Respiratory status in dairy farmers in France; cross sectional and longitudinal analyses

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Aims: To compare respiratory status in dairy farmers with that of non-farming controls.

Methods: Longitudinal study in the Doubs (France). From a cohort constituted in 1994 (T1), 215 (81.1%) dairy farmers and 110 (73.8%) controls were reevaluated in 1999 (T2). The protocol comprised a medical and occupational questionnaire, spirometric tests at both evaluations, allergological tests at T1, and a non-invasive measure of blood oxygen saturation ($\text{SpO}_2$) at T2.

Results: In 1999 analyses, the prevalence of chronic bronchitis was higher ($p = 0.013$), and $\text{FEV}_1/\text{VC}$ ($p < 0.025$) and $\text{SpO}_2$ ($-0.7\%$, $p < 0.01$) lower in dairy farmers than in controls. In a multiple linear regression model, farming, age, and smoking were significantly and inversely correlated with $\text{SpO}_2$. In the whole population, the mean annual decline in $\text{FEV}_1$ and $\text{FEV}_1/\text{VC}$ was $-13.4$ ml and $-0.30\%$, respectively. Farming was associated with an accelerated decline in $\text{FEV}_1/\text{VC}$ ($p < 0.025$) after adjustment for covariates. No relation between allergy and respiratory function changes was observed, except for $\text{FEF}_{25-75}$.

Conclusions: This prospective study shows that dairy farming is associated with an excess of chronic bronchitis, with a moderate degree of bronchial obstruction and a mild decrease in $\text{SpO}_2$.

Epidemiological studies have consistently shown a significant association between farming and an excess of respiratory symptoms. In a majority of cross sectional studies, respiratory function values are moderately although significantly lower in farmers when compared to non-farming controls. There are only few controlled longitudinal studies and interpretation of their results is difficult. Demonstration has nevertheless been made of an accelerated decline in expiratory flow rates and in forced vital capacity among grain elevator workers.8 Farmers are indeed exposed to a large variety of organic particles that may be responsible for inflammatory or allergic pulmonary reactions. Moreover, allergy is considered as a possible risk factor for the development of chronic obstructive pulmonary disease (COPD) or for an accelerated decline in respiratory function parameters in the general population, but its relation with respiratory function impairment has never been longitudinally studied in dairy farmers.

Two studies were conducted in two different geographic areas of the Doubs, a dairy farming province in France. The cross sectional analysis of the first study has shown a significant excess in respiratory symptoms and to a lesser degree in bronchial obstruction in farmers compared to non-farming controls. The longitudinal analysis of the same cohort has suggested that long term occupational exposure significantly accelerated the decline in respiratory function in male dairy farmers. The present study concerns the second cohort. In 1994, 265 dairy farmers were compared to 149 non-exposed control rural subjects. Results showed an excess of respiratory symptoms in dairy farmers which was mild and non-significant for asthma, but high for cough and phlegm. There was also a non-reversible bronchial obstruction in dairy farmers. Prevalence of IgE mediated allergy was generally lower in dairy farmers. Both groups were reevaluated five years later with the following objectives:

- To confirm the excess of lung disorders in dairy farmers and to evaluate their influence on blood oxygenation by measuring non-invasively oxygen saturation.
- To compare respiratory function parameter changes in both groups and to analyse the influence of allergy on these modifications.

METHODS

This study was undertaken with the cooperation of the Doubs Mutualité Sociale Agricole (Agricultural Health Insurance Mutual), whose medical department organises annual free examinations for all affiliated members in the province. The protocol was approved by the local review board for research involving human subjects. Informed written consent was obtained from each subject.

Population

The study population in 1994 consisted of two groups of both genders, 16–65 years of age. Details of population selection have been described previously. Briefly, a cohort of 353 dairy farmers and 189 control subjects was established in 1994. Two hundred and sixty five and 149 of these subjects took part in the 1994 investigations, respectively.

In 1999, each subject investigated in 1994 was contacted individually and an explanatory letter concerning the...
Dairy farming is consistently associated with an excess of lung disorders, especially chronic bronchitis. Dairy farmers have a slight degree of chronic obstruction and of accelerated decline in expiratory flows. They have a mild but significant decrease in blood oxygen saturation independently of bronchial obstruction. Atopy does not seem to play a role in these disorders.

**Objectives of the study**, its practical value, and some of the previous results, was sent to each subject. Half of the subjects who refused to participate in the present study were randomly contacted in order to obtain the reasons for their refusal.

The protocol comprised a medical and occupational questionnaire, spirometric tests at both evaluations, allergological tests in 1994, and a non-invasive measure of blood oxygen saturation ($S\text{PO}_2$) in 1999.

**Questionnaires**
Medical questionnaires were collected during the organised medical examinations, and were reviewed by the same investigator as in 1994. This questionnaire consisted of an adapted French version of the long version of the European Community Respiratory Health Survey questionnaire. Questions on respiratory symptoms, allergy, and definition of chronic bronchitis, dyspnoea, and asthma have been given previously. Non-smokers (NS) were defined as those having smoked on average less than one cigarette, one cigar, or one pipe a day for a year. Current smokers (CS) smoked this amount or more, and ex-smokers (ES) had stopped smoking at least one month before the time at which they filled out the questionnaire.

**Respiratory function tests**
Respiratory function tests were performed according to the American Thoracic Society recommendations. A portable pneumotachograph (Autospirio Minato Pal; Medical Science Company Ltd, Osaka, Japan) was used to measure slow vital capacity (VC), forced expiratory volume in one second (FEV$_1$), and forced mid-expiratory flow (FEF$_{25-75}$). The spirometer was calibrated daily for atmospheric pressure, humidity, and temperature, and periodically with a 1.5 l syringe. A minimum of three adequate measurements was required for each subject. Values were expressed as percentages of European Community for Steel and Coal reference values.

**Immunological analyses**
Immunological analyses were performed in 1994. Methods and results of these analyses have been reported previously. Briefly, each subject underwent skin prick tests (SPT) on the volar surface of the forearm for seven allergens: Dermatophagoides pteronyssinus, Acarus siro, cow dander, cat dander, mixed grass pollen, mixed betulacceae pollen, and an extract of mixed mouldy and non-mouldy hay from farms in the Doubs (laboratoire des Stallergènes, Fresnes, France). Total IgE were measured by the microparticulat enzymatic immunoassay (MEIA; IM x-IgE; Abbott, Rungis, France). Detection of serum IgE antibodies against a mixture of inhalant allergens was performed using the Phadiatop test with capsulated hydrophilic carrier method (Phadiatop, Cap system; Pharmacia Diagnostic AB, Uppsala, Sweden).

**RESULTS**

**Population characteristics**
The initial cohort included 414 subjects (T1). For the second evaluation (T2), 13 subjects were lost to follow up and four had died. Among the 397 remaining subjects, 325 (81.9%) agreed to participate in the present study and were reevaluated. Among the 72 subjects who did not participate, 40 randomly selected subjects were contacted by telephone. Twenty one dairy farmers and 11 control subjects finally completed a telephone questionnaire. Reasons for refusal included lack of time (14 farmers, six controls), lack of interest for this kind of study (four farmers, two controls), impossibility to attend the medical evaluation because of occupational activities (one farmer, two controls), omission (one control), and medical reasons (two dairy farmers).

**Oximetry data**
Arterial oxygen saturation was evaluated for each subject with the finger pulse oximeter Onyx model 9500 (Nonin Medical Inc., Plymouth, MN, USA). Three measurements at 30 second intervals were taken for each subject on the index finger of the left hand. Subjects were seated, and had been at rest for at least 15 minutes. The highest value of blood oxygen saturation using pulse oximetry ($S\text{PO}_2$) was retained with the corresponding pulse rate. The pulse oximeter was tested weekly for accuracy by comparing $S\text{PO}_2$ with the oxygen saturation of arterial blood gases.

**Statistical analysis**
Total IgE was transformed logarithmically (log$_10$). For univariate analyses, discrete variables were compared through $\chi^2$ tests, and continuous variables using Student’s $t$ tests. In multivariate models, adjustment was performed for potential confounders determined in the present analysis, but also for those generally considered as being determinants of respiratory function. Interactions were tested between all significant covariates. Assumption for residual normality was assessed by a normal probability plot of residuals.

First, a cross sectional analysis of 1999 data was performed to compare dairy farmers with controls. To correct for imbalances in age, sex, and smoking, a multiple logistic regression was used to compare the odds ratios for respiratory symptoms. Relations between lung function, $S\text{PO}_2$ and pulse rate, and exposure (farmers) were assessed by multiple linear regression models. Adjustment was made for smoking (as pack-years) in the respiratory function model, and for age (as a continuous variable), sex, and smoking for both $S\text{PO}_2$ and pulse rate models. Altitude (tableland versus plain), FEV$_1$/VC (as a continuous variable), and log(IgE) were added in another model analysing $S\text{PO}_2$.

Second, a longitudinal analysis of respiratory function was performed. Effect of exposure on the annual change in respiratory parameters ($1999$ value – $1994$ value)/number of years between the two visits) was tested by a multiple linear regression model adjusted for sex, height, the 1999 value of age, the number of pack-years smoked, and altitude. An analysis of variance and covariance with repeated measures was furthermore performed in order to evaluate the effect of covariates on respiratory function tests with no forward hypothesis of decline in lung function.

Statistical analyses were carried out using the BMDP statistical software package (BMDP, Los Angeles, CA, USA).

**Policy implications**
A “simple” finger pulse oximeter may be a relevant tool for epidemiological studies of respiratory status.
Individual characteristics, respiratory symptoms and function, and immunological evaluation at T1 were compared between reevaluated and non-reevaluated subjects (table 1). Non-reevaluated subjects were found to have slightly more respiratory symptoms and lower expiratory flow rates. For chronic bronchitis and FEV1, farmers were slightly more concerned by this loss of less healthy subjects than controls.

Non-smokers had higher prevalence of atopy, asthma, and asthma related symptoms (cough, wheezing, wheezing apart from a cold, woken by shortness of breath, woken by shortness of breath, and wheezing with breathlessness, and wheezing apart from a cold during the past year) was identical in both groups. Fourteen (6.6%) farmers and seven (6.4%) controls were self reported asthmatics. There was a higher prevalence of cough (15.9%, p = 0.05), chronic phlegm (15.9%, p = 0.10), and chronic bronchitis (7.5%, p = 0.013) in dairy farmers than in controls (8.2%, 10%, and 1.8%, respectively) after adjustment for age, sex, and smoking. Smoking significantly influenced chronic bronchitis and FEV1, respectively). However, the FEV1/VC ratio was significantly lower in exposed subjects (98.2% versus 100.0%, respectively, p < 0.025). Smoking was negatively correlated with FEV1 and FEV1/VC (p < 0.01).

Cross sectional analyses
Concerning respiratory symptoms, results show that the prevalence of atopy, asthma, and asthma related symptoms (attack of shortness of breath, woken by shortness of breath, wheezing, wheezing with breathlessness, and wheezing apart from a cold during the past year) was identical in both groups. Fourteen (6.6%) farmers and seven (6.4%) controls were self reported asthmatics. There was a higher prevalence of cough (15.9%, p = 0.05), chronic phlegm (15.9%, p = 0.10), and chronic bronchitis (7.5%, p = 0.013) in dairy farmers than in controls (8.2%, 10%, and 1.8%, respectively) after adjustment for age, sex, and smoking. Smoking significantly influenced chronic bronchitis and related symptoms (cough, phlegm, wheezing).

Respiratory function data were available for 212 dairy farmers and 109 control subjects. There was no significant difference between both groups for VC (103.5% for dairy farmers versus 100.5% for controls), FEV1 (101.5% versus 100.4%, respectively), and FEF25–75 (89.5% versus 92.1%, respectively). However, the FEV1/VC ratio was significantly lower in exposed subjects (98.2% versus 100.0%, respectively, p < 0.025). Smoking was negatively correlated with FEV1 and FEV1/VC (p < 0.01).

Table 1 Description of the study population in 1999

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Mean (SD)</th>
<th>n = 215</th>
<th>n = 110</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>51.7 (11.6)</td>
<td>43.9 (10.7)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, mean (SD)</td>
<td>174 (5.9)</td>
<td>176.3 (6.8)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Female, mean (SD)</td>
<td>161 (6.1)</td>
<td>162.5 (5.7)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers, &gt;10 pack years, n (%)</td>
<td>15 (6.9)</td>
<td>14 (12.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers, &lt;10 pack years, n (%)</td>
<td>10 (4.7)</td>
<td>10 (9.1)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Ex-smokers, n (%)</td>
<td>27 (12.6)</td>
<td>28 (25.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smokers, n (%)</td>
<td>163 (75.8)</td>
<td>58 (52.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean pack-years (SD)</td>
<td>18 (3.1)</td>
<td>13.4 (9.5)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Passive smoking, n (%)</td>
<td>22 (10.3)</td>
<td>12 (20.7)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Alcohol†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 g, n (%)</td>
<td>116 (55.5)</td>
<td>70 (67.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–50 g, n (%)</td>
<td>88 (42.1)</td>
<td>33 (31.7)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>&gt;50 g, n (%)</td>
<td>5 (2.4)</td>
<td>1 (1.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*χ² tests for qualitative variables; Student’s t tests for quantitative variables.
†n = 209 for dairy farmers, n = 104 for controls.
Table 3: SpO2 and pulse rate in dairy farmers and controls in 1999

<table>
<thead>
<tr>
<th>Available data</th>
<th>Dairy farmers (n = 192)</th>
<th>Control subjects (n = 101)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO2 Mean (SD)</td>
<td>96.9 (1.4)</td>
<td>97.6 (1.2)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Pulse rate Mean (SD)</td>
<td>71.2 (11.0)</td>
<td>74.4 (13.8)</td>
<td>NS*</td>
</tr>
</tbody>
</table>

*Multiple linear regression adjusted for age, sex, and smoking.

Table 5: Mean annual changes in respiratory function parameters between 1994 and 1999

<table>
<thead>
<tr>
<th>Time between the two surveys (y)</th>
<th>Farmers (n = 196)</th>
<th>Controls (n = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔVC, ml/y (SD)</td>
<td>0.05 (75.1)</td>
<td>3.53 (69.9)</td>
</tr>
<tr>
<td>ΔFEV1, ml/y (SD)</td>
<td>−1.58 (48.9)</td>
<td>−7.37 (54.7)</td>
</tr>
<tr>
<td>ΔFEV1/VC, %/y (SD)</td>
<td>−0.36 (1.2)</td>
<td>−0.19 (1.1)</td>
</tr>
<tr>
<td>ΔFEF25–75, ml/y (SD)</td>
<td>11.38 (116.7)</td>
<td>−6.69 (116.7)</td>
</tr>
</tbody>
</table>

DISCUSSION
Results of the current study are consistent with those of the 1994 cross sectional analysis and with those of other studies conducted in the same region.13–15 20 Our findings confirmed that dairy farmers present a persistent excess in respiratory symptoms and a moderate bronchial obstruction which were not found to be closely related to IgE mediated allergy. In addition, our results suggest that these lung disorders are accompanied by a small but significant decrease in blood oxygen saturation.

Differences in the prevalence of respiratory symptoms between exposed and control subjects at T2 were smaller than those observed at T1 and only kept significance for chronic bronchitis and chronic cough. This may be partly explained by a loss of less healthy subjects at T2 (table 1). The prevalence of asthma was similar in both groups. The observed prevalence of 6% is lower than that published for the French general population21 but is usual in the farming setting. These results did not confirm those of a Swedish study in which the prevalence of asthma was found to double over a period of 12 years in dairy farmers.22 In this Swedish study, the authors insisted on the importance of allergy to storage mites, which do not seem to play a major role in our region.13–15 Measures of lung function confirmed the tendency for bronchial obstruction in exposed subjects. Although still significant, the difference between farmers and controls was weaker than that observed at T1, possibly also because of a greater bronchial obstruction in non-reevaluated farmers (table 1).

This study is the first, to our knowledge, to measure SpO2 in farmers. There are no published recommendations for the use of pulse oximeters in epidemiological studies. All subjects were tested sitting at rest for at least 15 minutes, and the best of three measures was retained in the rare case of discrepancies between the three measures. A recent article suggested that the accuracy and reproducibility of SpO2 measures allowed the use of a pulse oximeter for epidemiological studies.23 Our results showed that SpO2 was significantly lower in dairy farmers. The fact that SpO2 was, as expected, correlated negatively to smoking and positively to the FEV1/VC ratio argues in favour of both the accuracy and relevance of the tool. Interestingly, after adjustment for FEV1/VC, exposure remained associated with a decreased SpO2. This suggests that other mechanisms than bronchial obstruction are involved. Exposure to organic dusts, including endotoxins, may induce inflammatory pulmonary reactions,24 25 and therefore explain at least part of the decrease in SpO2. Finally it cannot be totally excluded that more callous hands in farmers play a role in the observed results.
The longitudinal analysis showed that absolute values of VC were not significantly modified between T1 and T2 and that the decline in FEV₁ and FEV₁/VC was lower than expected (table 6). Such observations have been previously discussed.26,27 A learning effect and/or a too small number of reevaluations in our study may have played a role. Another possible explanation is that exclusion of 28 subjects from the longitudinal analysis might have led to the selection of a healthier population. Indeed, subjects encountering difficulties performing respiratory function tests have generally the worst values.28 Moreover, subjects excluded at T1 for this reason were mainly farmers. This may have resulted in an underestimation of the magnitude of lung function decrease in farmers. Nevertheless, the effect of exposure on the FEV₁/VC ratio was statistically significant (table 6), even if it is controversial to adjust for initial values.29 Adjustment for initial values can lead to an overcorrection and to an underestimation of the effect of exposure. The variance-covariance analysis, which takes into account correlations between repeated measures in a same subject without making hypotheses on the sense of the difference between T1 and T2 reproduced the results presented in table 6, with a significance at least equal to that obtained using the multiple linear regression model. We can therefore conclude that our farmers have an accelerated decline in expiratory flow rates.

We also tested the influence of allergy on respiratory function changes. Several studies, recently reviewed15–17 suggested that allergy might be an independent risk factor for the development of COPD and for an accelerated decline in lung function in the general population. In Finish farmers, studies20,21 showed that atopy (defined clinically and/or by positive skin prick tests to usual aeroallergens) was significantly correlated with chronic bronchitis. In a previous study, we had observed that IgG mediated allergy was significantly associated with an accelerated decline in the FEV₁/VC ratio.25 In the current study, however, we did not observe consistent correlations between indicators of IgE mediated allergy and lung function or oxygen blood saturation.

In conclusion, this study shows that dairy farming is associated with an excess of lung disorders which mostly consist of chronic bronchitis, and with a moderate degree of bronchial obstruction and a mild decrease in blood oxygen saturation. Allergy does not seem to play a significant role.

Acknowledgements

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References


Table 6 Regression models for annual changes in lung function

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>VC</th>
<th>FEV₁</th>
<th>FEV₁/VC</th>
<th>FEV₁/VC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>Age</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>Smoking</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>Male</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>Height</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>Altitude</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>log(IgE)</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
<tr>
<td>Initial value</td>
<td>-236.6</td>
<td>-127.2</td>
<td>11.81</td>
<td>7.28</td>
</tr>
</tbody>
</table>

A regression coefficient (coeff.) with a negative value indicates that the variable is associated with a decline of the lung function parameter. All listed variables were included simultaneously in the models; each coefficient and p value is controlled for all other covariates. Age, smoking, height, log(IgE), and initial values are continuous variables; exposure: controls = 0, farmers = 1; altitude: plain = 0, tableland = 1.

p < 0.05, *p < 0.025, **p < 0.01, ***p < 0.001.