36 – 1.71)
Cat	9	7.1	71	13.6	0.52	(0.27 – 1.02)
Dog	15	11.8	50	9.6	1.24	(0.72 – 2.13)
Horse	5	3.9	20	3.8	1.03	(0.39 – 2.69)
Altemaria alternata	7	5.5	21	4.0	1.37	(0.60 – 3.16)
Storage mites[#]	11	8.7	41	7.8	1.10	(0.58 – 2.09)
House dust mites[¶]	10	7.9	48	9.2	0.86	(0.45 – 1.65)
Any mite*	18	14.2	74	14.1	1.00	(0.62 – 1.61)
Hazel nut	5	3.9	30	5.7	0.69	(0.27 – 1.17)
Egg white	1	0.8	16	3.1	0.26	(0.34 – 1.92)
Peanut	4	3.1	27	5.2	0.61	(0.22 – 1.71)

*: Birch, Timothy, Cat, *A. alternata*, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*; [#]: *Acarus siro*, *Lepidoglyphus destructor*, *Tyrophagus putrescentiae*; [¶]: *D. pteronyssinus*, *D. farinae*; [+]: Storage mites, house dust mites. RR: relative risk (weighted for sex and heredity); 95% CI: 95% confidence interval; ISAAC: international study of asthma and allergies in childhood.

to dog at the age of 7–8 yrs was similar, RR = 0.83 (95% CI 0.47–1.49). The observed negative association between early cat exposure and sensitization to cat at school age was stronger among children of farmers compared to nonfarmers' children, RR = 0.66 (95% CI 0.29–1.49) *versus* RR = 0.82 (95% CI 0.58–1.15). However, for children of farmers, the relative risk of sensitization to dog at school age and early exposure to dog was 1.23 (95% CI 0.61–2.51). In the control group of children this risk estimate revealed a negative value, RR = 0.60 (95% CI 0.26–1.39). Note that the confidence intervals are very wide due to the small numbers of children in each group.

Discussion

This closed birth cohort of 7–8-yr-old children has shown that children who have lived all their life on the island of Gotland in the Baltic Sea, have fewer atopic disorders if they were raised in a farming than in a nonfarming environment. This was true for bronchial asthma, allergic rhinoconjunctivitis and atopic dermatitis. Furthermore, there was a reduced risk among children of farmers compared to nonfarmers of having both respiratory symptoms and sensitization to any ISAAC allergen. However, farming did not influence atopic sensitization (frequency of positive SPTs), even though the weal diameter and the number of positive tests were smaller among children of farmers. When a higher cut-off level for positive SPTs was used ($\geqslant$4 mm), RR estimates were obtained for sensitization to all allergens, but significance was only reached for ISAAC allergens among farmers' children compared to nonfarmers' children. The present data are similar to recently published reports from Canada, Finland and central Europe [6–10]. Ernst and Cormier [6] in Canada, Riedler *et al.* [7] in Austria and Braun-Fahrländer *et al.* [8] in Switzerland all showed reduced risks for symptoms and for sensitization to different allergens in SPT or blood samples among children raised in farming surroundings. Ernst and Cormier [6] also demonstrated a reduced risk of asthma, defined as current wheeze and airway hyperresponsiveness in methacholine tests. In two large questionnaire studies with cross-sectional and retrospective design, Von Ehrenstein *et al.* [9] in Germany reported a reduced risk of current wheeze and hay fever ever and Kilpeläinen *et al.* [10] in Finland for having rhinoconjunctivitis diagnosed by a doctor. Compared to other studies, the strength of the present study is the stability of the population during the last decade, the high response rate to the questionnaire and the excellent participation in the SPTs. Questionnaire studies and cross-sectional design have disadvantages in relation to control of certain types of bias, such as recall bias. However, there is little reason to believe that the key exposure variable, *i.e.* farming *versus* nonfarming environment, is affected by such bias. In contrast, it is possible that parents in the farmer population have a higher "tolerance" for allergic symptoms and do not report these as much as parents in a nonfarming population. This reporting bias could only be eliminated by objective measurements. To increase the precision, a questionnaire, which has been thoroughly validated and tested, including translation and back translation has been used. Further, an SPT methodology according to ISAAC instructions for training of the field workers and counting of their precision throughout the whole study was used. To avoid selection bias in the study cohort, only children raised on Gotland and children who had or had not lived their whole life on a farm were included. Furthermore, the number of missing values was negligible. As in other studies, it is difficult to exclude, for certain, that atopic families in earlier generations have left their farms for various reasons such as allergic disease in the family. In the present study, it has been shown that the frequency of a family history of having asthma or hay fever was equal in the farming population compared to the nonfarming population. Furthermore, among those who lived in a farming environment during their first year of life, but not at the time of the study, the prevalence of allergic respiratory disorders was intermediate between the prevalence among children of farmers and nonfarmers.

Both Riedler *et al.* [7] in Austria and Von Ehrenstein *et al.* [9] in Germany have reported a lower prevalence of atopic diseases and exposure to livestock. The present study also indicated that cow farming was related to a decreased risk for development of atopic symptoms. This inverse relationship between being raised on a farm with cows and childhood allergy may have several explanations. Repeated exposure to high levels of allergens may result in tolerance, as has been documented in experimental studies and is now being discussed in relation to the perinatal period in humans [16]. Another possibility is that increased concentrations of bacterial endotoxins, including lipopolysaccharides found in cowsheds, may direct the immune response towards Th1 responses, which has been shown to suppress the development of immunoglobulin-E (IgE)-antibodies [17, 18]. Other protective factors to discuss are diet factors and especially their influence on the gut microflora, which is important in relation to atopy [19]. Animal experiments and studies *in vitro* show that lactobacilli can change the interleukin profile and inhibit antigen-induced IgE production [20, 21]. This study's results concerning exposure to furred animals and atopic sensitization are based on very few observations, which makes it difficult to draw any conclusions. Thus, the interesting question about early exposure to pets and development of sensitization or tolerance remains to be solved.

In conclusion, the present study is, to the authors' knowledge, the first investigation that is based on a whole birth cohort of 7–8-yr-old children, and which examines the farming environment with respect to development of immunoglobulin-E-mediated sensitization and allergic disease. The study shows that farmers' children compared to nonfarmers' children have a lower prevalence of atopic manifestations and, even though the prevalence of atopic sensitization was the same among the two groups, farmers' children had a reduced risk for having both respiratory symptoms

and sensitization to any International Study on Asthma and Allergy in Childhood allergen. The present results indicate that living in a firming surrounding seems to have a beneficial influence on the risk of the development of some, but obviously not all atopic phenotypes

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