

Increasing prevalence of asthma over 12 years among dairy farmers on Gotland, Sweden: storage mites remain dominant allergens

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Summary

Background Earlier studies from several countries have shown that IgE-mediated allergy in rural populations is of considerable importance and that storage mites are dominant allergens.

Objective In an epidemiological follow-up study among farmers on the island of Gotland, Sweden in 1996 we wished to investigate the prevalence of respiratory allergy and to find out whether storage mites are still important allergens in a farming environment.

Methods A questionnaire concerning airway symptoms, social and working conditions and smoking habits was distributed to all Gotland farmers aged 15–65 years and was completed by 1577 (86.7%), of whom 1015 were dairy farmers. Based on the answers, 500 dairy farmers were invited to undergo a medical examination which included a skin-prick test (SPT) and blood sampling for RAST analyses. Prevalence figures (symptoms, RAST and SPT) given for the whole population ($n = 1015$) were based on the investigation of the 461 farmers who took part in the examination.

Results Immediate onset hypersensitivity was present in 41.7% of the 1015 farmers studied, which is almost the same figure as in 1984 (40.0%). The prevalence of asthma had increased significantly during the previous 12 years (5.3% vs 9.8%), as had asthma in combination with rhinoconjunctivitis (3.7% vs 7.0%). Rhinoconjunctivitis, on the other hand, had not changed significantly (36.5% vs 33.1%) and remained one of the most common symptoms. The prevalence of storage mite allergy in the farming population in 1996 was 6.5% and constituted an important cause of allergic symptoms.

Conclusion Over 12 years, Gotland dairy farmers have developed significantly more respiratory symptoms from the lower airways, although the proportion with atopy is unchanged. Storage mites are still dominant allergens for developing allergic disease.

Keywords: farmers, epidemiology, asthma, respiratory symptoms, storage mites

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Introduction

Many studies from different parts of the world have reported an increase in the prevalence of asthma and rhinoconjunctivitis, independently of age [1–4]. Although the

reason for this is not fully understood, it probably involves interactions between numerous endogenous and exogenous factors. Occupational allergies, asthma and rhinoconjunctivitis have also increased during the past decade [5]. Farmers are exposed to many different types of agents, several of which are risk factors for respiratory diseases such as asthma and farmer's lung [6]. Farm workers are generally believed to lead a healthy open-air life. However,

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the highest incidence of occupational allergic respiratory diseases in Finland has been detected among farmers and bakery workers [5]. Among farmers, the main causative agents were cow epithelium, floor dust and storage mites. Several studies have reported that IgE-mediated allergy is a problem of far greater importance in rural populations than farmer's lung [7,8].

Earlier studies from Scotland, England and the Nordic countries have shown that allergy to storage mites is of major importance as a cause of bronchial asthma and/or allergic rhinitis in rural settings [9–13]. In 1984 an epidemiological study concerning respiratory symptoms among farmers on the island of Gotland in the Baltic Sea found a prevalence of 40% for immediate onset hypersensitivity. The main cause of allergic respiratory symptoms was storage mites [7]. The prevalence of storage mite allergy was as high as 6.2%. Common inhalant allergens such as pollens and animal danders were of minor importance [11].

We present here a 12-year follow-up study of respiratory symptoms among the farming population on Gotland. The aim was to investigate whether the prevalence of airway symptoms had changed and whether storage mites were still a risk factor for the development of allergic diseases.

Material and methods

Study design

Registry information from the Federation of Swedish Farmers was used to select the study subjects. A questionnaire for self-administration was distributed in November 1995 to all farmers, aged 15–65 years, who owned 2 hectares or more on the island of Gotland. The questionnaire contained 53 questions concerning work-related and chronic symptoms from the upper and lower airways, social working conditions and smoking habits, including passive smoking. The questionnaire was completed by 1577 subjects, corresponding to 86.7% of the men and women of this age group mainly occupied with farming. The questions on disease, social working conditions, dust exposure and smoking habits were the same as those asked in 1984. As almost all subjects in the 1984 study were dairy farmers who handled hay or straw, only farmers that performed this kind of work were included in the further studies ($n = 1015$).

On the basis of the answers, the subjects were grouped according to symptoms: group 1, healthy subjects ($n = 529$); group 2, single-organ symptoms, those with immediate-onset symptoms from either the lungs or the nose/eyes ($n = 343$); group 3, multi-organ symptoms, those

with immediate-onset symptoms from both the lungs and the nose/eyes ($n = 132$) and group 4, suspected allergic alveolitis ($n = 11$). From the four groups, a random sample of 500 subjects aged between 15 and 65 years was adjusted to give the same age distribution as the whole material. These people were invited to undergo a thorough medical examination. Of these 500 farmers, 100 were healthy (group 1), 258 were from group 2 and had single-organ symptoms, 131 were from group 3 and had multi-organ symptoms, and 11 were from group 4 and had suspected allergic alveolitis, according to the classifications based on the questionnaire answers. Of the 500, 461 (92.2%; 415 men and 46 women) underwent the medical examination, which was performed on Gotland in April 1996. The attendance in the four groups was (1): 90/100, (2): 241/258, (3): 119/131 and (4): 11/11. Among the 39 dropouts nine had died or were not able to participate due to serious illness not related to allergy and six had changed occupation or moved away from Gotland.

The medical examination comprised a structured interview concerning history of allergic symptoms and a physical examination conducted by a physician with experience in allergic diseases. It also included a skin-prick test (SPT) performed by a trained nurse, blood sampling for determination of IgE antibodies and total IgE analyses. On the basis of the allergological interview and the questionnaire, all the farmers examined were finally allocated to one (or more) of the symptom groups (asthma or rhinoconjunctivitis or both and suspected allergic alveolitis) or an asymptomatic group. These groups were then further subdivided into atopic and non-atopic based on the results of the RAST analysis. The subjects were classified as atopic if they had at least one positive RAST to the allergens mentioned below. The diagnoses of asthma, rhinoconjunctivitis and suspected allergic alveolitis were based on the same criteria as in 1984 and were made by a physician experienced in allergology on the basis of the case history and physical examination. Asthma was considered to be present in people with a history of episodic shortness of breath, wheezing and breathing difficulties. Allergic rhinoconjunctivitis (seasonal or perennial) was defined as episodic rhinorrhoea, usually associated with nasal stuffiness and sneezing and lacrimation, in response to known or suspected allergen(s). The classification of suspected allergic alveolitis required the occurrence of repeated attacks of characteristic symptoms such as recurrent febrile reactions with respiratory symptoms during the previous 2 years. All prevalence figures (symptoms, SPT and RAST) pertaining to the whole population of dairy farmers ($n = 1015$) are based on the detailed investigations of the 461 farmers attending the examination, taking into consideration the selected fraction of subjects in the different symptom groups.

Skin-prick tests

Skin-prick tests were performed against the same allergens as in 1984 (birch 10 HEP, timothy grass 10 HEP, mugwort 10 HEP, *Aspergillus fumigatus* 1:20 w/v, *Cladosporium herbarum* 1:20 w/v, cat 10 HEP, dog 10 HEP, horse 10 HEP and *Dermatophagoides pteronyssinus* 10 HEP). Histamine chloride concentration was 10 mg/mL. The extracts were obtained from ALK (Allergologisk Laboratorium, Hørsholm, Denmark). Test procedures were performed according to Pepys [14] on the volar side of each forearm. A positive skin-prick test was defined as a ++ [15] and at least 3 mm.

Serum IgE

The IgE concentration in serum was determined using the Pharmacia CAP System, IgE FEIA (Pharmacia & Upjohn AB Diagnostics, Uppsala, Sweden) (kindly provided by Pharmacia & Upjohn). The cut-off was 2 kU/L.

Radioallergosorbent test (RAST)

The Pharmacia CAP System, RAST FEIA (Pharmacia & Upjohn AB Diagnostics) was used for quantifying circulating IgE antibodies to the same 10 allergens as in 1984 (birch t3, timothy grass g6, *C. herbarum* m3, dog e5, cow e4, *D. pteronyssinus* d1, *Lepidoglyphus destructor* d71, *Acarus siro* d70, *Tyrophagus putrescentiae* d72 and *Glycyphagus domesticus*, d73 (kindly provided by Pharmacia & Upjohn). The results are expressed in kU/L. All RAST values >0.20 kU/L were re-tested and a positive RAST was defined as ≥ 0.35 kU/L. If a value obtained from the second run differed by more than 25% from the first run, the sample was re-run a third time. A mean value was finally calculated from the second and third assay runs.

Statistical analyses

The continuous variables for IgE and RAST are described as geometric means and ranges for each group. Differences in IgE levels between groups were evaluated with the Mann–Whitney *U*-test. Differences in prevalence figures are given as 95% confidence intervals (95% CI). Based on the results of the clinical investigation and/or results of SPT and RAST, individuals with symptoms and positive allergen tests were identified among the 461 who underwent the medical examination. Given the distribution of these subjects in the four original symptom groups and the fraction of farmers included in each group (e.g. for healthy 90/529) the prevalence was estimated for the whole population of farmers ($n = 1015$).

Ethical considerations

The study was approved by the Ethics Committee of the Karolinska Institute in Stockholm.

Results

Population characteristics

The results of the questionnaire were based on 1015 subjects, of whom 90.3% were men and 9.7% women. The male and female subjects were of the same mean age, 44.8 years. Out of the 1015 farmers, 15.9% were current smokers and 57.2% had never smoked. The majority of the population had been occupied with farming for more than 10 years (80.6%) and were working full time, >40 h weekly (78.7%). Of the 461 farmers examined, 65 (14.1%) had participated in the 1984 examination.

Symptom groups

Immediate onset nasal/conjunctival or bronchial symptoms were present in 41.7% of the farming population, which is almost the same figure as in 1984 (40.0%). The prevalence of asthma had increased significantly during the previous 12 years (5.3% vs 9.8%, 95% CI for the difference in prevalence: 2%, 7%) as well as the prevalence of asthma among atopic subjects (3.1% vs 4.9%, 95% CI: –3%, –0.5%). In addition, there was a significant increase in the prevalence of asthma and rhinoconjunctivitis (3.7% vs 7.0%, 95% CI: –4%, –1%). On the other hand, there was a non-significant decrease of farmers with rhinoconjunctivitis, which still was the most common symptom, 36.5% vs 33.1% (95% CI: 0%, 6%). However, the prevalence of rhinitis among atopic subjects had decreased significantly from 14.8 vs 11.4% (95% CI: 0.5%, 5%). The prevalence of suspected allergic alveolitis was low (one farmer in the group studied) and had not changed significantly since 1984 (Table 1).

Skin-prick test results

The prevalence of positive SPT to the allergens tested in 1984 and 1996 were not compared statistically because the extracts used in 1984 and 1996 were from different suppliers. As in 1984, low proportions of positive SPTs were found for pollen (2.0–3.1%), animal danders (1.6–4.2%) and mould (0.3–2.1%). Notably, the highest proportion of positive SPT both in 1984 and in 1996 was obtained for *D. pteronyssinus* (6.0% vs 4.6%).

IgE and RAST results

The highest IgE levels, both in 1984 and in 1996, were found among the atopic farmers with asthma or asthma and

Table 1. Estimated prevalence of symptoms of the airways and eyes among farmers on Gotland, a comparison between 1984 and 1996

Symptoms	1984 (%)	1996 (%)	Difference (95% CI*)
Asthma	5.2	9.8	4.6 (2–7)
Rhinoconjunctivitis	36.5	33.1	3.4 (0–6)
Asthma and rhinoconjunctivitis	3.9	7.0	3.1 (–4–2)
Suspected allergic alveolitis	0.2	0.1	–0.1 (–1–1)
Asymptomatic	59.8	58.2	–1.6 (–6–2)

* 95% confidence interval for estimated difference in prevalence 1984 and 1996. If CI includes 0 the result is not significant.

rhinoconjunctivitis. The levels had not changed significantly (140 kU/L [11–1400] vs 97 kU/L [3–1262] and 130 kU/L [11–1400] vs 101 kU/L [3–1959]). The prevalence of atopy among farmers on Gotland increased from 1984 to 1996 (14.9% vs 18.8%, 95% CI: –2%, 9%) although the change was not statistically significant.

Although there was a tendency towards an increase in prevalence of positive RAST for pollens, animal danders, mould, *D. pteronyssinus* and the four storage mite species (Table 2) since 1984, these differences did not reach statistical significance. The most prevalent positive RAST

Table 2. Prevalence of positive RAST against storage mites and other common allergens among farmers, a comparison between 1984 and 1996

Allergen	1984 %	1996 %	Difference (95% CI*)
All storage mites	6.8	8.1	1.3 (–2–5)
<i>L. destructor</i>	6.8	6.6	–0.2 (–4–4)
<i>A. siro</i>	3.9	6.2	2.3 (–1–6)
<i>T. putrescentiae</i>	4.4	6.2	1.8 (–2–5)
<i>G. domesticus</i>	4.7	3.8	–0.9 (–4–2)
Birch	1.9	3.9	2.0 (–1–6)
Timothy	4.9	8.1	3.2 (–1–7)
Dog	0.9	3.4	2.5 (0–5)
Cow	3.8	5.7	1.9 (–1–5)
<i>C. herbarum</i>	0.4	2.2	1.8 (0–4)
<i>D. pteronyssinus</i>	5.2	7.3	2.1 (–1–6)

* 95% confidence interval for estimated difference in prevalence 1984 and 1996. If CI includes 0 the result is not significant.

(8.1%) was for timothy grass and storage mites. Interestingly, *L. destructor* remained the storage mite species for which a positive RAST was most common. Positive responses against *L. destructor*, *A. siro* and *T. putrescentiae* were about equally present in 1996, whereas in 1984 only half as many subjects reacted to *A. siro* as to *L. destructor*.

Among the 461 farmers studied, a positive RAST to at least one of the four storage mite species was noted in 57 farmers. Of these, 22 (38.6 %) were RAST positive against all four species. Positive RAST tests to storage mites in 1984 were most frequent among those under the age of 45 years, which also was the case in 1996; 73.0% and 63.2%, respectively. A total of 42/57 of the storage mite-sensitized farmers were also RAST positive to the house dust mite *D. pteronyssinus*. A positive RAST against all the five analysed species of storage and house dust mites was present in 20 subjects.

Every fourth farmer with asthma or asthma and rhinoconjunctivitis had a positive RAST to storage mites (Table 3). However, rhinoconjunctivitis was the predominant disease among farmers with positive RAST against storage mites (46/57). In addition, more than one-third (20/57) of the farmers with IgE antibodies to storage mites had asthma, one-fifth (16/57) had asthma and rhinoconjunctivitis, while five farmers with these IgE antibodies were asymptomatic. The distribution of symptoms was similar for each of the four storage mite species. The highest RAST values were found among farmers with asthma in combination with rhinoconjunctivitis. The calculated overall prevalence of storage mite allergy in the entire farming population on Gotland remained around 6% (6.2% and 6.5% in 1984 and 1996, respectively).

Discussion

The most striking finding of this large survey is the significant increase in the prevalence of asthma among dairy farmers on Gotland: asthma has almost doubled during a

Table 3. Positive RAST (≥ 0.35 kU/L) to storage mites, grouped according to symptoms

Symptoms	Subject (n)	Positive (n)	%
Asthma	83	20	24.1
Asthma and rhinoconjunctivitis	62	16	25.8
Rhinoconjunctivitis	254	46	18.1
Suspected allergic alveolitis	1	0	0
Asymptomatic	145	5	3.4

12-year period (5.3% vs 9.8%). The number of farmers with asthma in association with rhinoconjunctivitis has also increased significantly. In contrast, the prevalence of rhinoconjunctivitis among farmers has remained unchanged. The prevalence of any form of immediate-onset symptoms from the airways has not changed, which is probably due to a shift from upper respiratory symptoms to multiple airways symptoms. Among the asymptomatic farmers who also underwent the examination in 1984, 50% (6/12) had developed respiratory symptoms and 19/33, who in 1984 had rhinoconjunctivitis only, were now reporting symptoms from the lower airways as well. This shift towards multiple symptoms was demonstrated earlier by, e.g. Ciprandi and colleagues, who over a 10-year period found an increased prevalence of asthma in association with hay fever among Italian conscripts [16]. Our findings cannot be explained by a shift towards an older and more symptomatic population, as the mean ages were almost the same in 1984 and 1996 (43 vs 45 years) and the age distributions within the groups were similar. Thus, it appears that there are other, unknown, explanations for the increases of lower airway symptoms.

Previous epidemiological studies among a general population in Sweden have reported a prevalence of asthma of 5.1% among adults and 6.8% among teenagers [17,18]. Åberg, who studied asthma and allergic rhinitis in Swedish conscripts over a 10-year period (1971–1981) reported an increase in prevalence of both asthma (1.9 vs 2.8%) and allergic rhinitis (4.4 vs 8.4%) [19]. Most authors agree that the greater prevalence of asthma and rhinoconjunctivitis cannot be explained only by better awareness and reporting of the diseases combined with improved diagnostic methods, but that the rise is also due to a true increase [19,20]. In the speculation about the causes of the increase, environmental factors such as smoking habits, infections, air pollutants, indoor climate, changes in allergen load and introduction of new allergens are implicated [21].

In Finland there was an increase in the number of newly detected cases of occupational asthma and rhinoconjunctivitis from 1981 to 1991. One of the most common occupations affected was farming [5]. Earlier studies among farmers from different parts of Europe also show a high prevalence of asthma. From Denmark the prevalence in a rural population is reported to be 7.7% [22], and from Scotland 15% [6]. Allergic alveolitis seemed to be as rare in 1996 as in 1984 (estimated prevalence 0.1%). The incidence of farmer's lung has been decreasing worldwide, mainly because of better knowledge about preserving hay and the installation of ventilation equipment in barns [23].

One prominent finding from the present study is that a positive RAST to storage mites was as common in 1996 as in 1984 (8.1 vs 6.8 %). The agricultural environment often offers favourable conditions for the growth of mites, especially in the presence of high humidity. Farmers are

exposed when handling hay, straw and grain. There are many different species of storage mite. In Europe the predominant mite fauna in barns consists of *L. destructor*, *A. siro*, *Tyrophagus* spp. and *G. domesticus* [8,25–27]. The importance of sensitization to storage mites in the rural population has been demonstrated by many authors [7,8,10–13,28,29]. Iversen and Pedersen, for instance, who studied 187 dairy and swine farmers in Denmark, found a positive RAST to storage mites in 5.3% [13] and Marx *et al.* demonstrated a positive RAST to storage mites in more than 9% of a group of farmers with respiratory symptoms [30]. In addition, we found a tendency to an increase in prevalence of sensitivity to all mite species including *D. pteronyssinus*, except for *G. domesticus*. Earlier studies have demonstrated that these allergens are more significant among the rural population than allergens from pollens and animal danders [11,13]. The proportion of storage mite-sensitized farmers with respiratory symptoms does not appear to have changed over 12 years and storage mites remain an important cause of allergic symptoms from the airways. A majority of the storage mite RAST-positive farmers (73.7%) were also positive against *D. pteronyssinus*, which may be due to the fact that different mite species propagate in the same environment [25,27], as well as the existence of allergenic cross-reactivity between the two mite species [31].

Interestingly, a positive SPT or RAST to pollens or to animal danders was generally less common, which agrees with earlier reports regarding rural workers [11,13]. This feature remains unclear, since pollen counts do not differ between Gotland and the Swedish mainland [32] and most farmers keep cats and dogs. One could speculate that this is due to an early health-related selection of affected individuals, but a study from the Department of Stress Research at the Karolinska Institute, Sweden, has shown that farmers in fact have a lower risk of leaving their occupation than do people in other lines of work [33]. Why the agricultural setting might render subjects tolerant of pollens and danders but not mites remains to be elucidated.

Obviously, there are several difficulties when assessing time trends based on two separate epidemiological studies, but as the criteria for diagnosis in the two studies were based on the same questionnaire as well as a medical examination, the data should be comparable. Since the results from both 1984 and 1996 were judged by the same person (MvHH) we believe that the comparisons are valid. However, in this study we decided not to put too much weight on the prevalence of positive SPTs since the extracts used in 1996 were from different suppliers than those used in 1984 (Pharmacia Diagnostics and ALK). It is a well-known fact that the allergen potency in SPT extracts varies even when they are obtained from the same company (batch-to-batch variation). The number of sensitized

farmers, as measured by specific IgE, did not change markedly during the intervening 12 years even though positive test results seem to be more common in 1996. As the Pharmacia CAP system was used in 1996, we cannot rule out the possibility that the tendency towards an increased prevalence of positive RAST analyses may be due to the improved *in vitro* tests [34].

We observed an increase in the prevalence of atopy, which did not reach statistical significance, even though the farmers examined in 1996 seemed to be more severely affected in the airways than those examined in 1984. Since we did not pay too much attention to the prevalence of positive SPTs, we decided to classify atopy based on RASTs only. Recent studies indicate that the prevalence of atopy is unchanged [24], even though there is an increase in the proportion of atopic subjects with symptoms.

Several important findings were obtained from the present study. First, the severity of the symptoms examined has increased during the past 12 years although the affected proportion of the farming population is unchanged. Secondly, even though the farmers were thoroughly informed in 1984 about health hazards associated with farming and methods of reducing allergen exposure, storage mites remain dominating allergens. Finally, the findings stress the importance of improved allergen avoidance and control in the rural environment.

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