Does Living on a Farm during Childhood Protect against Asthma, Allergic Rhinitis, and Atopy in Adulthood?

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Recent studies of children suggest that factors encountered in a farm environment might protect against the development of allergy. However, it remains uncertain whether living on a farm in childhood is associated with a decreased risk of atopic diseases in adulthood. We analyzed data from 6,251 randomly selected adults 20 to 44 yr of age participating in the European Community Respiratory Health Survey (ECRHS). Subjects answered a detailed questionnaire and underwent specific IgE measurements to five allergens. After adjustment for potential confounders, including pet exposure in childhood, number of siblings, severe respiratory infection in childhood, and parental history of allergy, living on a farm in childhood was associated with a reduced risk of atopic sensitization in adulthood (OR = 0.76, CI 95% = 0.60–0.97). Compared with other adults, those who had lived on a farm as a child were less frequently sensitized to cat (OR = 0.63, CI 95% = 0.41–0.96) and to Timothy grass (OR = 0.68, CI 95% = 0.50–0.94), and were at lower risk of having nasal symptoms in the presence of pollen (OR = 0.80, CI 95% = 0.64–1.02). The protective effect of farming environment in childhood observed in this population-based sample of young adults provides evidence in favor of the hypothesis that environmental factors encountered in childhood may have a lifelong protective effect against the development of allergy.

Keywords: asthma; allergic rhinitis; immunologic sensitization; farm; epidemiologic studies

It has been suggested that improvements in public health and hygiene explain the increase in prevalence of allergic diseases observed in many industrialized countries (1). A theoretical basis for this so called "hygiene hypothesis" is that the type and level of stimulation from the microbial environment may influence the postnatal differentiation of T-helper lymphocytes. A lower exposure to infectious and commensal microorganisms during childhood may be responsible for a greater susceptibility to develop allergic disease (2–4). This hypothesis provides a possible explanation for the lower risk of atopic sensitization, hay fever, and asthma observed in young children exposed to older children at home or to other children at day care (5–8). It is also consistent with the recent reports of lower prevalence of hay fever and allergic sensitization in farmers' children as compared with nonfarmers' children and adolescents (9–13) and in students who had lived on a farm as compared with other students (14). However, it remains uncertain whether the protective effect observed in children may last lifelong or disappear with cessation of exposure.

To assess whether living on a farm in childhood is associated with a lower risk of atopic disease in adulthood, we compared the prevalence of asthma, allergic rhinitis, and atopic sensitization in adults from the general population participating in the European Community Respiratory Health Survey (15), according to whether they were or were not living on a farm during childhood.

METHODS

Data were collected as part of the European Community Respiratory Health Survey (ECRHS). The methods of this international two-stage study have been described extensively elsewhere (15–17). Briefly, at Stage I, 48 study centers randomly selected samples of subjects 20 to 44 yr of age who completed a short postal questionnaire about asthma and asthmalike symptoms. At Stage II, randomly selected subsamples of responders to the postal questionnaire were then invited for further tests. The questionnaire administered in Stage II included detailed questions on asthma and asthmalike symptoms, allergic rhinitis, smoking, and home environment. A list of questions was used to assess exposure to pet animals at the moment of the study and during childhood. An additional item was included to identify subjects who were brought up on a farm in 13 centers located in five countries (Belgium, France, Netherlands, Sweden, and New Zealand). The examination also included respiratory function testing with methacholine challenge, total IgE measurement, and specific serum IgE measurements to five allergens: house dust mite (HDM) (*Dermatophagoides pteronyssinus*), cat, *Cladosporium*, and Timothy grass for all centers, plus one "local" allergen (birch for Sweden, Belgium, The Netherlands, and northern France, *Parietaria* for southern France, and ragweed for New Zealand). The protocol was approved by the local institutional review boards for human studies, and informed written consent was obtained from all the subjects before testing. Subjects were defined as current asthmatics if they had had at least one asthma attack or had taken asthma medication in the previous 12 mo. Allergic rhinitis caused by pollen was defined as a positive answer to the question "When you are near trees, grass or flowers, or when there is a lot of pollen about, do you ever get a runny or stuffy nose or start to sneeze?" Allergic rhinitis caused by animals or dust was defined as a positive answer to the question "When you are near animals such as cats, dogs, or horses, near feathers, including pillows, quilts, or duvets, or in a dusty part of the house, do you ever get a runny or stuffy nose or start to sneeze?" The response rates to Stage I and to Stage II in each of the ECRHS centers have been described elsewhere (16, 17). For the 13 centers included in the present analysis, the median response rate to the postal questionnaire was 78.1%. The median response rate to Stage II was 64.9%.

Analysis

Contingency tables were analyzed using the chi-square test (or Fisher's exact test when there were too few subjects). Data from the 13 centers were analyzed within countries. Potential heterogeneity across countries in the association between farm exposure and allergic diseases was studied, and combined odds ratio (OR_c) were derived using standard methods for meta-analysis, with country included into the model as a random effect (18). As there was no evidence for heterogeneity between countries, logistic regressions were performed to estimate adjusted OR taking potential confounders into account, with country included into the model as an additional explanatory variable. Univariate and logistic regression were carried out using the SAS-PC statistical package (Release 8.1; SAS Institute Inc., Cary, NC). Tests for heterogeneity and combined ORs from model with country as a random effect were performed using the Statistical Software STATA (Release 6.0; Stata Corporation, College Station, TX).

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RESULTS

Information on whether a subject had lived on a farm in childhood was available for 6,251 of the 6,604 subjects who attended for Stage II. The proportion of subjects who had lived on a farm in childhood ranged from 2% (Antwerp-city, Belgium) to 30% (Umea, Sweden).

The proportion of subjects with asthma and wheeze, nasal symptoms, and atopic sensitization is shown in Table 1, according to whether or not they had lived on a farm as a child, in each country. In one country, the 12-mo period prevalence of "wheezing in the chest" was higher in subjects who had lived on a farm than in those who had not, but this difference disappeared when heavy smokers were excluded from the analysis. In most countries, symptoms of rhinitis and atopic sensitization were less frequent in subjects who had lived on a farm, although the difference was generally not statistically significant. Test for heterogeneity of the association between farm exposure in childhood and the risk of allergic disorders in adulthood did not show any evidence for heterogeneity between countries. When a combined odds-ratio (OR_c) was derived from odds ratios estimated separately in each country, living on a farm in childhood was not related to the risk of asthma (OR_c = 0.82, CI 95% = 0.53–1.27) or wheeze (OR_c = 1.09, CI 95% = 0.82–1.46). Subjects who had lived on a farm as a child were at lower risk than control subjects of having nasal symptoms when exposed to pollen (OR_c = 0.78, CI 95% = 0.62–0.99) (Figure 1A). No association was found for nasal symptoms caused by exposure to animals, feathers, or dust (OR_c = 0.92, CI 95% = 0.69–1.24). Subjects who had lived on a farm were at lower risk of being sensitized to at least one of the five allergens tested (OR_c = 0.68, CI 95% = 0.55–0.86) (Figure 1B). When specific allergens were considered, the risk of being sensitized was significantly reduced in subjects who had lived on a farm during childhood, for sensitization to cat (OR_c = 0.57, CI 95% = 0.38–0.83) and to Timothy grass (OR_c = 0.64, CI 95% = 0.45–0.90) (Figure 1C and 1D). Living on a farm in childhood was associated with a less marked and less certain reduction in risk of sensitization to house dust mite (OR_c = 0.78 CI 95% = 0.58–1.03). There was little evidence for an association between early life on a farm and sensitization to *Cladosporium* (OR_c = 0.87, CI 95% = 0.40–1.90).

The distribution of sex, year of birth, smoking, and pet exposure in subjects who had lived on a farm in childhood and in those who had not is shown in Table 2. As shown in Table 2, subjects who had lived on a farm were more likely to have had a cat or a dog in childhood, had more siblings, and were more likely to have had a serious respiratory infection before the age of 5 yr than were other subjects. No difference was found with regards to parental history of allergy.

The association between the characteristics of the subject in childhood and the risk of rhinitis and atopic sensitization is shown in Table 3. After adjustment for current and past exposure to cat and dog and, for number of siblings, respiratory infection in childhood, parental history of allergy, parental smoking, current smoking, and sex, living on a farm in childhood remained associated with a significantly reduced risk of atopic sensitization, and sensitization to cat and to Timothy grass, and with a reduced risk, although not significant (p = 0.08), of nasal symptoms caused by pollen (Table 3).

As the proportion of subjects who had lived on a farm in childhood was higher in the older subjects, whereas rhinitis and atopic sensitization were more frequent in the younger, the association between farming environment in childhood and the risk of rhinitis and atopic sensitization was assessed by birth cohorts (Table 4). When year of birth was taken into account, the percentage of subjects with symptoms of rhinitis or atopic sensitization was generally lower in subjects who had lived on a farm than in other subjects, but the difference was significant only in subjects born after 1961, for sensitization to cat, and sensitization to Timothy grass.

Information on current occupation was available in 4,792 subjects. There were only 55 subjects who were working in a farm environment. The proportion of farm workers was higher in subjects who had lived on a farm when they were children (35% versus 9%; p = 0.001). However, similar results were obtained for the association between farm exposure in childhood and the risk of atopy and hay fever in adulthood, after exclusion of subjects who were currently working on a farm.

DISCUSSION

In this population-based study of adults 20 to 44 yr of age the risk of atopic sensitization was lower in those subjects who had lived on a farm when they were a child than in those who had not. Living on a farm in childhood was associated with a reduced risk of sensitization to cat or to timothy grass, and a reduced risk of having nasal symptoms in the presence of pollen, in adulthood. No association was found between a farming environment in childhood and the risk of having asthma, wheeze, or nasal symptoms in the presence of animals or dust, in adulthood.

Data on symptoms and atopic sensitization were collected in a well standardized way in random samples of young adults from the general population as part of the ECRHS (15). To our knowledge, this is the first study showing that exposure to a farm environment in childhood is associated with a decreased risk of atopic sensitization and hay fever in adulthood. A lower risk of hay fever in farmers' children has been reported in several age groups of school children in Switzerland (9, 10), in children 5 to 7 yr of age living in Germany (11), in children 8 to 10 yr of age in Austria (12), in adolescents 12 to 19 yr of age in Canada (13), and in Finnish students 18 to 24 yr

TABLE 1. PERCENTAGE OF SUBJECTS WITH ASTHMA, WHEEZE, NASAL ALLERGIES, AND ALLERGIC SENSITIZATION WHO DID NOT LIVE ON A FARM IN CHILDHOOD (CONTROL SUBJECTS) AND WHO DID LIVE ON A FARM IN CHILDHOOD

	Subjects (*n*)		Asthma (%)			Wheeze (%)			Rhinitis Grass/Pollen (%)			Rhinitis Dust/Animals (%)			Atopic Sensitization (%)		
	Control	Farm	Control	Farm	p Value	Control	Farm	p Value	Control	Farm	p Value	Control	Farm	p Value	Control	Farm	p Value
Country																	
Belgium	1,084	34	2.7	2.9	0.61	22.3	23.5	0.87	21.6	14.7	0.34	40.9	23.5	0.05	36.2	21.7	0.16
France	1,013	71	4.4	4.2	0.99	17.8	28.2	0.03	27.9	22.5	0.33	37.8	33.8	0.50	28.4	29.3	0.88
Netherlands	1,137	79	2.6	1.3	0.72	19.4	24.0	0.32	18.2	15.4	0.53	26.9	22.8	0.42	38.9	27.8	0.07
Sweden	1,546	264	5.1	4.9	0.93	26.5	25.0	0.62	28.2	20.0	0.006	28.7	28.0	0.82	32.9	24.3	0.02
New Zealand	923	100	10.6	6.2	0.18	29.1	24.0	0.29	45.3	48.0	0.61	48.1	57.0	0.09	44.3	34.9	0.15
Total	5,703	548	4.9	4.4	0.63	23.2	25.0	0.33	27.7	24.5	0.12	35.4	33.0	0.27	35.4	27.0	0.001

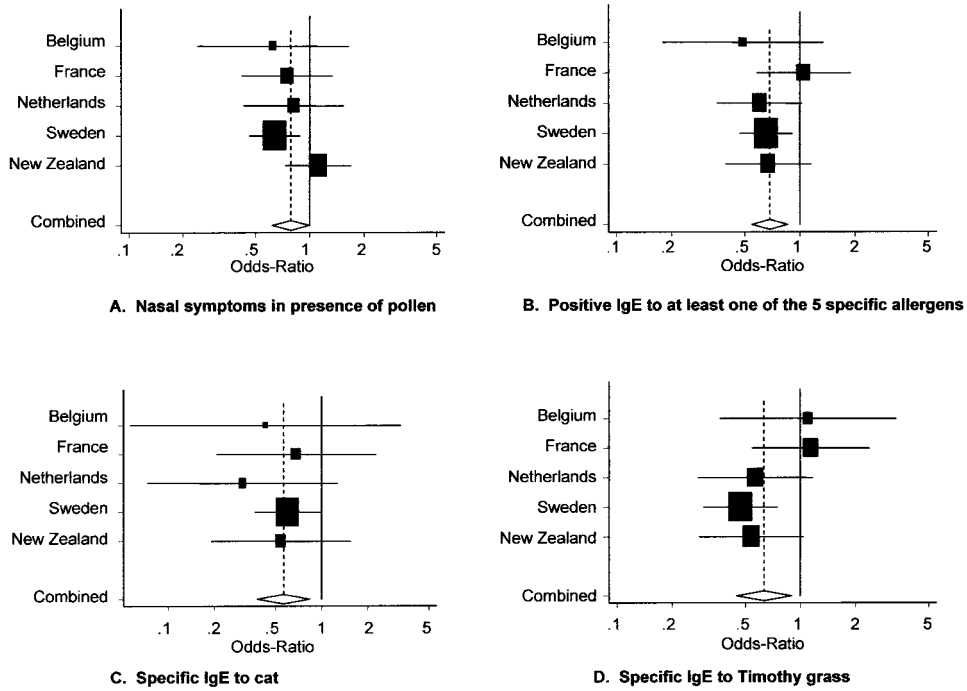

Figure 1. Odds ratios for the association between farm exposure and atopic disorder, and combined odds ratio derived using standard methods for meta-analysis, with country included into the model as a random effect. The area of each rectangle is proportional to the reciprocal of the variance of the estimate for the country. The *horizontal lines* and the *diamond* represent the width of the 95% confidence intervals of the odds ratio for each country and of the combined odds ratio, respectively.

of age (14). However, in most of these studies, the children were still living on a farm, and it remained uncertain whether farm exposure in childhood would have a long-lasting protective effect.

In the present study, the association between farm exposure and allergy was mostly seen in the younger age group. This might suggest that the protective effect of farm exposure decreases with time. However, subjects from younger age groups were from younger generations, and, because of the cross-sectional setting of the study, it is difficult to distinguish a possible interaction with age from a cohort effect. The prevalence of allergy was relatively low in the control subjects from the older generations. If individuals from older generations had encountered other protective factors, this may explain why the beneficial effect of farm is lower than in the younger. What is interesting to notice is that in control subjects we observed the generational increase that has been noticed for atopy and allergic rhinitis in western countries (19, 20), whereas in subjects who were exposed to a farming environment in childhood, there was no such generational increase.

Farm exposure in childhood has been found to be associated with a decreased risk of atopic sensitization, but the results regarding sensitization to specific allergen are not consistent (9, 10, 12). In a sample of children 13 to 15 yr of age, atopic sensitization to both outdoor allergens (Timothy grass, birch, mugwort) and indoor allergens (house dust mite, cat and dog dander) was less frequent in farmers' children than in other children (9). In another study of children 8 to 10 yr of age, living on a farm was associated with a decreased risk of sensitization to Timothy grass or birch pollen but not with sensitization to HDM and cat allergen, *Alternaria tenuis*, and *Cladosporium herbarum* (12). In our study, adults who had lived on a farm when they were children were at substantially lower risk of being sensitized to cat and to Timothy grass. Although the association between farm exposure in childhood and sensitization to HDM was weaker and not significant, the OR for HDM sensitization also showed a reduced risk in subjects who had lived on a farm.

In most studies of children, as in our study, no consistent association was found between living in a farm environment in childhood and the risk of asthma or wheeze (9, 11, 12, 14). It has been suggested that the different results observed for asthma and allergic rhinitis could be due to the large proportion of asthma cases not attributable to atopy (7, 21). In our study, 73% of asthmatic subjects had a positive specific IgE to at least one of the five allergens tested. The proportion of subjects with "atopic asthma" (i.e., current asthma and atopic sensitization) was similar among subjects who had lived on a farm in childhood and those who did not (3.6% versus 3.4%).

The negative association between farm exposure and atopic sensitization might be partly due to increased tolerance induction in subjects exposed to higher and repeated dose of aller-

TABLE 2. COMPARISON OF THE SUBJECTS WHO DID NOT LIVE ON A FARM IN CHILDHOOD (CONTROL SUBJECTS) AND SUBJECTS WHO LIVED ON A FARM IN CHILDHOOD

	Control (*n = 5,703*)	Farm (*n = 548*)	p Value
Sex, % women	52.2	48.4	0.09
Year of birth			
⩽ 1950	21.7	30.8	
1951–1960	38.8	44.7	
⩾ 1961	39.5	24.5	0.001
Smoking habits, %			
never smoker	66.1	70.5	
moderate smoker	21.3	21.1	
heavy smoker	12.6	8.5	0.02
Pets at the time of the study, %			
cat	26.3	31.6	0.008
dog	18.7	23.5	0.006
Pets in childhood, %			
cat	50.5	87.8	0.001
dog	51.2	78.8	0.001
Number of siblings, %			
0	9.7	7.0	
1	28.9	16.2	
⩾ 2	61.4	76.8	0.001
Respiratory infection in childhood, %	9.7	13.2	0.02
Parental history of allergy, %	41.5	39.1	0.3
Parental smoking, %	73.4	66.7	0.001

TABLE 3. ADJUSTED ODDS RATIOS* AND 95% CONFIDENCE INTERVALS FOR THE RISK OF ALLERGIC RHINITIS AND ATOPIC SENSITIZATION

	Rhinitis to Grass/Pollen	Rhinitis to Dust/Animals	Atopic Sensitization	Sensitization to Cat	Sensitization to Timothy Grass	Sensitization to House Dust Mite
Cat in childhood	1.05 (0.91–1.20)	1.10 (0.97–1.25)	0.96 (0.84–1.11)	0.91 (0.73–1.14)	0.94 (0.79–1.12)	0.97 (0.82–1.15)
Dog in childhood	0.94 (0.82–1.07)	1.03 (0.91–1.16)	0.85 (0.74–0.97)	0.93 (0.75–1.15)	0.87 (0.74–1.03)	0.93 (0.79–1.09)
Number of siblings†						
1	0.84 (0.67–1.07)	1.06 (0.85–1.32)	0.89 (0.69–1.14)	0.61 (0.43–0.86)	1.02 (0.76–1.38)	0.99 (0.73–1.35)
⩾ 2	0.80 (0.64–0.99)	1.00 (0.81–1.24)	0.78 (0.62–0.98)	0.59 (0.43–0.82)	0.85 (0.63–1.13)	0.90 (0.68–1.21)
Respiratory infection in childhood	1.32 (1.08–1.61)	1.54 (1.28–1.85)	1.12 (0.90–1.38)	1.32 (0.97–1.80)	1.05 (0.81–1.36)	1.21 (0.94–1.55)
Parental history of allergy	2.03 (1.79–2.29)	1.88 (1.67–2.11)	1.33 (1.17–1.52)	1.64 (1.33–2.02)	1.58 (1.35–1.86)	1.25 (1.06–1.46)
Parental smoking	1.04 (0.90–1.19)	1.01 (0.89–1.15)	0.98 (0.84–1.13)	0.81 (0.65–1.02)	0.87 (0.73–1.04)	0.94 (0.79–1.12)
Farm in childhood	0.80 (0.64–1.02)	0.97 (0.78–1.20)	0.76 (0.60–0.97)	0.63 (0.41–0.96)	0.68 (0.50–0.94)	0.81 (0.59–1.11)

* Adjusted for all variables presented in the table and for country, sex, current smoking, and current exposure to cat or dog.
† Odds ratio as compared with subjects with 0 sibling.

gens (12). If it was the case, one would expect that subjects who had lived on a farm should also be protected against sensitization to molds, which should be higher in a farm environment. However, in the present study there were very few subjects sensitized to *Cladosporium*, and the lack of association between farm exposure and sensitization to molds must be interpreted with caution.

Differences in lifestyle and other features related to the farm environment may also result in a lower risk of allergic diseases in farmers' families. In 1989, Strachan (1) speculated that infection transmitted by unhygienic contact with older siblings may prevent the development of allergic diseases. Increased number of siblings has been shown to be associated with a lower risk of atopy or allergic rhinitis in several studies (1, 6, 22–25). An inverse association between family size and atopy has already been described in the ECRHS (6, 23). In the present analysis, subjects who had lived on a farm during childhood were more likely to belong to larger families, but the protective effect of living on a farm was not explained by differences in the number of siblings.

Another possible explanation for the lower risk of atopic diseases in subjects who had lived on a farm is that, over generations, atopic families may have stopped farming because of symptoms related to exposure. However, the proportion of subjects with a parental history of allergy was similar in control subjects and subjects who had lived on a farm, suggesting that there was not such a "healthy farmer effect." Moreover, when the analysis was rerun only in subjects with no history of parental allergy, the results were virtually the same (results not shown).

Subjects who had lived on a farm in childhood were more likely to have had a cat or a dog in childhood. Pet exposure in childhood has been shown to be associated with a reduced risk of atopy and hay fever (6, 26–28). However, the protective effect of farm environment was still observed after pet exposure was taken into account. Exposure to other animals on farms may be responsible for the independent association observed between farm exposure and the risk of atopy and hay fever. In one study, regular contact with livestock and poultry was found to explain the association between farming and atopy (12), and in another, an inverse dose-dependent relationship was observed between frequency of contact with livestock and the risk of atopic diseases (11). It has been suggested that increased exposure to airborne bacterial compounds in stables where livestock is kept might prevent the development of allergy by triggering maturation of Th-1-type cells, thereby downregulating IgE levels (3, 11, 29). Lipopolysaccharides de-

TABLE 4. PERCENTAGE OF SUBJECTS WITH ALLERGIC RHINITIS AND ATOPIC SENSITIZATION, AND ASSOCIATION BETWEEN FARM EXPOSURE AND THE RISK OF ALLERGIC RHINITIS AND ATOPIC SENSITIZATION, ACCORDING TO YEAR OF BIRTH

	Year of Birth ⩽ 1950 (*n = 1,406*)	Year of Birth 1951–1960 (*n = 2,460*)	Year of Birth ⩾ 1961 (*n = 2,383*)
Rhinitis to grass/pollen, %	24.9	28.0	29.8†
Control	24.1	27.8	29.4†
Farm	23.7	24.6	25.4
Adjusted OR, (95% CI)*	0.96 (0.60–1.53)	0.80 (0.57–1.14)	0.74 (0.46–1.17)
Atopic sensitization, %	28.4	34.2	39.8†
Control	28.5	34.6	40.3†
Farm	23.6	27.8	30.1
Adjusted OR, (95% CI)*	0.89 (0.55–1.43)	0.85 (0.58–1.22)	0.67 (0.41–1.08)
Sensitization to cat, %	6.3	9.3	12.9†
Control	6.5	9.2	13.7†
Farm	5.0	9.1	4.9
Adjusted OR, (95% CI)*	0.82 (0.32–2.12)	0.89 (0.50–1.57)	0.31 (0.11–0.88)
Sensitization to Timothy grass, %	11.4	17.3	24.9†
Control	11.2	17.5	25.6†
Farm	9.3	15.7	11.7
Adjusted OR, (95% CI)*	1.09 (0.55–2.15)	0.94 (0.59–1.48)	0.37 (0.18–0.73)

* Odds-ratios and 95% confidence intervals (95% CI) for the risk of allergic rhinitis and atopic sensitization in subjects who had lived on a farm as compared with control subjects, adjusted for current and past exposure to cat and dog, and for number of siblings, respiratory infection in childhood, parental history of allergy, parental smoking, current smoking, sex, and country.
† $p < 0.01$ for the test for trend of a increasing frequency of rhinitis or atopic sensitization in younger generations.

rived from the cell walls of gram-negative bacteria are recognized as potent enhancers of interleukin (IL)-12 and interferon gamma production, and increased house-dust endotoxin concentrations have been shown to correlate with enhanced Th1-type cell response (2, 3, 30). Recently, Von Mutius and colleagues (29) have reported increased concentration of endotoxin in dust samples from houses and mattresses of children with regular contact to farm animals when compared with children from nonfarming families. Among other factors related to the farm environment that may result in a reduced risk of allergy, diet may play a role, either directly or through its effects on the intestinal microflora (31–37). The intestinal microflora is a source of bacterial stimulation that may exert a continuous pressure on the immune system (31). Higher counts of lactobacilli and eubacteria have been found in the intestinal microflora of infants from Estonia (where the prevalence of allergy is relatively low) as compared with infants from Sweden (32). It has been suggested that the consumption of mostly industrially processed and sterilized foods in Western Europe may have resulted in a reduction of lactic acid producing microbes (32, 33), whereas the ingestion of traditionally processed food, not treated with antimicrobial preservatives, may help to prevent the development of atopy (34). In the same way, the frequent consumption of vegetables preserved by spontaneous fermentation (in which live lactobacilli are common) may partly explain the lower risk of atopy observed in children of families with an anthroposophic lifestyle (35). Recently, research on the prophylactic use of probiotic bacteria suggested that administration of specific strains of *Lactobacillus* may have a beneficial effect in the treatment of food allergy and prevention of atopic eczema (36, 37). The effect of specific factors such as diet or contact with livestock should be thoroughly investigated in further studies.

In the present study we showed a negative association between farm exposure in childhood and the risk of atopy and hay fever in adulthood. This finding provides evidence in favor of the hypothesis that environmental factors encountered in childhood may have a lifelong protective effect against the development of allergy.

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APPENDIX

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