

Austrian children living on a farm have less hay fever, asthma and allergic sensitization

J. RIEDLER, W. EDER, G. OBERFELD* and M. SCHREUER†

*Paediatric Pulmonology, Children's Hospital Salzburg, *Environmental Medicine, Public Health Department and †Statistical Consultant, Department of Sociology, University of Salzburg, Salzburg, Austria*

Summary

Background and objectives In some studies, the prevalence of hay fever and asthma has been found to be lower in children from rural areas than in children from an urban environment. We hypothesized that living on a farm might be protective against development of allergic sensitization and allergic diseases.

Methods In a cross-sectional survey, parents of 2283 children aged 8–10 years from a mostly rural area in Austria answered a standardized questionnaire on allergic diseases and environmental factors. 1137 children performed a skin prick test to seven local allergens.

Results The prevalence of hay fever (3.1 vs 10.3%, $P=0.0002$), asthma (1.1 vs 3.9%, $P=0.017$) and a positive skin prick reactivity to at least one of the common local allergens (18.8 vs 32.7%, $P=0.001$) was significantly lower in children living on a farm than in children from a non-farming environment. In a multivariate logistic regression model, adjusting for genetic background, parent education, living and housing conditions and dietary factors did not change the odds ratio for the association of farming and allergic sensitization. Only after including 'regular contact with livestock and poultry' into the model did the odds ratio change significantly (cOR 0.48 95% CI 0.30–0.75 to aOR 0.75 95% CI 0.37–1.52) indicating an association between regular contact with farm animals and reduced risk of atopic sensitization.

Conclusion Possible explanations for the lower prevalence of hay fever, asthma and allergic sensitization in children living on a farm might be the development of immunotolerance or the stimulation of TH1 cells and suppression of TH2 cells by increased exposure of farm children to microbial antigens in the stables or farmhouses.

Keywords: allergic sensitization, asthma, farm, hay fever

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Introduction

The prevalence of hay fever and asthma in children is increasing and many studies have been looking into possible risk factors for this increase [1–6]. Comparisons between children from urban and rural areas have shown that atopy and allergic diseases might be reduced in rural areas and that air pollution might be a risk factor [7–9]. However, the

evidence is controversial and other factors associated with living under rural conditions could account for this finding [10–12]. Reports from Southern Bavaria and Switzerland suggest that a more traditional lifestyle or a different environment might explain the lower prevalence of allergic diseases in children from rural areas [13–15].

We, therefore hypothesized that children living on a farm have less hay fever, asthma and eczema and less allergic sensitization than children from a non-farming community. Further, we wanted to identify possible protective mechanisms for allergic sensitization.

Correspondence: J. Riedler, Paediatric Pulmonology, Children's Hospital, Muellner Hauptstrasse 48, A-5020 Salzburg, Austria (e-mail: j.riedler@lkasbg.gv.at).

Methods

Subjects

This cross-sectional survey was carried out in the county of Salzburg, Austria with a total population of 513 853 people. Sixty-five percent live in areas up to 6 inhabitants/ha and in the city of Salzburg, this rises to 20/ha. Most of the county is rural area with a high proportion of farmers. Farms are usually small and run by the members of the family and only occasionally by farm workers. Ninety percent of Austrian farmers have livestock or poultry.

The study took place from January to May 1997 and parents of all children in school grade 3 and 4 (age range 8–11 years) living in the Lungau (district with highest proportion of farmers) and children from 17 schools with a reasonable size from the other five districts of the county of Salzburg were invited to answer a questionnaire on respiratory and allergic diseases and environmental factors ($n = 2394$).

In phase 2 of the survey, all children who had reported 'yes' to at least one of the following questions [5] were asked to undergo a skin prick test: (1) 'In the last 12 months, has your child had problems with sneezing or a runny or blocked nose when he/she did not have a cold or the flu?' ($n = 261$). (2) 'Has your child ever had hay fever?' ($n = 216$). (3) 'Has your child had wheezing or whistling in the chest in the last 12 months?' ($n = 154$). (4) 'Has your child ever had asthma?' ($n = 76$). (5) 'Has your child ever had an itchy rash that was coming and going for at least 6 months?' ($n = 226$). (6) 'Has your child ever had eczema?' ($n = 225$). Since many children had a positive answer to more than one of these questions, the total number of diseased children invited was 679. A control group was selected at random, matched by sex, grade and school, from those who answered 'no' to all six questions ($n = 675$). All in all, 1354 children were invited for the skin prick test which was performed in the schools.

Questionnaire

The questionnaire included 85 questions on symptoms and a diagnosis of hay fever, respiratory symptoms, a previous diagnosis of asthma, 'asthmatic', 'spastic' or 'obstructive' bronchitis, symptoms and a diagnosis of eczema (ISAAC core questions [5], except the three 'bronchitis' questions), family history of allergic diseases, parental education, number of siblings, population density and sea level of the study area, questions about traffic and air pollution, passive smoking, indoor humidity, animal contact (livestock, poultry and pets), age of house, heating, airing, covering of floors, cleaning of carpets and floors, breast feeding and dietary factors.

With regard to farming, parents were asked 'does your child live on a farm?' and 'does your child have regular contact with livestock (cows, horses, sheep, pigs and goats) or poultry?'

Definitions

Symptoms of hay fever were defined by a positive response to 'in the last 12 months, has your child had problems with sneezing or a runny or blocked nose without a cold accompanied by itchy-watery eyes?'. 'Wheeze' was defined as a positive response to 'has your child had wheezing or whistling in the chest in the last 12 months?' A positive response to 'has your child ever had an itchy rash intermittently for at least 6 months?' was considered as indicative of eczema. Diagnostic labels were assessed by asking 'has your child ever had asthma, hay fever or eczema?'. A positive answer to 'did a doctor ever diagnose "asthmatic", "spastic" or "obstructive" bronchitis?' suggested possible asthma, as these terms are frequently used for asthma in our community [6].

Allergic sensitization was defined as skin test reactivity (weal diameter 3 mm) to one or more of the following allergens: house dust mites (*Dermatophagoides pteronyssinus* and *D. farinae*), cat fur, timothy grass, birch, *Cladosporium herbarum* and *Alternaria tenuis*.

Skin prick test

Skin prick tests were performed using *D. pteronyssinus*, *D. farinae*, cat fur, timothy grass, birch, *A. tenuis*, *C. herbarum*, histamine, and saline control solutions (Soluprick, ALK-laboratories, Copenhagen, Denmark). On the left forearm, the skin was pricked through each drop of allergen with a separate lancet (ALK skin prick lancet). Reactions to each skin test solution were measured 15 min after the pricks. The size of each weal in millimetres was documented as the mean of the longest diameter and the diameter perpendicular to it at its mid-point. The test was considered positive to a specific allergen if the weal was at least 3 mm greater than that resulting from the negative control. Children who failed to respond to histamine were excluded from the analysis ($n = 2$).

Statistical analyses

Data entry and analyses were made using SPSS for Windows (SPSS Inc., Chicago, IL, USA release 6.0 and 8.0). Prevalences of symptoms, diagnoses and allergic sensitizations were calculated for children living and those not living on farms and compared by chi square-test. To adjust for potential confounders or other variables that might explain the differences in allergic sensitization

Table 1. The association between a variety of variables under different labels and farming

Numerical variables	P-value (t-test)	Mean farming/ non-farming	95% CI of the difference between farming and non-farming
<i>Predefined confounders</i>			
Number of elder siblings	<0.0005	1.4/0.8	0.45 to 0.78
*Years in Kindergarten	<0.0005	1.5/2.2	-0.84 to -0.62
<i>Living conditions</i>			
Altitude in meters	<0.0005	869/720	120 to 180
Age of the house (year of construction)	<0.0005	1908/1971	47 to 78
Numbers of cigarettes currently smoked in the household	0.049	3.4/4.5	-2.1 to -0.003
<i>Infection and diet</i>			
Breastfeeding (days)	<0.0005	62/82	-29.3 to -11.5
Amount of margarine/sea-fish/salty snacks consumption in the previous year (assessed by factor analysis)	<0.0005		-0.44 to -0.23
Amount of butter/salt consumption in the previous year (assessed by factor analysis)	<0.0005		0.32 to 0.57
Categorical variables (dichotomous and ordinal)	χ^2 P-value		Correlation with farming Spearman's rho
<i>Predefined Confounders</i>			
*Sex	0.283		
*Genetic burden for asthma, allergic rhinitis or eczema	0.262		
Mother's education	<0.0005		-0.165
*Population density	<0.0005		-0.199
<i>Living conditions</i>			
Wall-to-wall carpeting in the child's room in the 1 st year of life	<0.0005		-0.097
Floor level of the child's bedroom	<0.0005		+0.099
Frequency of airing of the child's bedroom in winter	<0.0005		-0.185
*Airing of the child's bedroom during the night	0.054		-0.045
*Heating the child's bedroom during night	0.013		+0.017
Frequency of vacuum cleaning in the child's bedroom	<0.0005		-0.161
Surrogate question for traffic disturbance:			
Noise	0.027		-0.056
Fumes	0.237		
Surrogate question for fumes of wood or coal heating	0.547		
Location of the house with respect to foggy weather (covered, partly covered, clear)	<0.0005		-0.150
<i>Infection and diet</i>			
Frequency of coughing in the 1 st year of life	0.488		
*Frequency of coughing during school-age	0.073		-0.051
*Worm infection ever	0.041		-0.046
<i>Animal contact</i>			
*Pets	<0.0005		0.169
*Livestock and poultry	<0.0005		0.609

* Variables which remained in the final model

Table 2. Prevalence of hay fever, asthma and eczema in children living on a farm compared with children from a non-farming environment

	Prevalence (%)		P-value
	Living on a farm (n = 282)	Not living on a farm (n = 1710)	
Hay fever (ever)	3.1 (8/261)	10.3 (166/1614)	0.0002
Runny nose and itchy eyes last 12 months	4.1 (11/268)	7.8 (131/1677)	0.03
Asthma (ever)	1.1 (3/278)	3.9 (66/1693)	0.017
'Asthmatic, obstructive, spastic bronchitis'	10.3 (29/282)	15.2 (260/1710)	0.029
Wheeze last 12 months	4.7 (13/278)	7.5 (128/1701)	0.087
More than 4 asthma attacks last 12 months	0.7 (2/278)	0.8 (13/1697)	0.377
Eczema (ever)	11.4 (31/273)	10.9 (183/1678)	0.826
Itchy rash (ever)	9.1 (25/276)	11.0 (186/1693)	0.337

between children living on farms and those who do not, we compared the two groups with respect to variables concerning 'socioeconomic status', 'family history of allergic diseases', 'living conditions', 'infections', 'diet', 'animal contact' and 'air pollution' in a bivariate analysis by either *t*-test for metric variables or χ^2 for categorical variables. For the variables covered by each of these labels see Table 1. In a second step, all variables that showed a statistical difference were put in a multivariate logistic regression model with 'does your child live on a farm?' as dependent variable. All variables which had independent and statistically significant associations with the question on farming were then used as potential explanatory variables in a stepwise procedure to fit the final multivariate logistic regression model for allergic sensitization and subsequently to calculate the adjusted odds ratio for the effect of living on a farm.

Approval to conduct the survey was obtained from the Hospital Ethics Committee for Human Studies, from the Landesschulrat Salzburg and from the principals of the schools involved. Informed written consent was obtained from the parents of all children.

Results

Parents of 2394 children were invited to answer the questionnaire and 2283 agreed to participate, giving a response rate of 95.4%. Analysis was restricted to children with Austrian nationality, reducing the numbers to 2001. The mean age of these participants was 9.5 years (SD=0.7) of which 52% were boys. Of all the children, 14.1% lived on a farm and 81.3% of these children (232/282) had regular contact with livestock or poultry. Of the 1354 children invited for the skin prick test, 1137 agreed to participate (overall response rate 84%, symptomatic children 85.6%,

control children 82.3%) of which 1013 had Austrian nationality.

The prevalence of hay fever symptoms (4.1 vs 7.8%, $P=0.031$) and a diagnosis of hay fever (3.1 vs 10.3%, $P=0.0002$) was significantly lower in children living on a farm than in children from a non-farming environment. A diagnosis of asthma was also lower (1.1 vs 3.9%, $P=0.018$), and the difference in asthma symptoms did not reach significance (4.7 vs 7.5%, $P=0.087$). Similarly, a doctor's diagnosis of 'asthmatic or spastic or obstructive bronchitis' was significantly lower in farmers' children (10.3 vs 15.2%, $P=0.029$). The difference in asthma severity as assessed by frequency of asthma episodes was not significant. No difference was found for eczema (Table 2).

Children living on farms were less likely to have a positive skin prick reactivity to at least one of the common local allergens (18.8 vs 32.7%, $P=0.001$). The difference was much greater for outdoor allergens than for indoor allergens (Table 3) and did not reach significance for indoor allergens.

As living on a farm differs from living in a nonagricultural environment in many aspects (Table 1), possible explanatory variables were tested in a multivariate logistic regression model but did not account for the lower prevalence of allergic sensitization in children on farms (Table 4). Only after including 'regular contact with livestock and poultry' into the model did the odds ratio (living on a farm vs non-farming environment) for allergic sensitization change significantly from cOR 0.48, 95% CI 0.30–0.75 to aOR 0.75, 95% CI 0.37–1.52 (Table 4), indicating an association between regular contact with livestock and reduced risk of atopic sensitization. Children not living on a farm but having regular contact with livestock (37/868) also had a lower prevalence of allergic sensitization (13.5 vs 34.8%, $P=0.01$).

Table 3. Prevalence of allergic sensitization (skin prick test) to 7 common local allergens in children living on a farm compared with children from a non-farming environment

	Prevalence (%)		P-value
	Living on a farm (n = 138)	Not living on a farm (n = 868)	
At least one positive reaction \geq 3 mm	18.8	32.7	0.001
Timothy grass	7.2	21.4	0.00009
Birch pollen	0.7	8.3	0.001
<i>Dermatophagoides pteronyssinus</i>	12.3	15.8	0.294
<i>Dermatophagoides farinae</i>	8.0	10.6	0.344
Cat fur	9.4	12.2	0.345
<i>Alternaria tenuis</i>	0	0.1	0.689
<i>Cladosporium herbarum</i>	0	0.3	0.489

Discussion

The results of the present study show that Austrian children living on a farm have less hay fever, asthma and allergic sensitization than children from a non-farming environment. Regular contact with livestock and poultry, early in life, might protect against allergic sensitization and the development of allergic diseases.

Our findings are similar to reports from Switzerland on a lower prevalence of hay fever (aOR = 0.34, 95% CI 0.15–0.79) and allergic sensitization assessed by skin prick test (aOR = 0.4, 95% CI 0.27–0.72) in children whose parents were farmers [14]. Similarly, in a study from Germany, 5–6-year-old farmers' children had a lower risk for hay fever (cOR = 0.4, 95% CI 0.3–0.6) and asthma (cOR = 0.6, 95% CI 0.4–0.8) than their peers from non-farming families. Allergic sensitization was not assessed in this study. The

authors found a reverse relationship between the prevalence of these allergic diseases and the intake of whole milk and self-produced foods [15]. A study from Finland on 10 681 students aged 18–24 years, found a significantly lower prevalence of allergic rhinitis (OR = 0.5) in students who had lived on a farm than in students from a non-farming community [16]. Also in line with our findings is a study from Bavaria showing a lower risk for hay fever (aOR = 0.57, 95% CI 0.34–0.98) and bronchial hyperresponsiveness to cold air (aOR = 0.55, 95% CI 0.34–0.90) in children whose parents used wood or coal for heating [13]. The authors speculated that this type of heating be a marker of a more traditional lifestyle. In the present study, we asked various questions with regard to heating, but they did not explain the association between lower allergic sensitization and living on a farm. Austrian farms are usually small and run by the farmer and his family who all have regular contact with farm animals and differ in their lifestyle in many aspects from the nonagricultural community. This might be different from large farms in other countries where the farmers' children might have no close contact with livestock and do not differ in lifestyle.

A strength of our study is that we included a detailed standardized questionnaire on allergic diseases and an objective marker of atopy, i.e. a skin prick test and that both methods showed a similar strong and significant association of living on a farm and reduced risk for developing allergic sensitization and allergic diseases. A limitation, however, is, that we cannot provide an objective measure for exposure or a dose response relationship. The factor most strongly associated with the reduced risk for allergic sensitization in children living on a farm was 'regular contact with livestock and poultry'. This might relate to a direct or indirect contact as a protective mechanism or to a surrogate for something associated

Table 4. Changes in the odds ratio (OR) at the various stages of fitting the logistic regression model for the association of living on a farm and allergic sensitization

	n	OR	95% CI	P-value
Crude	1006	0.48	0.30–0.75	0.001
+ Predefined confounders*	899	0.48	0.29–0.79	0.004
+ Living conditions*	869	0.48	0.28–0.80	0.005
+ Infection and diet*	786	0.51	0.29–0.89	0.019
+ Regular contact with pets*	786	0.54	0.31–0.96	0.036
+ Regular contact with livestock and poultry*	786	0.75	0.37–1.52	0.426

* Variables which remained in the final model

with farming and allergy. As only about 10% of all farmers' children were not exposed to livestock (15/138 who had a prick test), the number of children living on a farm but not being exposed to livestock is too small to show whether protection against atopy occurred only in those farm children being exposed to livestock. However, the fact that children who did not live on a farm but who had regular contact with farm animals also had a lower prevalence of allergic sensitization lends support to our hypothesis that the protection against atopy is related to farm animal contact rather than the farming lifestyle (13.5 vs 34.8%).

Selection bias could also be a possible explanation for the reduced prevalence of allergic diseases in farmers' children. We cannot rule out with certainty that atopic children or atopic parents have been leaving the farms for generations. However, we consider this rather unlikely since adjusting for a family history of hay fever, asthma or eczema did not change the association between atopic sensitization and living on the farm (cOR = 0.48, 95% CI 0.30–0.75, aOR = 0.52, 95% CI 0.33–0.84). Further, children who had regular contact with farm animals but did not live on a farm also had a lower prevalence of allergic sensitization than children with no contact.

Breast feeding, dietary factors, frequency of respiratory infections, passive smoking and housing conditions have been looked at but found not to explain the difference. Of course, there might be other factors associated with these explanatory variables and development of allergic diseases which have not been considered.

Two main speculations come up which are related to allergy and 'contact with livestock and poultry': immune tolerance and bacterial stimulation of TH1 cells accompanied by suppression of TH2 cells. Higher and repeated exposure to allergens has led to tolerance via immune deviation in animals and humans [17,18]. The development of immune tolerance depends on the dose of the allergen, the type of antigen-presenting cell, the site of reaction and the time of allergen exposure. Since we found the greatest effect of farm living on pollen allergy and not on indoor allergens, one might speculate that very high exposure to these outdoor allergens early in life could have led to a state of tolerance as has been found in atopic children with milk proteins [19]. Farm animals are fed with grass and hay and thus the allergen contact to pollen might be different in children growing up on a farm and having regular contact with livestock as compared with children from a non-farming environment. Further studies are necessary to measure the exposure to grass pollen in farm children and relate this exposure to the prevalence of allergic sensitization.

Another speculation is a possible stimulation of TH1 cells and suppression of the production and release of immunoglobulin (Ig) E antibodies by increased exposure of farm children to microbial antigens in the stables or farmhouses.

Rats who were exposed to various microbial agents were less likely to become sensitized to inhaled allergens than rats who were protected against infections [20]. Along the same line is a study which showed that in mice the production of casein-specific IgE antibodies was suppressed by heat-killed *Lactobacillus plantarum* L-137 in correlation with an increase in interleukin (IL) -12 [21]. Increased IL-12 production leading to decreased levels of IgE and TH2-cytokines has been shown for various bacterial cell wall-derived substances such as lipopolysaccharides [22,23]. One might speculate that these substances are increased in stables and possibly in farmhouses and that they could lead to a stimulation and maturation of TH1 lymphocytes.

In conclusion, we have found a lower prevalence of hay fever, asthma and allergic sensitization in children living on farms than in children from a nonagricultural environment, suggesting a 'protective mechanism' of a farming environment. Further studies are necessary to investigate possible direct or indirect protective effects of regular contact with farm animals early in life on the development of allergic diseases in children.

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