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Risk factors associated with asthma and rhinoconjunctivitis among Swedish farmers

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Key words: allergens; asthma; environmental exposure; farmers; FEV₁; rhinoconjunctivitis; risk factors; sensitization.

Background: Earlier studies have shown a high prevalence of respiratory symptoms in farming communities and that storage mites constitute important allergens. We examined risk factors associated with asthma and rhinoconjunctivitis among Swedish farmers.

Methods: A population of 1015 small-scale dairy farmers was part of an epidemiologic survey. After selection based on symptom reports in a questionnaire, 461 of the farmers attended a medical examination, which comprised SPT, RAST analyses, and lung-function measurements. Risk factors for sensitization to different allergens, and development of asthma and rhinoconjunctivitis were assessed by multiple logistic regression.

Results: The prevalence of atopy was 26.7% among the farmers. For both asthma and rhinoconjunctivitis, sensitization to mites (OR=5.8 vs OR=3.8) and pollens (OR=10.3 vs OR=5.8) was a significant risk factor. There was a significant relationship between sensitization to mites and working time (OR=5.2). Environmental tobacco smoke and exposure to different animal species at the farm did not appear to affect the risk of allergen sensitization or respiratory symptoms. Farmers smoked less than the general population, but they more frequently had reduced FEV₁.

Conclusions: Allergen sensitization, especially to mites and pollens, was significantly associated with asthma and rhinoconjunctivitis in a farming community. The results point to allergen avoidance as a major goal for the prevention of occupational respiratory diseases among the farming population.

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An increased prevalence of asthma and rhinoconjunctivitis in industrialized countries has been reported during the last decade (1, 2), and this trend is not due merely to a change in diagnostic criteria but constitutes an increase per se (3). Recently, von Mutius et al. showed that the prevalence of atopy and respiratory disorders in two ethnically similar populations (children studied shortly after the reunification of Germany) was significantly lower among subjects living in the former East Germany than among subjects living in the former West Germany (4). The authors suggested that the Western lifestyle is a risk factor for the development of atopy, which in turn predisposes to asthma.

An association between occupation and development of allergy has been shown for several professions, and many agents are known to cause occupational rhinitis and asthma (5, 6) mediated by IgE antibodies. A high prevalence of respiratory symptoms among farmers has been demonstrated in studies from both Scotland and the Nordic countries (7–10); occupational asthma is the most common disease among farmers in Finland (11). Not only do farmers have a higher risk of developing asthma, but the asthma mortality rate among male farmers in Sweden is significantly higher than that in other occupational branches (12). Earlier studies have shown that farmers are more often sensitized to mites than the general population, and less to other common allergens, such as pollens and animal danders (8, 13, 14). Storage mites, together with cow epithelium and flour, have been reported as the most common causative agents of occupational asthma among farmers (11).

The aim of this epidemiologic study in a Swedish farming community was to determine whether exposure to common inhalant allergens and other risk factors is associated with atopy, asthma, and rhinoconjunctivitis.

Material and methods

Study design

An epidemiologic survey was performed in April 1996 among farmers aged 15–65 years, living on Gotland, an island in the Baltic Sea (15). Briefly, a questionnaire on symptoms from the airways and eyes, smoking habits, and working conditions was sent to all farmers aged 15–65 years who owned 2 hectares or more. Specific questions dealt with exposure to environmental tobacco smoke (in childhood and currently at home or during farm work), exposure to animals either at home and/or at the farm (all farmers were exposed

to cow, but, in addition, they could be exposed to horse, sheep/goat, swine, poultry, dog, or cat), number of years of farming, and use of dust masks (paper mask, half-mask, or air-stream helmet).

Out of the 1577 farmers who completed the questionnaire, 1015 were dairy farmers and were retained in the study. According to their answers in the questionnaire, the farmers were allocated to one of four groups:

- 1) single-organ hypersensitivity, farmers with immediate onset of symptoms from either the lungs or the nose/eyes ($n=343$)
- 2) multiple-organ hypersensitivity, those with immediate-onset symptoms from both the lungs and the nose/eyes ($n=132$)
- 3) suspected allergic alveolitis ($n=11$)
- 4) asymptomatic subjects ($n=529$).

From each of the four groups, a random sample of subjects aged 15–65 years was invited to attend a thorough medical examination. Of the 500 farmers selected, 100 were healthy, 258 had single-organ hypersensitivity, 131 had multiorgan hypersensitivity, and 11 had suspected allergic alveolitis, according to the questionnaire answers. The medical examination included interview by a physician with experience in allergic diseases, skin prick test (SPT), blood sampling for RAST analyses, and lung-function test. A total of 461 (92.2%) farmers attended the examination. The majority of the investigated farmers were men (90.3%), and the mean age was the same for men and women (44.8 years).

Asthma was considered to be present in subjects with a history of episodic shortness of breath, wheezing, and breathing difficulties ($n=83$). Allergic rhinoconjunctivitis (seasonal or perennial) was defined as episodic rhinorrhea, usually associated with nasal stuffiness and sneezing and lacrimation, in response to known or suspected allergen(s) ($n=254$) (15). From the results of the medical examination and the questionnaire, the prevalence of any form of immediate onset symptoms of some kind was estimated to be 41.7% in the whole group of 1015 farmers, with asthma present in 9.8% and rhinoconjunctivitis in 33.1%.

SPT

SPT were performed on the volar side of each forearm by a trained nurse. Thirteen allergens were tested: birch, timothy grass, mugwort, cat, dog, horse, cow (10 HEP), *Aspergillus fumigatus*, *Cladosporium herbarum* (1:20 w/v), *Dermatophagoides pteronyssinus*, *Lepidoglyphus destructor*, *Acarus siro*, and *Tyrophagus putrescentiae* (1000 NE/ml).

A positive (histamine chloride 10 mg/ml) and a negative reference were included. All extracts and controls were obtained from ALK, Allergologisk Laboratorium, Hørsholm, Denmark. A positive SPT was defined as 2+ and at least 3 mm.

Radioallergosorbent test (RAST)

The Pharmacia CAP System, RAST FEIA (Pharmacia & Upjohn, Diagnostic AB, Uppsala, Sweden), was used to quantify IgE antibodies against 21 allergens (birch, timothy grass, mugwort, rye, wheat, cat, horse, cow, dog, rat, mouse, house-dust mites [*D. pteronyssinus* and *Euroglyphus maynei*], storage mites [*A. siro*, *L. destructor*, *T. putrescentiae*, and *Glycyphagus domesticus*], *C. herbarum*, *A. fumigatus*, and nonstinging insects [*Gasterophilus intestinalis* and *Sitophilus granarius*]). A positive RAST was defined as ≥ 0.35 kU/l.

Atopy

Atopy was defined as at least two positive SPT at 2+ or one positive SPT at 3+ and/or one positive RAST.

Lung-function test

Measurements of forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), vital capacity (VC), FEV% (FEV₁/VC), and peak flow rate (PEFR) were conducted by an experienced nurse using a Vitalograph Alpha (Buckingham, UK). The Vitalograph was calibrated according to the manufacturer's instructions at least once daily. The test was done with the subject in an upright position and performed at least twice for each person. The test that yielded the highest value was accepted. Standardized reference values according to Berglund & Birath were used [16].

Statistical analysis

All prevalence rates (symptoms, SPT, and RAST) pertaining to the population of 1015 farmers constitute weighted estimates based on the detailed investigation of the 461 farmers attending the examination.

Univariate logistic regression analysis was used for calculation of odds ratios; each univariate factor was then tested separately in a multiple logistic regression model with adjustment for sex, age, and smoking (current smokers and nonsmokers). If the 95 % confidence interval (CI) did not

include 1.0, the odds ratio was statistically significant at $P < 0.05$.

Ethical considerations

The study was approved by the ethics committee of the Karolinska Institutet, Stockholm, Sweden.

Results

Population

Out of the 1015 subjects, a total of 80.7% had been farming for more than 10 years, 78.7% were working a minimum of 40 h per week, and 11.7% spent 20–39 h weekly on farm work. Almost one-third (30.9%) were occupied with pig-breeding. Current smoking was present in 15.9%, and 57.2% had never smoked. A history of parental smoking was present in 43.9%, and 16.1% of the farmers reported current daily exposure to environmental tobacco smoke.

SPT and RAST results

Based on SPT, sensitization to timothy grass reached the highest prevalence (3.6%) among the three different pollens, while sensitization to cow was most common (4.2%) among the animal danders. However, compared to storage mites (5.2–11.3%), pollens, molds, and animal danders were all represented with lower figures. It is notable that positive SPT were more common against storage mites than against the house-dust mite *D. pteronyssinus* (4.6%). In general, the RAST prevalence was slightly higher than the corresponding figures for SPT. The calculated prevalence rates for sensitization to respective groups – pollens, animal danders, and mites – were almost the same regardless of whether SPT or RAST results was used. The prevalence of atopy was calculated to be 26.7% in the whole population.

Out of the 461 farmers, 103 were sensitized to storage mites; i.e., they had at least one positive SPT and/or one positive RAST, corresponding to a prevalence of 17.1%. The corresponding figure for house-dust mites was 8.8% and for any mites species 18.8%. Furthermore, sensitization to pollens, animal danders, insects, and molds was present in 13.1%, 13.8%, 6.0%, and 4.2%, respectively.

Allergic sensitization, according to both SPT and RAST, was more frequent among farmers with asthma than among farmers with rhinoconjunctivitis. Among the allergens tested, the mite species were the most common allergens.

Furthermore, mites were the most prevalent allergens among farmers with asthma as well as rhinoconjunctivitis (Table 1).

Association between sensitization to different groups of allergens

The association of sensitization to groups of allergens with other variables, calculated with univariate logistic regression analysis, is shown in Table 2. Interestingly, all different allergen groups were significantly associated with each other. Sensitization to storage mites and sensitization to

Table 1. Proportions of positive SPT and RAST against common inhalant allergens among symptomatic and asymptomatic farmers (%)

Allergen	Asthma		Rhino-conjunctivitis		Asymptomatic	
	SPT	RAST	SPT	RAST	SPT	RAST
<i>Pollens</i>	–	36.1	–	22.8	–	4.8
Birch	13.3	18.1	7.9	9.4	0.7	1.4
Timothy grass	20.5	28.9	7.9	15.7	0.7	3.4
Mugwort	4.8	16.9	5.5	6.7	0	0.7
Wheat	nd	25.3	nd	16.9	nd	4.1
Rye	nd	26.5	nd	17.7	nd	3.4
<i>Animal danders</i>	20.5	25.3	17.3	16.5	2.8	6.2
Cat	14.5	12.0	7.5	7.8	0.7	4.8
Dog	13.3	13.3	8.3	6.7	0.7	1.4
Horse	7.2	4.8	3.5	2.8	0.7	0.7
Cow	10.8	18.1	7.5	11.4	1.4	2.1
<i>Mites</i>	–	31.3		23.6	–	3.4
<i>D. pteronyssinus</i>	20.5	26.5	11.0	17.7	0	1.4
<i>E. maynei</i>	nd	14.5	nd	9.8	nd	0.7
<i>A. siro</i>	27.7	21.7	21.3	14.9	6.9	2.1
<i>L. destructor</i>	27.7	16.9	23.6	14.2	2.8	2.8
<i>T. putrescentiae</i>	12.0	20.5	10.6	14.6	2.8	2.1
<i>G. domesticus</i>	nd	12.0	nd	8.7	nd	1.4
<i>Insects</i>	–	14.5		9.8	–	3.4
<i>S. granarius</i>	nd	13.3	nd	9.8	nd	3.4
<i>G. intestinalis</i>	nd	6.0	nd	3.9	nd	1.4
<i>Molds</i>	4.8	6.0	3.1	2.8	0.7	2.1
<i>C. herbarum</i>	0	2.4	0.4	0.4	0	0.7
<i>A. fumigatus</i>	4.8	3.6	3.1	2.4	0.7	1.4
<i>Rodents</i>	–	2.4	–	0.4	–	0
Rat	nd	1.2	nd	0.2	nd	0
Mouse	nd	2.4	nd	0.4	nd	0

nd: not done.

house-dust mites were strongly associated (OR=50.1, 95% CI: 22.9–123.4); in a multiple logistic regression analysis, adjusted for sex, age, and smoking, the OR was 36.9 (95% CI: 15.8–86.7). Sensitization to either storage or house-dust mites was most prominent in association with sensitization to animal danders (OR=5.1, 95% CI: 3.0–8.8) and molds (OR=3.6, 95% CI: 1.3–9.8) in the adjusted multiple model. There were significant correlations between smoking and sensitization to insects as well as between length of work week, reduced FEV₁, and sensitization to mites. However, no association was found for exposure to different animal species, years of farming, use of dust masks, or allergen sensitization (not shown in Table 2). Furthermore, exposure to environmental tobacco smoke in childhood and currently did not seem to affect the risk of allergen sensitization among either smokers or nonsmokers.

Association of sensitization with airway diseases

The most prominent risk factors for having any kind of respiratory symptom were sensitization to mites, pollens, animal danders, and insects and working full time (Table 3). In the multiple regression analysis, sensitization to pollens (OR=4.9, 95% CI: 2.3–10.7) and to mites (OR=3.3, 95% CI: 1.8–6.1) remained a significant risk factor for any respiratory symptoms.

In the univariate model, the risk of asthma as well as rhinoconjunctivitis was most clearly associated with sensitization to mites, pollens, and animal danders. In the adjusted analysis, sensitization to pollens (OR=10.3, 95% CI: 4.2–25.2) and to mites (OR=5.8, 95% CI: 2.7–12.6) was the only significant risk factor for asthma. Corresponding risk factors for rhinoconjunctivitis were sensitization to mites (OR=3.8, 95% CI: 2.0–7.1) and pollens (OR=5.8, 95% CI: 2.6–12.9), and working full time (>40 h/week) (OR=1.9, 95% CI: 1.1–3.3). No significantly elevated risk was associated with exposure to different animal species at home or at the farm (Table 4), or with years of farming and not using dust masks (not shown in Table 4). Reported exposure to environmental tobacco smoke in childhood or currently did not significantly affect the risk of airway disease in smokers, ex-smokers, or nonsmokers.

Lung function

The calculated prevalence of FEV₁ less than 80% of the predicted value was 16.0% in the whole population of farmers. After categorization according to symptoms, 12.6% of the subjects with rhinoconjunctivitis and 31.2% of those

Table 2. Odds ratios indicating association of sensitization to mites, pollens, animal danders, insects, and molds with smoking, length of work week, and FEV₁ <80% of predicted value

	Mites	Pollens	Animal danders	Insects	Molds
Pollens	3.3 (2.0–5.4)				
Animal danders	6.6 (4.0–11.1)	5.1 (3.0–8.7)			
Insects	8.1 (3.8–17.2)	8.7 (4.1–18.4)	6.4 (3.1–13.2)		
Molds	5.0 (2.1–12.1)	4.9 (2.0–11.6)	4.2 (1.7–10.2)	4.2 (1.4–12.1)	
Smoking	0.9 (0.5–1.6)	0.9 (0.5–1.7)	0.8 (0.4–1.6)	3.0 (1.4–6.4)	0.7 (0.2–2.7)
Work week of					
>40 h/week	5.2 (3.0–9.0)	0.8 (0.5–1.3)	1.0 (0.6–1.8)	1.7 (0.6–4.5)	1.0 (0.3–2.6)
FEV ₁ <80%	2.3 (1.4–3.9)	1.0 (0.6–2.0)	1.0 (0.6–2.0)	1.7 (0.7–4.0)	1.6 (0.6–2.0)

OR is given with 95% CI. If CI does not include 1.0, result is significant at $P < 0.05$.

with asthma had a FEV₁ below 80% of predicted value, while the corresponding figure among the asymptomatic farmers was 16.7%. A reduced FEV₁ was seen among 27.3% of the

current smokers and among 17.3% of the subjects that had ever smoked. A reduction of the FEV₁ by 20% or more was observed among 16.3% of the farmers who had worked full time for more than 10 years. The proportion of farmers with a reduced FEV₁ was similar among subjects breeding swine and those not doing so (17.1% vs 15.2%).

Table 3. Odds ratio for airway disease in relation to sensitization to different allergens, smoking, length of work week, and FEV₁ <80% of predicted value

	Any symptom	Asthma	Rhinoconjunctivitis
Mites	5.6 (2.9–10.9)	3.5 (2.1–5.8)	3.7 (2.3–6.1)
Pollens	5.6 (2.6–12.0)	4.9 (2.9–8.3)	4.5 (2.5–8.1)
Animal danders	3.5 (1.8–6.9)	4.1 (2.4–7.0)	2.4 (1.4–4.1)
Insects	2.8 (1.1–7.5)	2.7 (1.3–5.8)	2.8 (1.3–6.4)
Molds	2.1 (0.7–6.4)	2.5 (1.2–5.2)	1.2 (0.6–2.3)
Smoking	1.2 (0.7–2.0)	0.6 (0.3–1.2)	0.9 (0.5–1.4)
Work week of			
>40 h/week	1.8 (1.1–2.8)	1.1 (0.6–2.0)	1.6 (1.1–2.6)
FEV ₁ <80%	0.9 (0.7–2.0)	3.2 (1.8–5.6)	0.6 (0.4–1.0)

OR is given with 95% CI. If CI does not include 1.0, result is significant at $P < 0.05$.

Discussion

Several studies have shown that farmers have an elevated risk of developing airway symptoms (5, 8, 10, 17). The role of storage mites as a causative factor in respiratory allergy has been well established in rural as well as in urban populations (8, 9, 13, 18, 19). The findings in this study confirm that mites are important allergens in the farming environment, with almost one-fifth of the farmers sensitized to mites. Furthermore, mites were the most prevalent allergens among farmers with asthma and rhinoconjunctivitis. Storage mites are most common in barns and other places where hay, straw, and grain are stored (20, 21), but they can also be found in the indoor home environment (22). A recent study from Sweden found *L. destructor* in 100% of the hay samples from 30 investigated farms and *A. siro* in more than 80% (23). As for the indoor environment in rural homes, high numbers of both house-dust mites and storage mites, as well as large amounts of the house-dust mite allergens

Table 4. Odds ratio for airway disease related to exposure to different animal species

	Any symptom	Asthma	Rhinoconjunctivitis
Dog at home and/or at farm	1.4 (0.8–1.7)	1.0 (0.6–2.2)	1.2 (0.8–1.7)
Cat at home and/or at farm	1.2 (0.7–2.1)	1.1 (0.6–2.2)	1.0 (0.6–1.7)
Sheep/goat	0.8 (0.5–1.3)	0.9 (0.5–1.5)	0.9 (0.6–1.3)
Horse	0.9 (0.6–1.4)	0.9 (0.6–1.6)	0.9 (0.6–1.4)
Poultry	0.7 (0.5–1.1)	1.0 (0.6–1.8)	0.7 (0.5–1.1)
Swine	1.3 (0.8–2.0)	1.2 (0.7–2.0)	1.2 (0.8–1.8)

OR is given with 95% CI. If CI does not include 1.0, result is significant at $P < 0.05$.

Der p 1 and Der f 1, have been recorded (22, S. Parvaneh, in manuscript). Thus, storage mites as well as house-dust mites are part of the mite fauna of rural surroundings.

We observed a more than threefold increased risk of respiratory symptoms of some kind among farmers sensitized to mites or pollens and a more than fivefold elevated risk of asthma. Because asthma is a chronic disease which when inadequately treated may lead to a persistent impairment of lung function that may adversely affect the quality of life, it is desirable to prevent allergic sensitization.

In Finland, cow dander is reported to be an important cause of allergy among farmers. Terho et al. have demonstrated that 50 out of 70 farmers with allergic rhinitis had a positive reaction upon nasal challenge with cow dander (9). Among Swedish farmers, cow dander seems to be of less importance as an occupational allergen, although we found that cow was the most common cause of sensitization to animal danders, according to both SPT and RAST.

Various insect species can cause inhalant (24) as well as occupational allergies (25). Both the botfly (*G. intestinalis*) and the grain weevil (*S. granarius*) yielded nearly the same prevalence of sensitization as animal dander. A positive RAST against *G. intestinalis* was almost twice as frequent as against *S. granarius*, a finding which is in accordance with earlier findings from a farming community (26). Out of 34 subjects with positive RAST against either botfly or grain weevil, 23 were also sensitized to mites, a finding which probably reflects the fact that these insects and mites usually are found in the same habitat. The IgE-mediated response to timothy grass, wheat, and rye among the farmers

was twice as high as the response to birch, but still remained low compared to the response in the general population (27). Most of the farmers who were RAST-positive to timothy grass were also positive to wheat and/or rye, probably because of allergenic similarities between the allergens. A taxonomic relationship exists among the three different types of pollens, and cross-reacting allergens have been demonstrated (28, 29).

We obtained an almost four times higher prevalence of reduced FEV₁ than Bakke et al., who reported that 4.5% of a general population had a FEV₁ below 80% of predicted (30). Several earlier studies have demonstrated that farmers more often have a reduced FEV₁ and a more rapid decline in lung function than controls (31, 32). It is well documented that swine confinement workers in particular, but also grain and dairy farmers, have lower FEV₁ than the general population (33–35). The significant association of a FEV₁ below 80% of predicted value with asthma primarily represents a manifestation of the disease. We were not able to demonstrate any relation between swine-keeping and reduced lung function, possibly because most of the farms on Gotland are family farms with small numbers of swine. The relationship between smoking and reduction of FEV₁ is well established (36). In the univariate model, we found that smoking and sensitization to mites were risk factors for decreased FEV₁. The prevalence of smoking in rural communities has earlier been reported as almost 30% (37, 38). We found a lower prevalence of smoking (15.9%), which is more in accordance with the findings of Vergnenegre et al., who reported a prevalence of 18.1% of current smokers

among agricultural workers in France (39). The proportion of smokers among the Gotland farmers is lower than among Swedes in general, in whom the prevalence is estimated to be about 25 % (40).

The cross-sectional methodology used in this study is not optimal for assessment of causal relationships (41). For example, exposure to risk factors for allergy, such as environmental tobacco smoke and furred animals, as well as use of dust masks, may have changed after disease occurrence. Furthermore, the use of dust masks may be an indication of high exposure to dust in some cases and low exposure in others, making the interpretation difficult. On the other hand, substantial misclassification of pollen exposure is improbable since the pollen load was constant over several years (42, 43). In addition, two different studies performed by the authors in 1988 and 1992 revealed that the exposure to mites was constant (23, 44).

In conclusion, this study shows that in a small-scale, family-oriented farming community, sensitization to common allergens, especially mites and pollens, is associated with occurrence of asthma and rhinoconjunctivitis. However, no clear association was observed for exposure to environmental tobacco smoke or exposure to different animal species at the farm. The results point to allergen avoidance as a major goal for the prevention of occupational respiratory diseases among the farming population.

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