

Original article

Exposure to pets, and the association with hay fever, asthma, and atopic sensitization in rural children

Background: An increasing number of studies report pet exposure to be associated with lower risk of asthma and allergies. This 'protective pet effect' has been suggested to result from a modified T-helper (Th)2-cell response, or because of increased microbial load in homes where pets are kept. We examined the associations between pet contact and the occurrence of asthma and allergies in children of the rural Allergy and Endotoxin (ALEX) population, taking farm animal contact, endotoxin and cat allergen levels in mattress dust into account.

Methods: Information about contact with pets and farm animals, asthma and allergy were collected for 812 children by a standardized parents' questionnaire and an interview. Mattress dust endotoxin and cat allergen levels as well as specific IgE and IgG4 antibodies to Fel d1 were determined.

Results: Current contact with dogs was inversely associated with diagnosed hay fever (OR 0.26, 95% CI 0.11–0.57), diagnosed asthma (OR 0.29, 95% CI 0.12–0.71), sensitization to cat allergen (OR 0.48, 95% CI 0.23–0.99) and to grass pollen (OR 0.55, 95% CI 0.33–0.94), but not with increased IgG4 levels. Early and current contact with cats were associated with reduced risk of wheezing (OR 0.48, 95% CI 0.23–1.00, and OR 0.49, 95% CI 0.26–0.92, respectively) and grass pollen sensitization. Adjustment for farm animal contact but not for endotoxin and cat allergen exposure attenuated these associations and the effect of pet was stronger among farmers' children.

Conclusion: Although pet exposure was very frequent in this rural population, the inverse relation between current dog contact, asthma and allergy was mostly explained by simultaneously occurring exposure to stable animals or was restricted to farm children. In addition, a subtle form of pet avoidance may contribute to the protective effect of pet.

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Regular contact with stable animals has been shown to confer protection against the development of asthma and allergy in children (1–3). The amount of family farming activities, and the degree of the child's presence in stables and contact with farm animals have been shown to predict endotoxin levels in the mattresses of these children (4). Several studies suggest, that high endotoxin levels in mattress or floor dust of children are associated with a reduced risk for atopic diseases (5–8).

Yet, children in rural environments are not only exposed to farm animals but have frequent contact with pets as well. The role of pet exposure in the development of asthma and allergy is still controversial. An increasing number of studies, including a series of cohort studies support the notion of a protective 'pet effect' (9–13). Others, however, found an increased risk of sensitization associated with pet exposure (14–16) or no association between cat allergen exposure early in life and the

occurrence of asthma (17). It has been suggested that the 'protective effect' of pet keeping on asthma and allergy might be the result of a modified T-helper (Th)-2 cell response as exposure to cat allergen has been shown to produce IgG and IgG4 antibody response without sensitization or risk of asthma (18). Others have speculated that the inverse relation between pet exposure and the development of atopic sensitization, hay fever and asthma might be explained by the higher endotoxin levels found in homes where cats and dogs are kept (19). This view has been challenged by a recent longitudinal study from the US (20), reporting exposure to high levels of cat allergen and having a dog in the home to be associated with decreased risks for wheezing, independent of the effect of endotoxin in house dust.

The Allergy and Endotoxin (ALEX) study (5, 21) including school-aged children from rural areas of Germany, Switzerland and Austria provides a good

opportunity to evaluate these hypotheses as we not only measured endotoxin and the major allergen of cat dander, Fel d1, in the mattresses of the children but ascertained the details of timing, frequency, and intensity of children's exposure to pet as well as farm animals in a interview with the child's mother. In addition to specific IgE measurements in the serum samples of the children, IgG4 measurements were performed as well.

The aim of the present analysis was to evaluate the role of contact with cats or to dogs in this rural, partially farming population on the occurrence of asthma and allergy and to examine whether contact with farm animals, increased levels of cat allergen or endotoxin in house dust might explain the pet effect.

Materials and methods

Study population

The cross-sectional survey ALEX (Allergy and Endotoxin) was performed in rural areas of Austria, Germany and Switzerland as previously described (5, 21). In brief, 2618 of 3504 (74.7%) participating families consented to the measurement of specific IgE and IgG4 in their children's serum, and to the collection of dust samples from the respective child's mattress. Of these 1406 (53.7%), all children from farming families, all children from nonfarming families who reported regular contact with a farm environment, and a random sample of children from nonfarming families who were not exposed to a farm environment were invited to participate ($n = 901$). The final analysis was restricted to 812 children (319 farmers' children and 493 children from nonfarming families) with complete data and similar ethnic origin – as German, Austrian and Swiss nationality. The study population was representative of the rural population in the participating areas (21).

Approval to conduct the study was obtained from the three local ethics committees for human studies and from the principals of the schools attended by the children. Written informed consent was obtained from the parents of all children.

Parents' questionnaire and interview

Demographic factors, potential explanatory and confounding factors, and the prevalence of diseases and symptoms were assessed by a questionnaire given to the parents that included the questions of the International Study of Asthma and Allergies in Childhood (ISAAC) (22), as described previously (21). In an interview with the parents as part of the home visit, we obtained details of the timing of the child's exposure to pets and to farming activities. Exposure to pets was defined as contact with cats only, to dogs only and to dogs and cats. As few children were reported to have contact with dogs only, a variable combining any contact with dogs was used in the regression analyses. Contact with pets during the past 12 months (current) was distinguished from pet contact during the first year of life. Pet avoidance because of asthma or someone having an allergy in the family was assessed by asking 'Did you ever implement any action to reduce allergen levels in your house? If yes, did you remove any pets?' Exposure to farming during the first year of life was defined as exposure to stables during the first year of life, consumption of milk directly from the farm during the first year of life, or both. The child's current exposure to farm animals was expressed as a 'stable activity score', combining regular contact with

stable animals (No/Yes) and the frequency of staying in a stable (never/rarely or several times per week/at least daily). The score ranged from 0 (no contact with stable animals and never in a stable) to 3 (regular contact with stable animals and daily stable visit).

Dust collection

We collected with ALK filters (ALK, Copenhagen, Denmark) by vacuuming every mattress for 2 min/m² of surface area after removal of all sheets apart from mite impermeable mattress encasings and plastic sheets following the ISAAC phase II protocol (<http://isaac.auckland.ac.nz>). The material obtained was divided into two parts for the measurement of endotoxin and allergen content. All seven field workers (three in Germany, two in Austria, and two in Switzerland) were trained to ensure uniformity in sampling, using a standardized protocol.

Endotoxin and allergen analysis

Of the dust samples, one was stored at room temperature and transported in endotoxin-free vials within 1 week after collection to the central laboratory of the Institute for Occupational and Environmental Medicine of the University of Munich, Germany. Endotoxin content was measured by a kinetic limulus assay, and the details are given in Ref. (4). All endotoxin levels were within the limits of detection of the assay. The second dust sample was frozen at -20°C for at least 2 days and then transported to the Allergy Laboratory of the Department of Paediatric Pneumology and Immunology University Children's Hospital, Charité, Berlin, Germany (S. Lau), and stored at 4°C until it was analysed for *Felis domesticus* Fel d1 as previously described (14). The lower limit of detection was 16 ng Fel d1/g of dust. For allergen levels below the detection limit (0.2% of all measures), half the detection limit was considered.

Testing for specific IgE and IgG4 in serum

The level of specific IgE against airborne allergens in all serum samples was measured by fluorescence enzyme immunoassay (Pharmacia CAP System; Pharmacia Diagnostics AB, Uppsala, Sweden) in a central laboratory (Allergy Laboratory of the Department of Paediatric Pneumology and Immunology University Children's Hospital, Charité, Berlin, Germany). The serum concentration of specific IgE raised against a panel of aeroallergens (mixed-grass pollen, birch pollen, mugwort pollen, *Dermatophagoides pteronyssinus*, cat dander, dog dander and *Cladosporium herbarum*) was measured in all samples by fluorescence enzyme immunoassay (SX1, CAP; Pharmacia). In children with a positive SX1 result, responses to specific allergens (grass pollen, birch pollen, *D. pteronyssinus*, and cat dander) were measured. We defined atopic sensitization as at least one positive specific IgE test result of 0.35 kU/l or greater for the eight aeroallergens but additionally considered a cut-off level of 3.5 kU/l [corresponding to radioallergosorbent test (RAST) class 3 or higher] in the analyses.

IgG4 antibodies specific to cat dander were measured using fluorescent-enzyme immunoassay (FEIA) (CAP; Pharmacia) and diluting samples 1 : 10 in diluents provided with the kit. All measurements were conducted in a central laboratory (Respiratory Center, Tucson, AZ, USA). Allergen-specific IgG4 were expressed as microgram per litre. The limit of sensitivity of the assay was 15 µg/l, and undetectable samples (1.4% of all measures) were assigned a value of 10 µg/l. The mean IgG4 antibodies to Fel d1 was

121 kU/l (SD 170). IgG4 antibody levels were dichotomized into high and low levels using the median of 86.3 kU/l as cut-off.

Statistics

Chi-square statistics, geometric means, 95% confidence intervals, and *t*-test on log-scale data were calculated to describe differences in exposure characteristics of children exposed or not exposed to pets. Logistic regression models were performed to study the association between pet exposure, and asthma, hay fever and atopic sensitization. In our basic model we adjusted for sex, age, study area, family history of asthma or hay fever, parents' educational levels, number of older siblings, and pet avoidance because of asthma or allergies in the family. In addition, sensitivity analyses of the association between current pet exposure and allergy outcomes were performed by sequentially including pet exposure in the first year of life, endotoxin levels in mattress dust (log-transformed, EU/m²), cat allergen levels in mattress dust (log-transformed, µg Fel d1/g), farming exposure in the first year of life, and the child's current stable activity. To evaluate a potential interaction between pet exposure and the child's farming status, we ran the basic model for farmers' children and nonfarmers' children separately. We also included an interaction term for pet exposure and farming status in the logistic regression analyses and calculated likelihood ratio tests (LRT) for interaction. Besides including a variable for avoidance of pets because of asthma or allergies in the family into the basic model, we also restricted the analyses to families who did not report pet avoidance to evaluate the effect of residual confounding. As families with a history of asthma or hay fever might be less prone to keep pets, the analyses were repeated restricting the sample to children without a family history of asthma or hay fever. Data analysis was performed with STATA 8 (Stata corporation, College Station, TX, USA). A two-sided alpha level of 5% was considered significant.

Results

The study population consisted of 319 farmers' children with a mean age of 9.42 years (SD 1.63), and 493 children from nonfarming families, living in the same rural areas with a mean age of 9.49 years (SD 1.60). Fifty-one per cent of all children were boys. Farmers' families and nonfarming families of the respective study area differed in many socio-demographic and lifestyle aspects as previously described (1, 4, 23). Table 1 presents the exposure characteristics of the study population, stratified by the child's farming status. Farmer's children were significantly more likely to have contact with pets currently and during the first year of life and to be involved in farming activities. However, because of our selection procedure, contact with the farm environment was also quite common among nonfarmers' children. Only 1.7% (14/812) of the families reported avoidance of pets because of someone having allergy in the family. Although higher levels of endotoxin were found in mattress dust of farm children, no significant differences were observed with respect to Fel d1 levels.

Figure 1A,B displays the levels of Fel d1 and endotoxin in mattress dust of school-aged children exposed to pets

Table 1. Exposure characteristics of the study population

	Farmers' children [n = 319; n (%)]	Nonfarmers' children [n = 493; n (%)]	P-value*
Contact with pets in the first year of life			
No	109 (34.2)	330 (67.1)	<0.001
Cats only	92 (28.8)	97 (19.7)	
Dogs only	26 (8.2)	25 (5.1)	
Dogs and cats	92 (28.8)	40 (8.1)	
Current contact with pets			
No	30 (9.4)	179 (36.5)	<0.001
Cats only	129 (40.6)	166 (33.8)	
Dogs only	12 (3.8)	36 (7.3)	
Dogs and cats	147 (46.2)	110 (22.4)	
Pet avoidance due to asthma or allergies in the family	2 (0.6)	12 (2.4)	0.034
Exposure to farming in the first year of life†	274 (85.9)	203 (41.2)	<0.001
Current exposure to farm animals‡			
0	4 (1.3)	141 (28.8)	<0.001
1	22 (6.9)	164 (33.5)	
2	138 (43.5)	162 (33.1)	
3	153 (48.3)	22 (4.5)	
Current mattress endotoxin levels (EU/mg of dust)	37.8 (35.5–40.2)	22.8 (21.5–24.1)	<0.001
[geometric mean (95% CI)]			
Current mattress cat allergen levels (µg Fel d1/g of dust)	5.41 (4.40–6.63)	5.80 (4.61–7.30)	0.673
[geometric mean (95% CI)]			

The values are n (%).

* P-value for farmers' children vs nonfarmers' children.

† First stay in stable and farm milk consumption in the first year of life.

‡ Stable activity score: regular contact with farm animals (no, yes) and frequency of staying in stable (never, at least weekly, at least daily).

in the first year of life and currently. Contact with cats in the first year of life and currently specifically increased Fel d1 levels, whereas endotoxin levels were associated with pet keeping, in general.

The results of the basic multivariate regression model examining the association between pet exposure and allergy endpoints are given in Table 2. Exposure to cats only during the first year of life tended to be associated with a reduced risk for wheezing ($P = 0.050$), sensitization to cat allergen (RAST class ≥ 1) ($P = 0.061$), and grass pollen sensitization (RAST class ≥ 3) ($P = 0.021$), but not with overall sensitization (SX1). There was also a negative association with diagnosed asthma in sensitized children, however, because of the reduced numbers, the confidence intervals were wide. Exposure to dogs in the first year of life was not associated with any of the clinical outcomes, but was inversely associated with sensitization to grass pollen (RAST class ≥ 3) ($P = 0.039$) and non-significantly with cat dander. Current contact with dogs, however, was inversely associated with most of the clinical outcomes as well as with sensitization to cat allergen (RAST class ≥ 1) ($P = 0.047$) and grass pollen (RAST class ≥ 3) ($P = 0.029$). Current exposure to cats

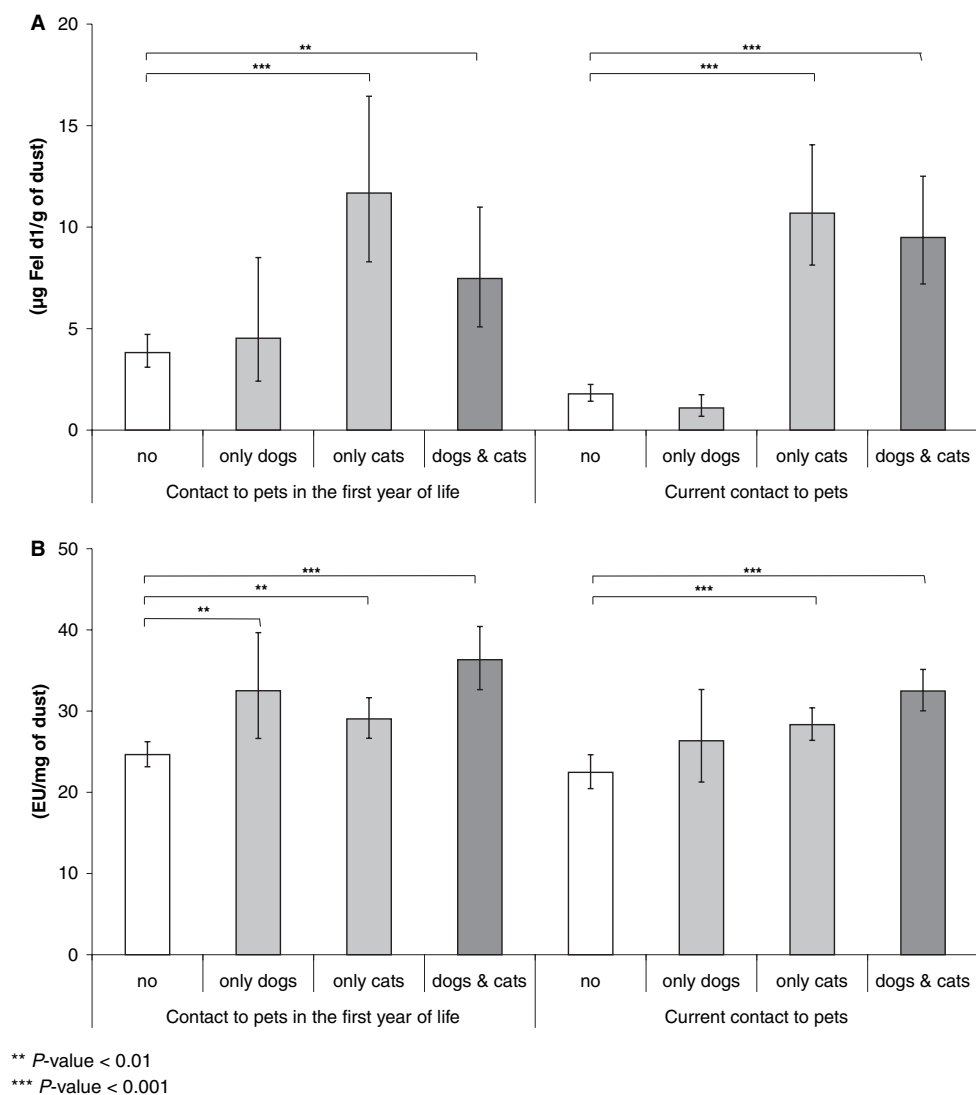


Figure 1. Mattress cat allergen (µg Fel d1/g) and endotoxin (EU/mg) levels (geometric means and 95% CI) of children with contact with pets.

only showed no association with hay fever and diagnosed asthma. Yet, an inverse association was observed for diagnosed asthma in sensitized children ($P = 0.035$), for wheezing ($P = 0.025$) and sensitization to grass pollen (RAST class ≥ 3) ($P = 0.027$). IgG4 against cat allergen was slightly but nonsignificantly increased in children with exclusive early ($P = 0.261$) and current ($P = 0.131$) contact with cats. When the analyses were repeated excluding all children from families who reported pet avoidance, or restricted to children without a family history of atopic diseases, the results remained essentially the same (data not shown).

To evaluate the effect of a series of variables that might explain or confound the association between current exposure to dogs and allergy outcomes we added these variables sequentially to the basic model as shown in Table 3. Adjustment for pet exposure in the first year of

life strengthened the inverse association with hay fever and diagnosed asthma but attenuated the association with sensitization to grass pollen. Inclusion of current endotoxin and cat allergen exposure did not greatly attenuate the association between current contact with dogs and allergic symptoms. However, adjustment of farming exposure in the first year of life, and particularly current exposure to stable and farm animals reduced the effect of dog exposure for most outcomes, although the inverse association between dog exposure and diagnosed hay fever and diagnosed asthma remained statistically significant. The analyses were then repeated for the subsamples of children from farming and nonfarming families. Among farmers' children current exposure to dogs was associated with a reduced risk for all investigated health endpoints, although due to the small sample size the confidence intervals were very wide. Among

Table 2. Associations between pet exposure and asthma and allergy

	Raw prevalence [n (%)]	Exposure to pets in the first year of life* [adj. OR (95% CI)§]		Current exposure to pets† [adj. OR (95% CI)§]	
		Cats only	Dogs‡	Cats only	Dogs‡
Diagnosed hay fever	65 (8.0)	0.69 (0.34–1.41)	0.64 (0.30–1.36)	0.84 (0.45–1.57)	0.26 (0.11–0.57)
Current hay fever symptoms	81 (10.1)	0.97 (0.51–1.85)	0.94 (0.50–1.79)	0.86 (0.47–1.56)	0.39 (0.20–0.78)
Diagnosed asthma	57 (7.0)	0.85 (0.40–1.81)	0.90 (0.39–2.05)	0.85 (0.43–1.66)	0.29 (0.12–0.71)
Asthma in sensitized	39 (4.9)	0.58 (0.21–1.59)	0.64 (0.21–1.90)	0.39 (0.16–0.93)	0.22 (0.08–0.63)
Current wheeze	79 (9.9)	0.48 (0.23–1.00)	0.76 (0.39–1.46)	0.49 (0.26–0.92)	0.57 (0.31–1.04)
Wheezing in sensitized	44 (5.8)	0.60 (0.23–1.55)	0.99 (0.43–2.30)	0.45 (0.19–1.04)	0.56 (0.25–1.27)
Atopic sensitization SX1					
RAST class ≥ 1	289 (35.6)	0.94 (0.63–1.39)	0.77 (0.51–1.16)	1.27 (0.84–1.91)	0.91 (0.60–1.38)
RAST class ≥ 3	171 (21.1)	0.81 (0.50–1.30)	0.72 (0.44–1.19)	0.94 (0.59–1.51)	0.78 (0.48–1.26)
IgE against grass allergen					
RAST class ≥ 1	208 (25.7)	0.87 (0.56–1.34)	0.75 (0.48–1.17)	1.01 (0.65–1.56)	0.75 (0.48–1.18)
RAST class ≥ 3	119 (14.7)	0.50 (0.28–0.90)	0.55 (0.31–0.97)	0.55 (0.32–0.94)	0.55 (0.33–0.94)
IgE against cat allergen					
RAST class ≥ 1	69 (8.5)	0.47 (0.21–1.04)	0.59 (0.27–1.29)	0.76 (0.39–1.47)	0.48 (0.23–0.99)
RAST class ≥ 3	20 (2.5)	0.42 (0.10–1.73)	0.39 (0.08–1.92)	0.51 (0.16–1.71)	0.34 (0.09–1.35)
IgG4 levels against cat allergen above Median	398 (49.8)	1.23 (0.86–1.76)	1.07 (0.73–1.55)	1.34 (0.92–1.95)	1.17 (0.80–1.70)

* Reference category: no contact with cats or to dogs in the first year of life.

† Reference category: no current contact with cats or to dogs.

‡ Combined category of dogs and cats + dogs only.

§ Adjusted for sex, age, study area, family history of asthma or hay fever, parent's education level, number of older siblings, and pet avoidance due to asthma or allergies in the family.

nonfarmers' children, current exposure to dogs remained inversely related to hay fever and hay fever symptoms and sensitization to grass pollen, whereas associations with wheeze, asthma and sensitization to cat dander were much weaker. The interaction term between dog exposure and farming status was of borderline significance for diagnosed asthma (LRT; $P = 0.058$) and for wheezing (LRT; $P = 0.159$) but nonsignificant for sensitization to cat dander (LRT; $P = 0.415$).

Discussion

The present analyses examined the role of pet keeping in a rural, partially farming population on the occurrence of childhood asthma and allergy. In contrast to several other recent publications (9, 11, 12, 24–26) no clear associations between pet exposure in the first year of life and asthma or allergy endpoints were observed. Early exposure to a farming environment which has previously been shown to confer protection from the development of asthma and allergy (21) remained independently associated with a reduced risk of hay fever, asthma and atopic sensitization. Current contact with dogs was associated with a reduced risk of hay fever, asthma, wheezing, and sensitization to cat allergen and grass pollen. The inverse association between exclusive exposure to cats was limited to wheezing, atopic asthma and grass pollen sensitization. The stronger protective effect associated with dog contact may simply reflect exposure to more

than one pet as in most cases exposure to dogs coincided with contact with cats as well. In a recent prospective cohort study (11) a reduced risk of allergic sensitization was only observed in children exposed to two or more dogs or cats in the first year of life. We cannot determine whether this interpretation also holds true for the present study because the number of pets a child was exposed to has not been recorded.

Several studies have shown that keeping a dog is associated with higher indoor endotoxin levels (4, 19) and it has been postulated that this higher microbial exposure might explain the 'protective' effect of dog on asthma and allergy. However, when current indoor endotoxin levels were added to the regression models as a potential explanatory variable, the inverse association between dog exposure, asthma and hay fever was not greatly affected. Similarly, a recent longitudinal study from the US found exposure to dog to be associated with a reduced risk of wheezing in young children independent of house dust endotoxin levels (20). These findings support the notion, that the effects of pet exposure and endotoxin on allergic outcomes work through different albeit unknown immunological mechanisms. It has been postulated that the observed inverse association between exposure to cat allergen and asthma may result from a modified Th2 immune response, inducing IgG4 antibodies which are not associated with an increased risk of asthma (18). Although, in the present study, current and early contact with cats was associated with a decreased risk of wheezing and atopic asthma, no significant increase in IgG4 levels

Table 3. Sensitivity analysis of the association between current contact with dogs* vs asthma and allergy outcomes

	Diagnosed hay fever	Current hay fever symptoms	Diagnosed asthma	Current wheeze	SX1, RAST ≥ 3	IgE grass, RAST ≥ 3	IgE cat, RAST ≥ 1
Basic models† (BM)	0.26 (0.11–0.57)	0.39 (0.20–0.78)	0.29 (0.12–0.71)	0.57 (0.31–1.04)	0.78 (0.48–1.26)	0.55 (0.33–0.94)	0.48 (0.23–0.99)
BM + pet exposure in the first year of life	0.23 (0.09–0.58)	0.31 (0.14–0.67)	0.17 (0.06–0.51)	0.59 (0.29–1.18)	0.85 (0.50–1.44)	0.67 (0.37–1.20)	0.50 (0.22–1.15)
BM + current mattress endotoxin level	0.24 (0.10–0.61)	0.42 (0.20–0.90)	0.31 (0.12–0.83)	0.54 (0.27–1.07)	0.80 (0.48–1.33)	0.59 (0.34–1.05)	0.59 (0.28–1.27)
BM + current mattress cat allergen level	0.26 (0.11–0.63)	0.34 (0.16–0.74)	0.26 (0.10–0.67)	0.48 (0.25–0.94)	0.78 (0.46–1.34)	0.64 (0.35–1.16)	0.51 (0.23–1.14)
BM + farming exposure in the first year of life‡	0.31 (0.14–0.71)	0.45 (0.23–0.90)	0.35 (0.14–0.85)	0.64 (0.34–1.19)	0.92 (0.56–1.50)	0.71 (0.41–1.24)	0.52 (0.25–1.10)
BM + current stable activity§	0.42 (0.18–0.97)	0.57 (0.28–1.18)	0.29 (0.12–0.74)	0.70 (0.36–1.36)	0.95 (0.56–1.60)	0.79 (0.45–1.41)	0.66 (0.31–1.43)
BM for farmers' children ($n = 319$)	0.28 (0.03–2.83)	0.48 (0.08–2.81)	0.03 (0.00–0.47)	0.19 (0.04–0.86)	0.64 (0.22–1.89)	0.54 (0.14–2.01)	0.22 (0.04–1.33)
BM for nonfarmers' children ($n = 493$)	0.34 (0.14–0.82)	0.46 (0.21–1.02)	0.51 (0.19–1.35)	0.93 (0.46–1.87)	0.86 (0.48–1.54)	0.64 (0.34–1.20)	0.69 (0.30–1.57)

The values are adj. OR (95% CI), adjusted for sex, age, study area, family history of asthma or hay fever, parent's education level, number of older siblings, pet avoidance because of asthma or allergies in the family, and current contact with cats only.

* Reference category: no current contact with cats or with dogs.

† Basic models from Table 2 additionally adjusted for potential confounding factors.

‡ First stay in stable and farm milk consumption in the first year of life.

§ Regular contact with farm animals (no, yes) and frequency of staying in stable (never, at least weekly, at least daily).

against cat dander was observed. Thus, the proposed mechanism behind the 'protective' effect of cat on asthma does not seem to be of importance in this study population. The hypothesis of a modified Th2 immune response has also been challenged by a recent Swedish study indicating that although all children had an immune response to cat, the presence of IgG4 antibodies was not associated with less allergy (27).

Deliberate avoidance of pets might be an other explanation for the protective 'pet effect' observed in many studies. In the present study, only a small proportion of families (1.7%) reported that pets had been given away because of presence of allergic disease in one of the family members. Adjustment for pet avoidance did not influence our results. Yet, as many families with a history of allergic diseases are counselled to avoid keeping pets, we cannot discount an unmeasured bias in the association between pet exposure and allergic diseases. A Swedish study reported that one-fourth of the Swedish population reported avoidance behaviour towards pets and concluded that this might explain the protective effect of exposure to pets during childhood on asthma and allergies (28). When we restricted our sample to children without a family history of asthma and allergy to address the issue of primary pet avoidance we still found an inverse relation between contact with dogs and allergy outcomes making primary pet avoidance an unlikely explanation for the observed pet effect in our population. Nevertheless, the discrepancy between the effects on asthma and allergy observed in the present study for current and early pet exposure might indicate parental avoiding behaviour which was not measured in the questionnaire. To address this question we compared the 30 children (8%) who had contact with pets in the first year of life but no current pet contact with children who had early and current contact with pets and found the latter to be significantly less likely to suffer from asthma and to be sensitized to grass pollen and cat dander. Thus, the association between current pet contact, asthma and allergic sensitization might at least partially be explained by a sort of pet avoidance of which parents are not aware.

Most but not all of the inverse association between current dog exposure and allergic sensitization, wheezing and hay fever symptoms was attenuated and no longer statistically significant when current contact with stable animals was introduced into the regression models. Only the association with diagnosed hay fever and asthma remained statistically significant. Conversely, current exposure to endotoxin in mattress dust and early farm exposure remained independently associated with a reduced risk of asthma and allergy as previously reported (5, 21).

In addition, a stronger association between current dog contact and asthma or sensitization to cat dander was observed in farmers' children. In nonfarmers' children only the inverse relation between contact with dogs and hay fever remained statistically significant. We can only

speculate about the reason for such differential effects as the mechanism behind a protective effect of pet exposure is still unknown. Pet contact of farm children might be more intense as many more cats and dogs are usually found on a farm compared with a nonfarming household. It is also conceivable that compared with pets from nonfarming environments, pets living on farms carry a broad spectrum of microbes leading to a different and more intense stimulation of a farm child's immune system.

Based on the present analyses we conclude that although pet exposure was very frequent in this rural population, the inverse relation between current dog contact, asthma and allergy was mostly explained by simultaneously occurring exposure to stable animals or restricted to farm children. In addition, a subtle form of pet avoidance may contribute to the protective pet effect. However, the cross-sectional design of our study limits our ability to draw firm conclusions. Prospective studies

are needed to definitely clarify the role of pet exposure in a farming environment.

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