

Reduced risk of hay fever and asthma among children of farmers

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Summary

Background The prevalence of atopic diseases is on the rise. Traditional lifestyles may be associated with a reduced risk of atopy.

Objectives To test the hypothesis that children living on a farm have lower prevalences of atopic diseases. To identify differences in living conditions between farmers and other families which are associated with the development of atopic conditions.

Design Cross-sectional survey among children entering school (aged 5–7 years). A written questionnaire including the ISAAC core questions and asking for exposures on a farm and elsewhere was administered to the parents. **Setting:** School health entry examination in two Bavarian districts with extensive farming activity. **Subjects:** 10 163 children.

Main outcome measures The prevalence of doctor's diagnoses and symptoms of hay fever, asthma and eczema as assessed by parental report.

Results Farmers' children had lower prevalences of hay fever (adjusted odds ratio = 0.52, 95% CI 0.28–0.99), asthma (0.65, 0.39–1.09), and wheeze (0.55, 0.36–0.86) than their peers not living in an agricultural environment. The reduction in risk was stronger for children whose families were running the farm on a full-time basis as compared with families with part-time farming activity. Among farmers' children increasing exposure to livestock was related to a decreasing prevalence of atopic diseases (aOR = 0.41, 95% CI 0.23–0.74).

Conclusions Factors related to environmental influences on a farm such as increased exposure to bacterial compounds in stables where livestock is kept prevent the development of allergic disorders in children.

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Introduction

There is conflicting evidence about the lower risk of atopic diseases in children in rural compared with urban areas [1–8]. Within Germany, lower prevalences of asthma and hay fever were shown in the eastern part of the country immediately after reunification in 1991 [9]. The recent increase in hay fever and atopic sensitization but not in asthma prevalence in children of former East Germany suggests that environmental factors operating early in life determine the development

of atopic diseases [10]. Factors associated with western living conditions like high socioeconomic status [11], western diet [12], increased allergen exposure due to insulated housing conditions [13], reduced burden of infections early in life [14], and smaller sibship size [15,16] have been proposed to explain the differential development of atopic diseases. If the adoption of a 'westernized' lifestyle is related to an increase in atopic disorders, more traditional lifestyles such as those encountered in a farming environment should be associated with decreased prevalences of these diseases.

We aimed to test the hypothesis that children living on a farm have lower prevalences of atopic diseases, and to identify differences in living conditions between farmers

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and other families which are associated with the development of atopic conditions in children. We studied all first graders at school entry health examinations in two Bavarian counties with extensive agricultural activity.

Methods

Study population

A cross-sectional study was performed in two rural Bavarian districts (Niederbayern [1 143 000 inhabitants] and Oberpfalz [1 054 000 inhabitants]) with a high proportion of farmers among the general population. All children attending obligatory school entry health examinations from February to August 1997 were invited to participate in this study and their parents were given a questionnaire for self completion ($N = 13\,345$).

Questionnaire

The questionnaire included the ISAAC core questions on symptoms of asthma, allergic rhinitis and atopic eczema which have been reported in detail elsewhere [17]. In addition, parents were asked: 'Did a doctor ever diagnose any of the following diseases in your child? (a) asthma; (b) asthmatic, spastic or obstructive bronchitis; (c) bronchitis'. Children were defined as having asthma if their parents reported that asthma had been diagnosed at least once or that a doctor had diagnosed asthmatic, spastic or obstructive bronchitis more than once. The prevalence of hay fever and atopic eczema was assessed as a doctor's diagnosis of the disease [18]. Symptoms of hay fever were assessed by asking about a runny nose without a cold being accompanied by itchy-watery eyes in the last 12 months [18]. Current rash was assessed by asking about an itchy rash coming or going in specified skin areas for at least 6 months in the past 12 months [17].

Farming was assessed by asking: 'Do you live on a farm?' and if so, 'Does your family run the farm on a (a) full-time basis, (b) part-time basis, (c) small scale basis, (d) only for home consumption or (e) not at all?' Children were classified as exposed to 'farming' if they lived on a farm and their parents were engaged in farming activity of any degree. 'Farming' categories were then combined to (a) full-time activity and (b) part-time activity, the latter including categories b, c and d.

The questionnaire also asked about potential risk factors and confounders such as gender, sibship size, parental education and the family history of hay fever, asthma or eczema in first degree relatives. In addition, factors possibly associated with farming status such as housing characteristics, passive smoking, child's health care practices and dietary habits were assessed. Among children living on a farm the frequency of contact with livestock was inquired.

Statistical analysis

The lifetime prevalence of doctor-diagnosed atopic disorders (hay fever, asthma, eczema) and the 12-month period prevalence of related symptoms (runny nose and itchy eyes, wheeze, itchy rash) was computed for farmers' and non-farmers' children. Crude and adjusted odds ratios were calculated using chi-square tests and logistic regression analysis. The number of older siblings, parental education, family history of atopic diseases and use of wood or coal for heating or cooking were included in the adjusted analyses. SAS software (version 6.12) was used in all calculations.

To determine differences in the distribution of variables between farmers' offspring and other children chi-square statistics and Mantel Haenszel tests for trend were used for binary and ordered categorical variables, respectively. The relation to outcome variables was additionally studied for those covariates which were significantly ($P < 0.05$) associated with farming. Since these covariates may be surrogate measures for the farming status, their independent effect was furthermore assessed in a multivariate logistic regression model adjusting for farming activity.

Among farmers' children the association between exposure to livestock and the prevalence of atopic diseases was assessed using a combined outcome variable defined as having at least one of the following doctor's diagnoses: hay fever, asthma or eczema. Contact with livestock was subdivided into three levels: (a) no or rare, (b) occasional and (c) frequent. The risk associated with increasing animal contact was calculated in a logistic regression model adjusting for the same covariates as before.

Results

From February 1997 to August 1997 13 345 children (age 5–7 years) were seen at the obligatory school entry health examinations. Table 1 shows the selection of the study population ($N = 10\,163$) which included 1181 (12.0%) farmers. Of these, 450 families were running the farm as a full-time job.

Table 1. Selection of study population

Population	Subjects, <i>n</i> (%)
Target population	13 354
Study population	10 163 (76.2)
German nationality	9835 (73.7)
Farmers' children	1181 (12.0)
<i>Of all farmers' children</i>	
Full-time farming activity	450 (38.1)
Part-time farming activity	731 (61.9)

Table 2. Prevalence of atopic diseases in children of farming and non-farming parents

	Prevalence in percentage			
	Non-farming (<i>n</i> = 8466)	Farming (<i>n</i> = 1181)	Part-time farming (<i>n</i> = 731)	Full-time farming (<i>n</i> = 450)
Doctor's diagnosis of hay fever [†]	4.9 (411/8383)	1.8*** (21/1172)	2.1*** (15/724)	1.3*** (6/448)
Runny nose and itchy eyes in the past 12 months [‡]	5.4 (448/8360)	2.9*** (34/1169)	3.2* (23/722)	2.5* (11/447)
Doctor's diagnosis of asthma [†]	6.4 (529/8235)	3.4*** (39/1147)	3.7** (26/709)	3.0* (13/438)
Wheeze in the past 12 months [‡]	8.1 (673/8326)	5.6* (65/1167)	5.4* (39/722)	5.8 (26/445)
Doctor's diagnosis of eczema [†]	15.5 (1289/8299)	13.8 (160/1163)	14.2 (102/720)	13.1 (58/443)
Itchy rash in the past 12 months [‡]	7.2 (582/8058)	6.0 (68/1125)	5.8 (40/696)	6.5 (28/429)

* $P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$ in comparison with non-farmers' children. [†]Lifetime prevalence. [‡]12-month period prevalence.

The prevalence of a doctor's diagnosis of hay fever (1.8 vs 4.9%, $P \leq 0.001$) and hay fever symptoms (2.9 vs 5.4%; $P \leq 0.001$) was significantly lower in farmers' offspring as compared with children from a nonagricultural environment (Table 2). Similarly, the prevalence of a doctor's diagnosis of asthma (3.4 vs 6.4%; $P \leq 0.001$) and current wheeze (5.6 vs 8.1%; $P \leq 0.05$) was significantly lower in farmers' children, whereas no such difference was observed for eczema. The effects were stronger in children of farmers with full-time activity as compared with their peers with only part-time farming parents, suggesting a dose-response relationship (Table 2).

Significant differences in exposure between children of farming parents and other families are shown in Table 3. The prevalence of atopic diseases was lower in parents and siblings of children living on a farm as compared with other children. Farmers had a lower level of education and sibship size was larger among these families. Indoor dampness was more prevalent among farming families as was the use of wood or coal for heating. Differences in the use of homeopathic medicine and antibiotics were also found with farming parents using less of these treatments. Finally, the consumption of whole milk, but not skim milk (data not shown) was higher among farmers' offspring than among other children.

Among farmers' children the crude odds ratios for hay fever (cOR 0.35; 95% CI 0.23–0.55), hay fever symptoms (0.53; 0.37–0.75), asthma (0.51; 0.37–0.71) and wheeze (0.67; 0.52–0.87) were significantly reduced. After adjustment for the number of older siblings, parental education, family history of atopic diseases and wood or coal heating in the house the adjusted OR for hay fever (aOR 0.52; 95% CI 0.28–0.99) and wheeze (0.55; 0.36–0.86) remained significantly decreased. For part-time and full-time farming activity the crude risk estimates for hay fever (part-time: cOR 0.41; 95% CI 0.24–0.69, full-time: 0.26; 0.12–0.59), asthma

(part-time: 0.56; 0.37–0.83, full-time: 0.45; 0.26–0.78) and related symptoms were all significantly reduced, except for wheeze among full-time farmers' children. However, after adjustment, the odds ratios were significant only for wheeze among part-time farmers (aOR 0.49; 95% CI 0.27–0.86) and for asthma among full-time farmers (0.38; 0.15–0.97) (Table 4).

Of all farmers, 88% (*n* = 1039) kept livestock. Sixty-four percent had cows, 57.2% poultry, 41.3% pigs, 13.5% horses, 6.8% goats and 6.2% sheep (data not shown). Increasing exposure to livestock was associated with a reduced risk for the development of atopic disease among farmers' children (aOR = 0.41, 95% CI 0.23–0.74) (Table 5).

Discussion

We have shown a lower prevalence of hay fever, asthma and wheeze in children of farmers compared with their peers not living in an agricultural environment. Interestingly, a gradient with lower prevalences of hay fever and asthma among children of full-time farmers as compared with offspring of parents with part-time farming activity was found. Among farmers' children, increasing exposure to livestock was related to a significant decrease in the prevalence of atopic diseases. The findings suggest that factors related to traditional living conditions on a farm prevent the development of allergic disorders in children.

Methodological aspects

The ISAAC core questions on asthma and hay fever were used as an internationally standardized instrument to assess the prevalence of allergic diseases in children [19]. The validity of the ISAAC core questions on hay fever and rhinitis symptoms was assessed in a Swiss study on 2954 schoolchildren aged 7–14 years. Skin test reactivity was

Characteristic	Non-farming (N = 8466) % (n/N)	Farming (N = 1181) % (n/N)
Family history of atopic disease‡	46.0 (3897/8466)	35.4*** (418/1181)
Parental education		
Low	43.2 (3408/7886)	55.5*** (604/1089)
Medium	36.6 (2887/7886)	34.5 (376/1089)
High	20.2 (1591/7886)	10.0*** (109/1089)
Number of older siblings		
None	45.6 (3800/8326)	37.4*** (438/1170)
One	38.5 (3202/8326)	34.1** (399/1170)
Two or more	15.9 (1324/8326)	28.5*** (333/1170)
Wood and coal as energy source for heating and cooking	12.4 (698/5631)	75.6*** (541/716)
Indoor dampness	7.0 (588/8377)	8.7* (102/1173)
Antibiotic treatment in the first 3 years		
≤ 2 times	63.2 (5127/8108)	67.2** (751/1118)
3–5 times	26.3 (2129/8108)	24.5 (274/1118)
≥ 6 times	10.5 (852/8108)	8.3* (93/1118)
Homeopathic treatment for fever	7.0 (583/8343)	5.0** (58/1163)
Consumption of whole milk		
< once/week	32.8 (2563/7816)	16.7*** (189/1132)
1–2x/week	13.5 (1055/7816)	12.1 (137/1132)
≥ 3/week	53.7 (4198/7816)	71.2*** (806/1132)

Table 3. Differences in living conditions between children of farming and non-farming parents†

†Only variables which were significantly associated with both, farming and outcome, and in addition had an effect independent of farming are included in Table 2. ‡Hay fever and/or asthma and/or eczema in first degree relatives. * $P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$ in comparison with non-farmers.

used as a reference. The questions showed a specificity above 90% with positive predictive values ranging from 63.7 to 70.0%, whereas sensitivity was low (25.7–28.4%) [20]. Therefore, the ISAAC core questions on hay fever and rhinitis are highly specific and appropriate to exclude atopy in epidemiological surveys. The low sensitivity may result in an underestimation of the true prevalence of hay fever and related symptoms. This may reduce the strength of the observed associations and bias our results towards the no effect level.

Variation in the awareness of allergic and respiratory diseases between farmers and other subjects may have influenced both physicians' labelling and parental report of doctors' diagnoses, and children's symptoms of allergic diseases. However, consistent differences in the prevalence of hay fever and asthma were shown between 'part-time' and 'full-time' farmers' offspring, and it seems unlikely that these two groups would differ substantially with respect to physicians' labelling and parental report.

The results reported herein are in line with findings from two previous investigations in which objective markers of asthma and atopy were assessed. Results of a Swiss study showed a significant reduction in the risk for sneezing

attacks during pollen season (aOR = 0.34, 95% CI 0.12–0.89) and atopic sensitization as assessed by SX₁ (aOR = 0.31, 95% CI 0.13–0.73) in children whose parents indicated farming as their occupation. In addition, the risk of atopic sensitization was lower in children from full-time farmers (aOR 0.24, 95% CI 0.09–0.66) than from part-time farmers (aOR 0.54, 95% CI 0.15–1.96) [21]. In a previous Bavarian survey, the risks for hay fever (aOR = 0.57, 95% CI 0.34–0.98), skin test reactivity (OR = 0.67, 95% CI 0.49–0.93) and bronchial hyperresponsiveness (OR = 0.55, 95% CI 0.34–0.90) were all significantly lower in children living in homes where coal or wood was used for heating as compared with children exposed to other heating systems. Coal and wood stoves were assumed to be a surrogate for 'living on a farm' [22]. In fact, the use of coal and wood was predominantly reported by farmers (75.6 vs 12.4%, Table 3) in this study confirming our previous assumption

Genetic factors

Atopic diseases occurred less frequently in parents and siblings of children living on a farm than in the families

Table 4 Atopic diseases in children of farming vs non-farming parents with subgroup analysis for full-time and part-time farming activity: crude and adjusted odds ratios

	Farming (<i>N</i> = 1181)		Part-time farming activity (<i>N</i> = 731)		Full-time farming activity (<i>N</i> = 450)	
	Crude OR (95% CI)	Adjusted* OR (95% CI)	Crude OR (95% CI)	Adjusted* OR (95% CI)	Crude OR (95% CI)	Adjusted* OR (95% CI)
Doctor's diagnosis of hay fever†	0.35 (0.23–0.55)	0.52 (0.28–0.99)	0.41 (0.24–0.69)	0.63 (0.31–1.29)	0.26 (0.12–0.59)	0.31 (0.10–1.03)
Runny nose and itchy eyes in the past 12 months‡	0.53 (0.37–0.75)	0.89 (0.54–1.47)	0.58 (0.38–0.89)	0.98 (0.56–1.74)	0.45 (0.24–0.82)	0.70 (0.31–1.58)
Doctor's diagnosis of asthma†	0.51 (0.37–0.71)	0.65 (0.39–1.09)	0.56 (0.37–0.83)	0.80 (0.45–1.40)	0.45 (0.26–0.78)	0.38 (0.15–0.97)
Wheeze in the past 12 months‡	0.67 (0.52–0.87)	0.55 (0.36–0.86)	0.65 (0.47–0.91)	0.49 (0.27–0.86)	0.71 (0.47–1.06)	0.66 (0.36–1.23)
Doctor's diagnosis of eczema†	0.87 (0.73–1.04)	1.09 (0.82–1.44)	0.90 (0.72–1.12)	1.09 (0.78–1.52)	0.82 (0.62–1.09)	1.09 (0.72–1.65)
Itchy rash in the past 12 months‡	0.83 (0.64–1.07)	1.04 (0.70–1.54)	0.78 (0.56–1.09)	0.97 (0.61–1.56)	0.90 (0.61–1.33)	1.13 (0.64–2.00)

*Adjusted for older siblings, parental education, family history of atopic diseases, and wood or coal as energy source for heating and cooking. †Lifetime prevalence. ‡12-month period prevalence.

of their peers. A genetic selection bias may have contributed to our observations as generations of farmers with hay fever or asthma may have moved into other occupations. However, controlling for a positive family history of atopic disease did not significantly change the estimate for 'farming'. Analogous, the gradient between children of parents running a farm on a part-time vs a full-time basis remained almost unchanged after adjusting for atopic diseases in the family (data not shown). In contrast, parental education explained in part the difference in prevalence between children of parents with part-time or full-time farming activity (data not shown). This supports the notion that farmers moved to other part-time jobs as a result of economic constraints, rather than atopic diseases in the family. Moreover, the increase in hay fever and asthma

prevalence in the general population was observed merely within the last few decades [10,23–25]. Differential reproduction of 'nonallergic' phenotypes among farmers will presumably require more time to take effect. Although we cannot exclude with certainty that the genetic background contributes to some extent to the protective farming effect, environmental factors related to the lifestyle of these families are more likely to account for the lower prevalence of atopic diseases among farmers and their children.

Environmental influences

The lifestyle of children living on a farm differs from living conditions of other children. In line with previous findings a shorter duration of parental education [11], a larger sibship

Table 5. Exposure to livestock in children of farming parents (*N* = 1181): relation to atopic diseases†

	Exposure		
	No or rare contact	Occasional contact	Frequent contact
Prevalence of atopic diseases† (%)	22.9 (46/201)	18.8 (68/362)	13.6* (80/589)
Adjusted‡ OR (95% CI)	1.0	0.88 (0.50–1.57)	0.41 (0.23–0.74)

* $P < 0.005$ (Mantel-Haenszel χ^2 test for trend). †Defined as doctor's diagnosis of hay fever and/or asthma and/or eczema. ‡Adjusted for older siblings, parental education, family history of atopic diseases and wood or coal as energy source for heating and cooking.

size [15,16] and the use of coal and wood for heating [22] were associated with a lower risk of atopic disorders and were more common among farmers. When including parental education, older siblings and a positive family history of atopic disease into the regression model, all adjusted odds ratios for farming remained significant (data not shown). After additional adjustment for coal or wood as heating source the odds ratios for hay fever symptoms and asthma became non-significant. Farming and use of coal or wood as heating source were highly correlated and in most models use of coal or wood as heating source had no independent significant effect. This may indicate an overadjustment resulting in conservative effect estimates. Among part-time and full-time farmers similar relations were found. Furthermore, small numbers within the farming activity categories reduced the power of the subset analyses. These findings strongly suggest that the protective 'farming effect' cannot be attributed to confounding factors.

Indoor dampness increased the risk for atopic disorders in this population as has been shown previously [26,27]. However, farmers reported more indoor dampness parallel to a lower disease prevalence (Tables 2 and 3) supporting the notion that a strong protective factor operates in the agricultural environment. Use of antibiotics was related to a higher prevalence of hay fever and asthma. The less frequent use of antibiotics by farmers' offspring compared with other children may result in an enhanced infectious burden which has been suggested to protect against the development of asthma and allergies [14]. Furthermore, use of homeopathic medication was less common among farmers' children and was positively related to atopic disorders and severity of symptoms (data not shown), both having a lower frequency in the farming group. This suggests that parents of children with more severe symptoms are more likely to apply homeopathic remedies. The consumption of whole, but not skim milk was associated with a decreased prevalence of hay fever and asthma (data not shown). This is in line with recent studies which indicate a protective effect of foods rich in fatty acids [12]. Alternatively, increased consumption of whole milk may reflect an increased intake of milk originated directly from the farm. This 'raw', unpasteurized milk may contain a higher microbial load, particularly of *Lactobacillus*, than industrially processed skim milk. In mice, food allergy has been shown to be suppressed after injection of heat-killed *Lactobacillus plantarum* L-137 [28] which supports our notion. Though farmers' children used less antibiotics and homeopathic medication, and drank more whole milk than their peers, none of these factors explained the protective 'farming effect' in the multivariate models.

Exposure to livestock

Interestingly, among farmers' children a strong inverse,

dose-dependent association between factors related to exposure to livestock and atopic disorders was found (Table 5). In childhood, allergies against cows, pigs and chickens are uncommon. Therefore, it seems unlikely that the inverse relation is due to allergen avoidance. In occupational medicine increased concentrations of bacterial compounds such as endotoxin and its purified derivate lipopolysaccharide were found in stables where livestock is kept [29]. These potent pro-inflammatory agents may direct the immune response towards TH1 responses [30,31] which have been shown in laboratory studies to suppress the development of immunoglobulin E antibodies [32]. Hence, elevated exposures to bacterial compounds (lipopolysaccharides) in the microbial environment of farm stables may reduce the risk of developing atopic diseases through the promotion of TH1 responses.

In summary, we observed a protective 'farming effect' suggesting that environmental factors related to living conditions on a farm may protect against the expression of allergic diseases in children. Further studies are needed to identify the effective environmental influences, eventually leading to a new strategy of prevention against the development of atopic disorders in childhood.

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