Effect of farming environment on sensitisation to allergens continues after childhood

H O Keskela, K K Happonen, S T Remes, J Peckanen

Methods: A population based sample of 202 women who did not live on a farm and 231 who did. The subjects filled in a questionnaire and underwent skin prick tests for several common and farming related allergens.

Results: The prevalence of sensitisation to any of the allergens was similar in the two groups (37.1 vs 34.6% (p = NS). However, compared with women who did not live on a farm, the women who lived on a dairy farm showed a low prevalence of sensitisation to pollens (4.4 v 17.3%, p = 0.01) and cats (3.5 v 10.4%, p = 0.047). The risk of sensitisation to pollens and pets was lowest among women with both a childhood and adulthood farming environment and was dose dependently associated with current contact with farm animals. However, this contact increased the risk of sensitisation to bovine dander.

Conclusion: The farming environment may reduce sensitisation to common allergens also after early childhood. However, it may also increase sensitisation to farm allergens.

METHODS

Study population

This study was carried out in the 17 municipalities of the former Kuopio County. The study area consisted of mostly rural areas with few small towns. The present study is connected with a study about the effect of the farming environment on children.
Skin prick tests

The testing was carried out in the 2001, during winter to avoid the influence of pollen season, by a single fieldworker, according to the International Study of Asthma and Allergies in Childhood protocol.22

A panel of 10 allergens was used (Soluprick SQ, ALK-Abelló, Copenhagen, Denmark). Seven of the allergens were standardised (birch, timothy grass and mugwort pollens, cat, dog, horse dander, and house dust mite (Dermatophagoides pteronyssinus), and three were not (bovine dander, cockroach, and storage mite (Lepidoglyphus destructor)). The concentration of the standardised extracts was 10 histamine equivalent prick; the concentrations of the non-standardised extracts were 100 biological units (storage mite) and 1:100 weight/volume (bovine dander and cockroach). Histamine dihydrochloride (10 mg/ml) and glycerol (50%) were used as positive and negative controls, respectively. The same batch of each solution was used throughout the study. For a test to be included in the final analyses, the reaction to the positive control had to be at least 3 mm, and the reaction to the negative control had to be 1 mm or less. A reaction of 3 mm or greater to the allergens was considered positive.

Statistical analysis

Prevalence of the various characteristics and the sensitisation to common allergens between the groups were compared by Fisher’s exact test (two groups) and χ² test (more than two groups). Student’s t test was also used in between-groups comparisons. The confounders for the logistic regression models were chosen in the following way: A potential confounder was chosen if its prevalence varied significantly between the study groups (table 1) and if it could potentially affect the main outcome—that is, sensitisation to allergens. The following potential confounders were found: childhood farming environment, passive smoking during childhood, currently having cat or dog mostly indoors, and never, ex, and current smoking. The confounder was included in the final models if adjusting for the potential confounder changed the odds ratio (OR) of a particular farming characteristic by 10% or more. In addition, we performed the logistic regression analysis including all the above-mentioned potential confounders plus age in the models. It changed the results very little (data not shown). The interaction effect of childhood farming environment and current farming environment on sensitisation to allergens was tested by creating a new variable (“the interaction variable”) by multiplying the childhood farming exposure (0 or 1) with adulthood farming exposure (0 or 1). All analyses were carried out using SPSS for Windows 10.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

Population

Of the 676 women invited to the study, 311 (75.6%) participated in skin prick testing and a total of 466 (68.9%) women returned the questionnaire. Twenty-eight subjects with a positive reaction to the negative control and four subjects with a negative reaction to histamine were excluded from the analyses. Complete data including acceptable skin prick test results and questionnaire were obtained from 433 women (64.1% of invited). Of the 165 women who did not participate in skin prick testing, there were more women who did not live on a farm (58.8%) than those who did (41.2%).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Basic characteristics of the subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not living on a farm, n = 202</td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>39.2 (5.7)</td>
</tr>
<tr>
<td>Mean (SD) body mass index (kg/m²)</td>
<td>25.2 (4.1)</td>
</tr>
<tr>
<td>Ex smokers (%)</td>
<td>23</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>10</td>
</tr>
<tr>
<td>Mean (SD) length of education (years)</td>
<td>13.0 (2.7)</td>
</tr>
<tr>
<td>Having cats or dogs indoors currently (%)</td>
<td>34</td>
</tr>
<tr>
<td>Parental atopy (%)</td>
<td>40</td>
</tr>
<tr>
<td>Mean (SD) number of older siblings</td>
<td>1.8 (1.7)</td>
</tr>
<tr>
<td>Childhood farming environment (%)</td>
<td>49</td>
</tr>
<tr>
<td>Having had pets during childhood (%)</td>
<td>73</td>
</tr>
<tr>
<td>Passive smoking during childhood (%)</td>
<td>69</td>
</tr>
<tr>
<td>Allergic dermatitis during childhood (%)</td>
<td>23</td>
</tr>
<tr>
<td>Childhood day care attendance (%)</td>
<td>2.0</td>
</tr>
</tbody>
</table>

*Due to the skewed distribution, Mann-Whitney U test was used.

The continuous variables are expressed as means and standard deviations in parenthesis, and compared by Student’s t test between the groups. The categorical variables are expressed as percentages, and the comparisons between the groups were carried out using Fisher’s exact test.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Prevalences of sensitisation to specific allergens, expressed in percentages</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not living on a farm, n = 202</td>
</tr>
<tr>
<td>Living on a dairy farm, n = 113</td>
<td>Living on a farm with other types of animal husbandry, n = 38 (8, 11, 19)</td>
</tr>
<tr>
<td>Timothy grass</td>
<td>9.4</td>
</tr>
<tr>
<td>Birch</td>
<td>10.4</td>
</tr>
<tr>
<td>Mugwort</td>
<td>6.9</td>
</tr>
<tr>
<td>Any of the pollens</td>
<td>17.3</td>
</tr>
<tr>
<td>Dog</td>
<td>13.9</td>
</tr>
<tr>
<td>Cat</td>
<td>10.4</td>
</tr>
<tr>
<td>Dog or cat</td>
<td>15.8</td>
</tr>
<tr>
<td>House dust mite</td>
<td>7.9</td>
</tr>
<tr>
<td>Cockroach</td>
<td>8.9</td>
</tr>
<tr>
<td>Storage mite</td>
<td>10.9</td>
</tr>
<tr>
<td>Horse</td>
<td>2.5</td>
</tr>
<tr>
<td>Bovine dander</td>
<td>0.0</td>
</tr>
<tr>
<td>Any of the allergens</td>
<td>37.1</td>
</tr>
</tbody>
</table>

†Fisher’s exact test between the groups “not living on a farm” and “living on a farm”.

‡χ² test between the groups “not living on a farm”, “dairy farm”, “other animal husbandry”, and “crop farm”.

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Of the 433 women with acceptable skin test and questionnaire, there were 202 who did not live on a farm and 231 who did (table 1). The distribution of various types of farms is expressed in table 2. Typically for eastern Finland, small dairy farms predominated, containing a mean of 25 cows. The women who lived on a farm were asked whether they actively participated in the farm work and the results of this question are expressed in table 2. The subjects were also asked whether they had quitted farming or had decided not to become a farmer due to allergic symptoms. Only six subjects answered yes to this question—three who did not live on a farm and three who did.

### Sensitisation to allergens

The overall prevalence of sensitisation to any allergens did not differ between the women who did not live on a farm and the women who lived on various types of farms (table 2). However, the prevalence of sensitisation to pollens and pets (and cat especially) was lowest among women who lived on a dairy farm (table 2). On the contrary, the prevalence of sensitisation to bovine dander was most common among these women. Table 3 shows that the lowest risk of sensitisation to pollens and pets was among women with both a childhood and adulthood farming environment. However, these women also showed the highest prevalence of sensitisation to bovine dander. The “interaction variable” tended to associate with sensitisation to pollens (p = 0.067) but not with sensitisation to pets (p = 0.91). Table 4 shows that the intensity and duration of animal husbandry was dose dependently associated with a decreased risk of sensitisation to pollens. Such an association could also be shown in sensitisation to pets, though less clearly. Again, an opposite pattern could be observed in sensitisation to bovine dander. The duration and intensity of animal husbandry correlated significantly (p<0.001, χ² test) demonstrating that those with the most frequent visits to the animal shed usually had worked for the longest time with farm animals.

### DISCUSSION

This study showed that the overall prevalence of sensitisation to allergens does not differ between women who live on a farm and women who do not. However, there were clear differences in the targeting of sensitisation. The women who lived on dairy farms showed decreased risks of sensitisation to pollens and pets and an increased risk of sensitisation to bovine dander, in a dose dependent manner with respect to current contacts with farm animals. When the effects of childhood and adulthood farming environment were analysed separately, those with both childhood and adulthood farming exposure showed the lowest risks of sensitisation to pollens and pets. These findings suggest that the farming environment affects sensitisation to allergens throughout life, not just during childhood.

Our findings indicate that the immune deviation hypothesis may not fully explain the low prevalence of sensitisation to common allergens among adult farmers as this deviation is thought to be established by 5 years of age. Therefore, other mechanisms should be considered. Recently the term “immune modulation” has been introduced whereby both Th1 and Th2 responses are enhanced or suppressed in concert, throughout life. This immune modulation might involve the action of the so called T regulatory cells. These cells form a heterogeneous family. A subset called adaptive T regulatory cells acquires suppressive activity in the periphery under certain conditions of antigenic stimulation. It is tempting to speculate that there is a farm related factor which could stimulate the adaptive T regulatory cells, which, in turn, could suppress IgE mediated responses.
to common allergens throughout the life. The dose dependent association between the decreased risk of sensitisation to pollens and pets and the current contacts with dairy cattle suggests that this factor is somehow associated with farm animals. This finding is in close agreement with studies on children. However, direct exposure data, like dust and endotoxin levels, have not been measured in the present study, which can be considered as a weakness of the study.

Previous studies comparing the sensitisation to common allergens between adult farmers and a control group corroborate our findings. Rautalähtö et al. showed that dairy farmers in eastern Finland are less sensitised to cats, dogs, and mugwort than teachers. Filipiak found that farmers in southern Germany have lower risk for sensitisation against pollens and mites than non-farmers. In a recent study from Norway atopy (defined as a presence of IgE antibodies against common allergens) tended to be less prevalent among livestock farmers compared with crop farmers. In addition, prevalence of atopy was inversely associated with the duration of farm work. Unfortunately, IgE antibodies against bovine dander were not measured in that study.

What is the clinical importance of the present findings? Living on a farm was associated with decreased risks of sensitisation to pollens and pets. Sensitisation to these particular allergens is constantly associated with allergic rhinitis and asthma in the Nordic countries. We have previously reported considerably decreased risks of pet and pollen induced upper airway symptoms in the present farmer population. Therefore, a lifelong exposure to a farming environment might decrease the risk of allergic diseases by decreasing the risk of sensitisation to those allergens, which are most often associated with these diseases. However, the sensitisation to bovine dander was most common among women with the longest and most intensive exposure to cattle, suggesting that the heavy bovine allergen burden had outweighed the postulated protective farm effect. As a result, the overall prevalence of sensitisation to allergens did not differ between the women who lived on a farm and those who did not live. The sensitisation to bovine dander was also clinically important since our previous study showed that 28% of the present farmer population suffered from farm work related upper airway symptoms which were strongly associated with a positive skin test result to bovine dander. Thus, the present study does not suggest that farming would attenuate the overall prevalence of sensitisation to clinically important allergens. Furthermore, our findings suggest that when examining the effects of the farming environment on sensitisation to allergens, omitting the relevant farm related allergens from the test panel can lead to underestimation of skin test positivity.

One weakness of the present study is the somewhat lower participation rate among women who did not live on a farm. This may have lead to an overestimation of the prevalence of skin test positivity among them, as subjects with allergic symptoms may have been more keen to participate in allergy testing. However, this bias has less effect on the observed associations between the intensity of animal husbandry and the risks of sensitisation to various allergens. The present results are also potentially affected by the “healthy worker effect”. However, in the present study all subjects were asked whether they had quitted farming or had decided not to become a farmer due to allergic symptoms. Only six subjects answered yes to this question—three who did not live on farm and three who did. A Swedish follow up study also speaks against significant health based selection among farmers.

In conclusion, the present study suggests that the farming environment affects sensitisation to allergens throughout life and not just during early childhood. The net effect of the farming environment may not be necessarily protective as the decreased risk of sensitisation to common allergens like pets and pollens was accompanied by the increased risk of sensitisation to bovine dander.

Main messages
- The effect of the farming environment on sensitisation to allergens is not restricted to early childhood.
- An adulthood farming environment may decrease the risk of sensitisation to pollens and pets.
- Bovine husbandry seems to increase the risk of sensitisation to bovine dander.

Policy implications
- The mechanisms of the effects of an adulthood farming environment on sensitisation to allergens should be studied further.
- Sensitisation to bovine dander causes work related allergic symptoms. Thus, interventions to prevent this sensitisation should be considered in bovine farmers.

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Ethics approval: informed written consent was obtained from every participant and the study was approved by the Ethical Committee for Human Research of Kuopio University Hospital, Finland.

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