

Which factors explain the lower prevalence of atopy amongst farmers' children?

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Summary

Background The inverse association between farming and atopy in children has been attributed to microbial exposure, especially through livestock. Very little is known about other potential explanatory factors.

Objective To explore potential differences in lifestyle and environmental factors between farmer and non-farmer families, and whether these factors could explain the association between farming and childhood atopy.

Methods A cross-sectional study, including 366 farmers' and 344 non-farmers' children in eastern Finland. Information regarding exposure and background characteristics was gathered by a written questionnaire. Atopy was defined as having one or more positive skin prick test reactions (> 3 mm) against the six common aeroallergens.

Results Regardless of the current farming type, atopy was less frequent among the farmers' children than the non-farmers' children (aOR 0.56, 95% CI 0.40–0.78). Remarkable differences were seen in many lifestyle factors (including diet) between the farmer and non-farmer families, but only a few of the explored factors were associated with atopy. The frequency of current livestock contacts seemed to have an inverse, dose-dependent association with atopy (aOR 0.46, 95% CI 0.22–0.97 for daily vs. no contact). Having lived on a dairy farm in infancy (aOR 0.51, 95% CI 0.28–0.93), or having had cats or dogs in infancy (aOR 0.60, 95% CI 0.42–0.85), decreased the risk of atopy at school age. The inverse association between farming and atopy was not explained by the sociodemographic factors, or by differences in conventional risk factors of atopy. Animal contacts explained partially, but not completely, the association.

Conclusion Higher frequency of animal contacts is one factor, but probably not the only one, explaining the inverse association of farming and atopy in children. The importance of early life exposures may have recently been over-emphasized, and current exposures discounted, when studying the risk factors of childhood atopy.

Keywords atopy, children, epidemiology, farm, risk factors, skin prick test

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Introduction

Farmers' children have been shown to have smaller risk of both allergic sensitization [1–6] and symptoms of allergy [1, 3, 5–9] than their non-farmer peers. The reduced risk has been attributed to the exposure to a farm-related microbial environment, especially the microbial exposure by the livestock animals [3, 10, 11]. The microbial matter is easily brought inside the farmers' homes [11, 12]. Thus, even newborn children can be exposed to the microbial matter of the stables, as measurable levels of such matter are carried into the farmers' bedrooms and mattresses [11].

It seems reasonable to assume that there are also additional factors to the microbial exposure that could partially explain the inverse association between farming and childhood allergy. A few years ago a study from Sweden found a significantly lower risk of atopy among the children from families adopting the anthroposophic lifestyle [13]. Farmer families may resemble these families in the respect that they often have a more traditional lifestyle when compared with non-farmer families. For example, there may be differences in diet, exercise level, the use of medications, or the exposure to air pollution, just to mention a few. All of these factors have been associated with atopy, although the results have often been controversial [14]. However, studies assessing potential explanatory factors (other than microbial exposure) for an inverse association between farming and allergy in children are scarce.

We compared the prevalence of atopic sensitization amongst 366 farmer's and 344 non-farmer's children, and explored the environmental factors that could explain the potential

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differences in atopy among the farmers' and non-farmers' children.

Materials and methods

Sampling of the study population

The study area consisted of mainly rural areas with few small towns in the province of Eastern Finland, including the 17 communities around Kuopio town. From this area, all children ($n = 1011$) aged 6 to 15 years whose fathers were farmers, and an equal number of randomly selected children whose fathers were not farmers, were drawn from the population register in November 2000. The sample was subsequently restricted to the elementary-school children (age 6 to 13 years) in order to keep the number of required school visits to a feasible level. The resulting sample included 715 farmers' and 806 non-farmers' children. From these 1521 children, only children whose mothers lived at the same address as the child were included (694 farmers' and 780 non-farmers' children). Furthermore, only one (randomly selected) child per each farmers' family was included, and for each child a randomly selected control (one control per family) was drawn from the same community. Thus, 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 mothers of the children filled in a written questionnaire on background characteristics, dietary habits, pet ownership, various family and environmental exposures, and farming characteristics, such as the presence of livestock. Diet was assessed by using the questions from the FINRISK study [15] and the PARSIFAL study (unpublished), and partially by the questions developed for this study. The food frequency questionnaire was not used. The children whose parents answered 'yes' to the question 'Is your family involved in farming?' in the written questionnaire were defined as farmers' children.

Atopy was used as the main outcome variable in this study. The children with positive reactions against one or more of the following allergens were defined as having atopy: birch, timothy grass and mugwort pollens, cat and dog epithelial danders, and house dust mite (*Dermatophagoides pteronyssinus*). Skin prick tests were performed in the local elementary schools between January and March 2001. The testing was carried out in winter (i.e. with snow on the ground) to avoid the influence of the pollen season. The standardized ALK (Allergologiska Laboratorium, Copenhagen, Denmark) allergen solutions, same batches throughout the study, were used. The concentration of the extracts was 10 HEP (HEP = histamine equivalent prick). Histamine dihydrochloride (10 mg/mL) and glycerol (50%) were used as positive and negative controls, respectively. 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. In addition, 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.

Study of mothers

Mothers of the index children were subsequently invited to a parallel study on allergies and farming environment among farmers' wives. This study started shortly after the main study, in February 2001; all the mothers of the children joining the study from February onwards were invited to the study on mothers. Mothers were administered a separate written questionnaire on maternal diseases and exposures. Some questions on perinatal exposures of the index children were added to the end of the maternal questionnaire.

Statistical analyses

The data were analysed using STATA [16]. For categorical variables, the Pearson chi-squared test was used. In addition, logistic regression was used for categorical exposure variables for testing trends. Uni- and multivariate logistic regression models were fitted to examine the association between exposure variables and atopy, the association between environmental or lifestyle characteristics and farming, and to adjust for potential confounders [17]. 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 years, 10 to 15 years, ≥ 15 years). In addition, the models assessing the risk factors of atopy were adjusted for current farming (see above for definition). The possibility of effect modification by parental atopy, or by current farming, was evaluated by adding the appropriate interaction terms into the logistic models. A two-sided alpha level of 5% was considered significant.

Ethics

The research nurse asked for 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

Characteristics of the study population

The questionnaire was returned by 765 children (82.8%), of whom 714 participated in skin prick testing (overall participation percentage 77.3%). The children of the farmer fathers participated more often (82.9%, $n = 383$) than the other children (71.7%, $n = 331$) ($P < 0.001$). No significant differences were observed in the age of the non-participating children (mean age 8.7, SD 2.3) and 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 due to > 1 mm reactions in the negative control. The remaining 710 children form the material for the present study.

Farmers' children tended to be older (mean age (SD): 9.4 (2.3) years) than the non-farmers' children (mean age 9.0 (2.3) years) ($P = 0.013$). Interestingly, the proportion of children whose parents or grandparents had quitted farming, or avoided becoming a farmer, was almost identical among the current

farmers' and non-farmers' children (Table 1). The farming status of the family *per se* changed in one-tenth of all children between infancy and the present time (Table 2).

Lifestyle factors

In general, there were no significant associations between conventional risk factors of atopy and farming (Table 1). Among the early life exposures (Table 2), smoking during the first year of the index child was more common among the non-farmer mothers (11.9%) and fathers (36.9%) than among the farmer mothers (4.1%) or fathers (19.7%) (mothers $P < 0.001$; fathers $P < 0.001$). No association was observed with the duration of breast-feeding and farming (not shown).

As expected, farming was associated with many 'traditional lifestyle' factors (Table 1). However, no significant differences were seen in reporting of visible dampness or mould between the farmer (10.7%) and non-farmer homes (8.4%) ($P = 0.31$), or in reporting of mould odours in farmer (6.8%) and non-farmer (6.7%) homes ($P = 0.94$). Likewise, the children's current frequency or level of exercising was neither associated with farming nor with atopy (not shown).

Diet

Farmers' children used more often butter (farmers 9.8% vs. non-farmers 2.3%, respectively) or butter-oil mix (42.1% vs. 29.5%) and less often margarine (44.0% vs. 67.1%) on bread than the non-farmers' children ($P < 0.001$). A similar trend was seen in the use of fat in cooking. Farmers' children drank full milk or farm milk daily more often (37.4% vs. 4.1%, $P < 0.001$), and skim milk less often (18.1% vs. 32.3%, $P < 0.001$), than the non-farmer's children. None of these factors, however, was significantly associated with atopy (Table 1 and 2).

Interestingly, the consumption of fresh vegetables seemed to be inversely associated with atopy (Table 1). This inverse association was stronger for vegetables grown on the farm or on a nearby farm, than for vegetables bought from the grocery store (not shown). The association did not significantly change if the children reporting avoidance of certain foods due to allergy were excluded. In contrast, the consumption of boiled vegetables, or fruit and berries, was not significantly associated with atopy.

Eating any kind of fish at least once a week was more common amongst the non-farmers' than the farmers' children (32.6% vs. 24.9%, respectively, $P = 0.023$); no such association was observed in oily fish (5.2% vs. 7.1%, $P = 0.30$). No consistent associations were seen in the consumption of eggs, yoghurt, meat or sausage, or whole meal products and farming. Only a few families used organic foods (8.3%) or fermented vegetables (0.8%). None of these dietary factors was, however, associated with atopy (not shown).

Farm type

Atopy was less frequent among the farmers' children (27.9%, $n = 102$) than among the non-farmers' children (39.5%, $n = 136$). The inverse association between farming and atopy was seen irrespective of the type of farming, although it was significant only for dairy or other livestock farming (Table 1). No significant interactions were found between farming and parental asthma, hayfever or eczema in relation to atopy in children (not shown).

Livestock and household pets

Having had animals in infancy, either pets or livestock, was inversely associated with atopy at school age (Table 2); the children with both livestock and household pets in infancy had about 60% lower risk of atopy, when compared with the children with no animals (Fig. 1). Excluding the children whose families had reported avoidance or removal of household pets due to allergy did not significantly alter the results (not shown).

Also, current animal ownership (either livestock or pets) was inversely related to atopy (Table 1). In addition, a dose-response relationship was observed between the frequency of current livestock contacts and atopy (Table 3). This inverse trend was similar for all types of livestock, although a small number of children in each subgroup made the numbers unstable. The avoidance of animal contacts due to asthma or allergy seemed not to be responsible for this trend, as the results remained stable if the children reporting avoidance were excluded, or if they were re-classified as being exposed to livestock (not shown).

The risk of atopy was lowest amongst the children whose families had some sort of animals (either livestock, dogs or cats), both currently and when the child was an infant (aOR 0.47, 95% CI 0.28–0.76), followed by those who had animals only currently (aOR 0.59, 0.32–1.09), and those who had animals only in infancy (aOR 0.65, 0.31–1.36), when compared with the children with animals neither currently nor in infancy. These findings were relatively similar when dogs, cats or livestock animals were analysed separately. The influence of animal exposures on atopy in children was similar irrespective of the farming status or parental history of hayfever (not shown).

Combined analysis

Although the conventional risk factors of atopy were significantly associated with atopy in our study, they were not able to explain the lower risk of atopy among the farmer's children (Table 4). Neither adding the sociodemographic factors nor sibling or day care exposure in infancy to the logistic model were able to change the farming-atopy association; only addition of animal contact variables into the models significantly reduced the farming effect. However, although animal exposure seemed to be an important determinant of the farming-atopy association in children, animal exposure could not entirely explain the inverse association between farming and atopy.

Discussion

There were three main results in our study. First, a reduced prevalence of sensitization against common aeroallergens was observed among the farmer's children, irrespective of the farming type. Secondly, despite identifying extensive differences in many lifestyle and environmental characteristics between the farmer and non-farmer families, only a few of these factors were able to explain the lower frequency of atopy among the farmer's children. Thirdly, our results support the previous observations on possible protective effect of exposure to animals, either livestock [18] or household pets [19], on atopic sensitization.

Our results on the lower risk of atopy among the children of families with cats, dogs or livestock are in agreement with the

Table 1. Home, family and farming characteristics between the current farmers' and non-farmers' children, and association of these factors with atopy at school age

Risk factor	Percentage (n) children with a risk factor		<i>P</i> ‡	Adjusted† odds ratio (OR) for atopy OR (95%CI)
	Non-farmers' children (<i>n</i> = 344) % (<i>n</i>)	Farmers' children (<i>n</i> = 366) % (<i>n</i>)		
Farming				
No	—	—		1.0
Yes, part or full time				0.56 (0.40–0.78)***
Main line of production at present				
No farming	99.7 (343)	0 (0)	< 0.001	1.0§
Dairy farming	0 (0)	53.6 (196)		0.62 (0.41–0.93)*
Other livestock	0.3 (1)¶	15.3 (56)		0.46 (0.23–0.89)*
Plant farming	0 (0)	28.4 (104)		0.67 (0.40–1.10)
Other or not defined	0 (0)	2.7 (10)		0.31 (0.40–1.10)
Dogs at home at present				
No	59.9 (206)	43.7 (160)	< 0.001	1.0
Yes	40.1 (138)	56.3 (206)		0.74 (0.52–1.04)
Cats at home at present				
No	74.4 (256)	33.1 (121)	< 0.001	1.0
Yes	25.6 (88)	66.9 (245)		0.66 (0.45–0.96)*
Dogs or cats at home at present				
No	48.3 (166)	18.3 (67)	< 0.001	1.0
Yes	51.7 (178)	81.7 (299)		0.61 (0.42–0.88)**
Gender				
Male	51.7 (178)	51.9 (190)	0.96	1.0
Female	48.3 (166)	48.1 (176)		0.61 (0.44–0.85)**
Parental hayfever				
No	44.4 (144)	49.9 (176)	0.16	1.0
Yes	55.6 (180)	50.1 (177)		1.54 (1.10–2.16)**
Parental education				
≤ 10 years	11.8 (40)	14.1 (51)	0.44	1.0
10–15 years	53.2 (181)	48.8 (177)		0.92 (0.55–1.54)
≥ 15 years	35.0 (119)	37.2 (135)		0.93 (0.54–1.61)
				<i>P</i> for trend 0.87
Number of older siblings				
0	30.3 (104)	23.2 (85)	< 0.001	1.0
1	39.4 (135)	29.0 (106)		0.75 (0.49–1.15)
2	22.2 (76)	29.8 (109)		0.98 (0.62–1.55)
≥ 3	8.2 (28)	18.0 (66)		0.58 (0.32–1.06)
				<i>P</i> for trend = 0.28
Years in the current house				
≤ 6 years	43.6 (150)	12.0 (44)	< 0.001	1.0
7–17 years	48.0 (165)	46.7 (171)		1.12 (0.73–1.70)
≥ 17 years	8.4 (29)	41.3 (151)		0.81 (0.46–1.43)
				<i>P</i> for trend = 0.56
Child's bedroom floor				
Wood	32.6 (112)	42.9 (157)	0.017	1.0
Plastic	64.2 (221)	54.6 (200)		1.09 (0.77–1.54)
Other	3.2 (11)	2.5 (9)		0.75 (0.27–2.08)
Fireplace in use				
No	18.9 (65)	4.4 (16)	< 0.001	1.0
Occasionally	65.1 (224)	74.0 (271)		1.29 (0.74–2.25)
Regularly	16.0 (55)	21.6 (79)		1.07 (0.56–2.06)
				<i>P</i> for trend = 0.95
Consumption of fresh vegetables				
Less than once per week	14.8 (51)	16.1 (59)	0.63	1.0
1–6 times per week or more	85.2 (293)	83.9 (307)		0.60 (0.38–0.95)*
				<i>P</i> for trend = 0.95

Usual type of fat in cooking††				
Vegetable oil	25.1 (85)	17.6 (64)	< 0.001	1.0
Margarine	31.9 (108)	14.8 (54)		1.21 (0.74–1.99)
Butter-margarine mix	17.7 (60)	19.0 (69)		1.20 (0.71–2.03)
Butter	25.4 (86)	48.6 (177)		1.08 (0.68–1.73)
				<i>P</i> for trend = 0.86
Quitted farming due to allergy				
No	89.7 (280)	89.2 (295)	0.83	1.0
Yes, parents	2.6 (8)	2.1 (7)		0.79 (0.25–2.49)
Yes, grandparents	7.7 (24)	8.8 (29)		0.87 (0.45–1.71)

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. †Adjusted for gender, age, parental hay fever, parental education, the number of older siblings, day care during the first year of life, and current farming. ‡The difference in exposure or characteristic between the farmers' and non-farmers' children. §Current farming omitted from the model due to collinearity. ¶The family with a horse stable. ††Mutually exclusive groups; in subjects with multiple responses the group with the highest animal fat content has been appointed. The six cases reporting no use of fat were excluded.

Table 2. Exposure to environmental factors during the first year of life among the farmers' and non-farmers' children, and association of these factors with atopy at school age

Risk factor	Percentage (<i>n</i>) children with a risk factor		<i>P</i> ‡	Adjusted† odds ratio (OR) for atopy OR (95%CI)
	Non-farmers' children (<i>n</i> = 344) %(<i>n</i>)	Farmers' children (<i>n</i> = 366) % (<i>n</i>)		
Farming in infancy				
No	89.5 (308)	7.9 (29)	< 0.001	1.0
Yes, part or full time	10.5 (36)	92.1 (336)		0.68 (0.48–0.95)*§
Main line of production in infancy				
No farming	89.5 (308)	7.9 (29)	< 0.001	1.0
Dairy farming	4.7 (16)	55.7 (204)		0.68 (0.46–1.00)
Other livestock	2.6 (9)	17.2 (63)		0.51 (0.28–0.93)*
Plant farming	2.6 (9)	17.5 (64)		0.74 (0.42–1.32)
Other or not defined	0.6 (2)	1.6 (6)		0.46 (0.09–2.38)
> 1 month in day care during the first year of life				
No	85.4 (293)	94.3 (345)	< 0.001	1.0
Yes	14.6 (50)	5.7 (21)		0.54 (0.29–0.99)*
Dogs at home in infancy				
No	67.6 (232)	53.0 (193)	< 0.001	1.0
Yes	32.4 (111)	47.0 (171)		0.74 (0.53–1.05)
Cats at home in infancy				
No	76.4 (262)	48.6 (51.4)	< 0.001	1.0
Yes	23.6 (81)	51.4 (187)		0.82 (0.57–1.19)
Dogs or cats at home in infancy				
No	56.0 (192)	31.3 (114)	< 0.001	1.0
Yes	44.0 (151)	68.7 (250)		0.60 (0.42–0.85)**
Maternal smoking in infancy				
No	88.1 (303)	95.9 (351)	< 0.001	1.0
Yes	11.9 (41)	4.1 (15)		0.64 (0.32–1.27)
Use of farm milk in infancy¶				
No	91.0 (202)	51.0 (123)	< 0.001	1.0
< 1 time/week	3.6 (8)	11.6 (28)		0.92 (0.40–2.11)
1–6 times/week	4.1 (9)	11.2 (27)		0.95 (0.41–2.22)
Daily	1.4 (3)	26.1 (63)		1.16 (0.59–2.29)
				<i>P</i> for trend 0.73

* $P < 0.05$, ** $P < 0.01$. †Adjusted for gender, age, parental hay fever, parental education, the number of older siblings, day care during the first year of life, and current farming. ‡Farmers vs. non-farmers. §Current farming omitted from the model due to collinearity. ¶Information available only for part of the children (*n* of missing equally common in both farmer and non-farmer groups).

proposal that animal-derived endotoxin or other microbial products may decrease the risk of atopy in children [20, 21]. The results from Austria support this idea [18], showing a significant weakening in the association between farming and atopy (from OR 0.48 (0.30–0.75) to OR 0.75 (0.37–1.52)) only after adding regular contact to livestock into the multivariate model. As in their study, the impact of livestock was stronger in our data than that of pets (not shown). A heavier level of microbial exposure through livestock, in comparison with household pets, might be a likely explanation for these findings. An alternative explanation is that massive animal allergen

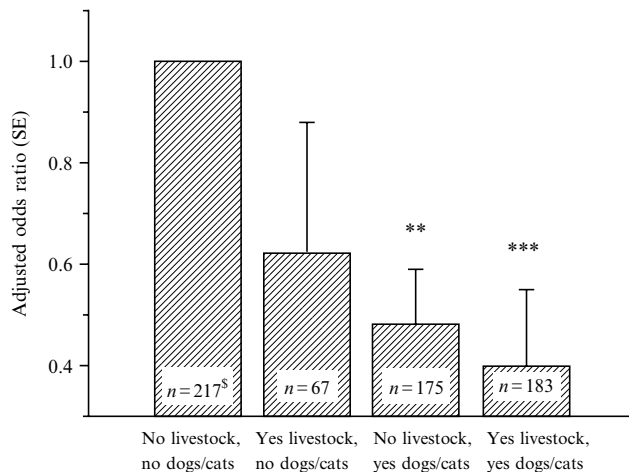


Fig. 1. The risk of atopy in children, according to whether the families had or did not have livestock and/or household pets (cats or dogs) during the first year of life of the index child. ** $P < 0.01$, *** $P < 0.001$ vs. reference group. (P -values adjusted for gender, age, parental hayfever, parental education, day care during the first year of life, farming during the first year of life, and the number of older siblings; logistic regression.) \$Reference group. SE = standard error.

exposure decreases the risk of atopy by tolerance induction [22]. Animal exposure may thus involve multiple, simultaneous and interacting mechanisms that determine the final impact of exposure on the atopic phenotype [23].

Although animal exposures were able to explain a significant proportion of the 'farming effect' on atopy, they were unable to explain the entire difference. These findings suggest that there are still other, unknown factors related to farming that could partially explain the lower prevalence of atopy amongst the farmer's children. However, despite large differences in the family and lifestyle characteristics between the farmers and non-farmers, very few of these factors were associated with atopy or explained the reduced risk of atopy among the farmer's children. Similar observations were made in the study from Austria [18]. We were especially curious to see whether any of the dietary differences might have explained the farming effect. A study from Austria, Germany and Switzerland suggested that consumption of unpasteurized farm milk in early life might protect against the development of atopic diseases, possibly due to microbial contamination of the farm milk [3]. However, we were unable to repeat these findings. In Finland, the amount of consumption of pure farm milk is probably small in infancy, as it is recommended to give either breast-milk or formulas for infants until the age of 1 year. There may also be variation in the microbial content of farm milk between the countries. The influence of recall bias can not be excluded, as the infant dietary data were collected retrospectively. More studies are clearly needed to further evaluate the possible atopy-protecting effects of farm milk.

Among the other dietary factors, only consumption of fresh vegetables seemed to be inversely related to atopy. This finding might be explained by soil-derived microbial content or by the vitamin E content of fresh vegetables [24]. The former explanation seems more likely, given the stronger association for vegetables grown on the farm or a nearby farm compared with the vegetables bought from the grocery store. It has been

Table 3. The association of atopy with the frequency of current livestock contacts among all children

Frequency of livestock contacts	Atopic % (n)	OR crude (95% CI)	OR adjusted (95% CI)*
No (n = 176)	44.9 (79)	1.0	1.0
Occasional (n = 358)	31.3 (112)	0.56 (0.39–0.81)	0.65 (0.43–0.96)
Weekly (n = 113)	29.2 (33)	0.51 (0.31–0.84)	0.73 (0.41–1.28)
Daily (n = 62)	21.0 (13)	0.33 (0.17–0.64)	0.46 (0.22–0.97)
P for trend		< 0.001	0.048

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

Table 4 The association of current farming and atopy, and the influence of different model adjustment on this association

Model*	OR for atopy	95%CI	P
Current farming†	0.59	0.43–0.81	0.001
+ sociodemographic factors‡	0.58	0.42–0.81	0.001
+ older siblings and day care§	0.56	0.40–0.78	0.001
+ animals, infancy¶	0.68	0.47–0.98	0.040
+ animals, current**	0.74	0.50–1.10	0.13

*The model in each row includes all variables mentioned in the previous rows. †Unadjusted model. ‡Gender, age, parental hayfever, and parental education. §The number of older siblings, and being > 1 month in day care during the first year of life. ¶The presence of animals (dogs, cats or livestock) at home in infancy. **The presence of animals (dogs, cats or livestock) at home currently.

suggested that the changes in dietary fatty acids, including increased use of *trans* fatty acids [25] and polyunsaturated fatty acids [26], may have contributed to the increased prevalence of atopy [27]. However, we were unable to show consistent associations between the consumption of dietary fat, or any other specific foods, and atopy. One explanation for these negative findings could be measurement error, as accurate measurement of diet is difficult [28]. The influence of diet on the development of atopy remains to be elucidated. Various elements of the diet, approached as different foods and as various dietary constituents [28], should all be considered.

It is important to consider the possibility of bias in a cross-sectional study like this. We noted that the farmers' children participated slightly more often than the non-farmers' children. However, to explain the inverse association between farming and atopy entirely by selection bias, the proportion of atopic children among the non-participating farmers should have been much higher relative to the non-participating non-farmers, which we think is not probable. The selection bias due to the 'healthy farmer effect', i.e. the selective avoidance of farming by atopic families, seems improbable as well. The proportion of parents or grandparents who had quitted or not become farmers due to allergy was equal among the farmers' and non-farmers' children; even if all the non-farmer children of these families were re-defined as atopic, the inverse association between farming and atopy remained. In livestock exposure, taking reported avoidance of animal contacts into account in the analyses did not significantly influence the results. Recent studies showing significantly increased concentrations of microbial products (endotoxin) in the homes of farmers with livestock [11] suggest that it would actually be difficult, if not impossible, to avoid exposure to animal-derived material while living on a livestock farm. Finally, excluding the children of families reporting avoidance or removal of household pets due to allergy from the analyses related to cats and/or dogs and atopy slightly weakened, but never reversed, the inverse association.

We used skin prick test reactivity as an outcome measure. Skin prick tests offer an objective marker of atopic sensitization, avoiding the potential for reporting bias. Our definition of atopy was based on sensitization against any of the allergens that we considered as common in our area. House dust mite may be an exception, as it is not ubiquitous in our climate. Excluding house dust mite from the definition of atopy, however, did not change our results, and there was no difference in house dust mite sensitization between the farmers' and non-farmers' children.

A recent study compared the prevalence of atopy among the conscripts and young farming students in Denmark [29]. That study showed lowest prevalences of atopic sensitization among the farmers who had grown up on a farm. However, also the farmers who had not grown up on a farm had lower prevalences of atopy than the controls. It could be argued that avoidance of farming, i.e. the 'healthy farmer effect', could explain the latter findings. However, in spite of differences in markers of atopic sensitization, the differences in symptoms were minor between the controls and the farmers not grown up on a farm, arguing against the possibility of selection bias [29]. Also, in our study the inverse associations between the farm-related exposures and atopy were stronger for the current exposures than for those encountered in infancy. In addition, we observed the dose-response relationship between atopy and the frequency of

current livestock contacts. Although greater measurement error for previous exposure may partially explain our results, they are in agreement with the proposal that also exposures after early life may influence the degree of atopic sensitization [29]. Therefore, the importance of exposures in infancy may have recently been over-emphasized.

In conclusion, our results agree with the earlier reports on lower prevalence of atopy in children living on a farm. Increased exposure to livestock or household pets seems to be a likely factor, but probably not the only one, which explains the decreased prevalence of atopy amongst farmers' children. In addition to early life, also later exposures may influence the occurrence of atopic sensitization. The potential influence of diet on atopy or on the relationship between farming and atopy deserves further investigation.

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References

- Braun-Fahrlander C, Gassner M, Grize L et al. Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. SCARPOL team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution. *Clin Exp Allergy* 1999; 29:28–34.
- Pekkanen J, Xu B, Jarvelin MR. Gestational age and occurrence of atopy at age 31 – a prospective birth cohort study in Finland. *Clin Exp Allergy* 2001; 31:95–102.
- Riedler J, Braun-Fahrlander C, Eder W et al. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *Lancet* 2001; 358:1129–33.
- Downs SH, Marks GB, Mitakakis TZ, Leuppi JD, Car NG, Peat JK. Having lived on a farm and protection against allergic diseases in Australia. *Clin Exp Allergy* 2001; 31:570–5.
- Ernst P, Cormier Y. Relative scarcity of asthma and atopy among rural adolescents raised on a farm. *Am J Respir Crit Care Med* 2000; 161:1563–6.
- Leynaert B, Neukirch C, Jarvis D, Chinn S, Burney P, Neukirch F. Does living on a farm during childhood protect against asthma, allergic rhinitis, and atopy in adulthood? *Am J Respir Crit Care Med* 2001; 164 (10, Part 1):1829–34.
- Kilpeläinen M, Terho EO, Helenius H, Koskenvuo M. Farm environment in childhood prevents the development of allergies [see comments]. *Clin Exp Allergy* 2000; 30:201–8.
- Klintberg B, Berglund N, Lilja G, Wickman M, van Hage-Hamsten M. Fewer allergic respiratory disorders among farmers' children in a closed birth cohort from Sweden. *Eur Respir J* 2001; 17:1151–7.
- von Ehrenstein OS, Von Mutius E, Illi S, Baumann L, Bohm O, von Kries R. Reduced risk of hay fever and asthma among children of farmers [see comments]. *Clin Exp Allergy* 2000; 30:187–93.
- Lewis SA. Animals and allergy [editorial; comment]. *Clin Exp Allergy* 2000; 30:153–7.
- von Mutius E, Braun-Fahrlander C, Schierl R et al. Exposure to endotoxin or other bacterial components might protect against the development of atopy. *Clin Exp Allergy* 2000; 30:1230–4.
- Pasanen AL, Kalliokoski P, Pasanen P, Salmi T, Tossavainen A. Fungi carried from farmers' work into farm homes. *Am Ind Hyg Assoc J* 1989; 50:631–3.

- 13 Alm JS, Swartz J, Lilja G, Scheynius A, Pershagen G. Atopy in children of families with an anthroposophic lifestyle. *Lancet* 1999; 353:1485–8.
- 14 von Mutius E The environmental predictors of allergic disease. *J Allergy Clin Immunol* 2000; 105 (1, Part 1):9–19.
- 15 Vartiainen E, Jousilahti P, Alfthan G, Sundvall J, Pietinen P, Puska P. Cardiovascular risk factor changes in Finland, 1972–97. *Int J Epidemiol* 2000; 29:49–56.
- 16 Stata Corporation. Stata Statistical Software: Release 7.0. College Station, Texas: Stata Corporation, 2001.
- 17 Hosmer DW Jr., Lemeshow S. *Applied Logistic Regression*. New York: John Wiley & Sons, 1989.
- 18 Riedler J, Eder W, Oberfeld G, Schreuer M. Austrian children living on a farm have less hay fever, asthma and allergic sensitization [see comments]. *Clin Exp Allergy* 2000; 30:194–200.
- 19 Svanes C, Jarvis D, Chinn S, Burney P. Childhood environment and adult atopy: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; 103 (3, Part 1):415–20.
- 20 Bischof W, Koch A, Gehring U, Fahlbusch B, Wichmann HE, Heinrich J. Predictors of high endotoxin concentrations in German homes. *Proc Healthy Buildings* 2000; 1:251–6.
- 21 Liu AH. Endotoxin exposure in allergy and asthma: reconciling a paradox. *J Allergy Clin Immunol* 2002; 109:379–92.
- 22 Platts-Mills T, Vaughan J, Squillace S, Woodfolk J, Sporik R. Sensitisation, asthma, and a modified Th2 response in children exposed to cat allergen: a population-based cross-sectional study. *Lancet* 2001; 357:752–6.
- 23 Gereda JE, Klennert MD, Price MR, Leung DY, Liu AH. Metropolitan home living conditions associated with indoor endotoxin levels. *J Allergy Clin Immunol* 2001; 107:790–6.
- 24 Fogarty A, Lewis S, Weiss S, Britton J. Dietary vitamin E, IgE concentrations, and atopy. *Lancet* 2000; 356:1573–4.
- 25 Weiland SK, von Mutius E, Husing A, Asher MI. Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe. ISAAC Steering Committee. *Lancet* 1999; 353:2040–1.
- 26 Dunder T, Kuikka L, Turtinen J, Rasanen L, Uhari M. Diet, serum fatty acids, and atopic diseases in childhood. *Allergy* 2001; 56:425–8.
- 27 Kankaanpää P, Sutas Y, Salminen S, Lichtenstein A, Isolauri E. Dietary fatty acids and allergy. *Ann Med* 1999; 31:282–7.
- 28 Willet W. *Nutritional Epidemiology*, 2nd edn. Monographs in Epidemiology and Biostatistics, Vol. 30. New York: Oxford University Press, 1998.
- 29 Portengen L, Sigsgaard T, Omland O, Hjort C, Heederik D, Doekes G. Low prevalence of atopy in young Danish farmers and farming students born and raised on a farm. *Clin Exp Allergy* 2002; 32:247–53.