

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 (SpO₂) at T2.

Results: In 1999 analyses, the prevalence of chronic bronchitis was higher ($p = 0.013$), and FEV₁/VC ($p < 0.025$) and SpO₂ (-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 SpO₂. In the whole population, the mean annual decline in FEV₁ and FEV₁/VC was -13.4 ml and -0.30% , respectively. Farming was associated with an accelerated decline in FEV₁/VC ($p < 0.025$) after adjustment for covariates. No relation between allergy and respiratory function changes was observed, except for FEF₂₅₋₇₅.

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 SpO₂.

Epidemiological studies have consistently shown a significant association between farming and an excess of respiratory symptoms.¹⁻³ 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 studies⁴ and interpretation of their results is difficult.⁵ Demonstration has nevertheless been made of an accelerated decline in expiratory flow rates and in forced vital capacity among grain elevator^{6,7} and swine confinement workers.⁸ These lung disorders may theoretically have repercussions on gas exchanges, but this has to our knowledge never been investigated. Their causes and mechanisms have not been elucidated.¹ Organic dust exposure seems to play a determinant role, especially in the development of chronic airflow obstruction.⁹ Farmers are indeed exposed to a large variety of organic particles that may be responsible for inflammatory or allergic pulmonary reactions.¹⁰ 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,^{11,12} 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.¹³ 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.¹⁴ The present study concerns the second cohort.^{15,16} 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.¹⁵ Prevalence of IgE mediated allergy was generally lower in dairy farmers.¹⁶ 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.¹⁵ 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

Abbreviations: CPOD, chronic obstructive pulmonary disease; CS, current smoker; ES, ex-smoker; FEF₂₅₋₇₅, forced mid-expiratory flow; FEV₁, forced expiratory volume in one second; NS, non-smoker; SpO₂, blood oxygen saturation; VC, vital capacity

Main messages

- 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 (SpO₂) 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.¹⁷ Questions on respiratory symptoms, allergy, and definition of chronic bronchitis, dyspnoea, and asthma have been given previously.¹⁵ 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.¹⁸ A portable pneumotachograph (Autospiro Minato Pal; Medical Science Company Ltd, Osaka, Japan) was used to measure slow vital capacity (VC), forced expiratory volume in one second (FEV₁), and forced mid-expiratory flow (FEF₂₅₋₇₅). 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.¹⁹

Immunological analyses

Immunological analyses were performed in 1994. Methods and results of these analyses have been reported previously.¹⁶ 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 betulaceae 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 microparticle 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).

Policy implications

- A "simple" finger pulse oximeter may be a relevant tool for epidemiological studies of respiratory status.

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 (SpO₂) was retained with the corresponding pulse rate. The pulse oximeter was tested weekly for accuracy by comparing SpO₂ with the oxygen saturation of arterial blood gases.

Statistical analyses

Total IgE was transformed logarithmically (log₁₀). For univariate analyses, discrete variables were compared through χ^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, SpO₂ 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 SpO₂ and pulse rate models. Altitude (tableland versus plain), FEV₁/VC (as a continuous variable), and log(IgE) were added in another model analysing SpO₂.

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).

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).

Table 1 Demographic, clinical, spirometric, and allergological characteristics in 1994 for reevaluated and non-reevaluated farmers and control subjects

| | Reevaluated (n = 325) | | Non-reevaluated (n = 89) | |
|--|--------------------------|------------------------|--------------------------|------------------------|
| | Farmers | Controls | Farmers | Controls |
| <i>Demographic data</i> | | | | |
| Age (y), mean (SD) | n = 215 46.1 (11.5) | n = 110 38.3 (10.7) | n = 50 44.6 (10.0) | n = 39 36.7 (9.2) |
| Male, n (%) | 121 (56.3) | 51 (46.4) | 32 (64.0) | 20 (51.3) |
| Female, n (%) | 94 (43.7) | 59 (53.6) | 18 (36.0) | 19 (48.7) |
| <i>Smoking status, n (%)</i> | | | | |
| Current smokers | 24 (11.2) | 30 (27.3) | 14 (28.0) | 9 (23.1) |
| Ex-smokers | 29 (13.5) | 21 (19.1) | 3 (6.0) | 5 (12.8) |
| Non-smokers | 162 (75.3) | 59 (53.6) | 33 (66.0) | 25 (64.1) |
| Pack-years, mean (SD) | 16.4 (14.9) | 8.6 (9.4) | 21.3 (15.7) | 11.7 (15.9) |
| <i>Altitude, n (%)</i> | | | | |
| Plain | 97 (45.1) | 48 (43.6) | 28 (56.0) | 17 (43.6) |
| Tableland | 118 (54.9) | 62 (56.4) | 22 (44.0) | 22 (56.4) |
| <i>Symptoms, n (%)</i> | | | | |
| Asthma | n = 214 12 (5.6) | n = 110 4 (3.6) | n = 50 4 (8.0) | n = 39 1 (2.6) |
| Wheezing, LY | 12 (5.6) | 0 | 3 (6.0) | 2 (5.1) |
| Wheezing with breathlessness, LY | 9 (4.2) | 0 | 2 (4.0) | 2 (5.1) |
| Wheezing apart from a cold, LY* | 7 (3.3) | 0 | 4 (8.0) | 2 (5.1) |
| Usual morning cough | 24 (11.2) | 4 (3.6) | 9 (18.0) | 2 (5.1) |
| Usual morning phlegm | 27 (12.6) | 2 (1.8) | 9 (18.0) | 1 (2.6) |
| Chronic bronchitis | 14 (6.5) | 1 (0.9) | 6 (12.0) | 0 |
| Dyspnoea | 43 (20.1) | 12 (10.9) | 6 (12.0) | 7 (17.9) |
| <i>Respiratory function, mean (SD)</i> | | | | |
| % VC | n = 198 102.7 (14.2) | n = 106 99.7 (13.0) | n = 47 101.0 (14.8) | n = 38 102.3 (13.5) |
| % FEV ₁ | 99.3 (14.9) | 98.0 (13.7) | 95.1 (11.6) | 98.4 (15.6) |
| % FEV ₁ /VC | 96.3 (8.7) | 99.7 (16.6) | 95.0 (10.5) | 96.2 (11.3) |
| % FEF ₂₅₋₇₅ | 85.8 (24.0) | 87.2 (27.2) | 79.8 (20.8) | 85.3 (23.8) |
| <i>Immunological tests</i> | | | | |
| Total IgE, mean (SD) | n = 212 102.6 (468.3) | n = 102 69.1 (10.0) | n = 49 204.9 (459.5) | n = 39 56.8 (81.2) |
| Phadiatop +, n (%) | 30 (14.2) | 20 (19.4) | 11 (22.4) | 7 (17.9) |
| Skin prick tests +, n (%) | 78 (36.8) | 43 (40.2) | 16 (32) | 15 (39.5) |

SD, standard deviation; LY, last year; VC, vital capacity; FEV₁, forced expiratory volume in one second; FEF₂₅₋₇₅, forced mid-expiratory flow.

Reevaluated and non-reevaluated subjects were compared using χ^2 tests for qualitative variables, and Student's *t* tests for quantitative variables.

**p* < 0.05.

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 control subjects.

Table 2 presents individual characteristics of reevaluated dairy farmers and control subjects at T2. Seventy seven of the 215 dairy farmers had officially retired between 1994 and 1999, but 32 of them still had an occupational exposure.

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 2 Description of the study population in 1999

| | Dairy farmers (n = 215) | Control subjects (n = 110) | <i>p</i> value* |
|--------------------------------|-------------------------|----------------------------|-----------------|
| <i>Age, y</i> | | | |
| Mean (SD) | 51.7 (11.6) | 43.9 (10.7) | <0.001 |
| <i>Height</i> | | | |
| Male, mean (SD) | 174.2 (5.9) | 176.3 (6.8) | <0.05 |
| Female, mean (SD) | 161.6 (6.1) | 162.5 (5.7) | NS |
| <i>Smoking</i> | | | |
| Smokers, >10 pack years, n (%) | 15 (6.9) | 14 (12.7) | |
| Smokers, ≤10 pack years, n (%) | 10 (4.7) | 10 (9.1) | <0.001 |
| Ex-smokers, n (%) | 27 (12.6) | 28 (25.5) | |
| Non-smokers, n (%) | 163 (75.8) | 58 (52.7) | |
| Mean pack-years (SD) | 18.3 (16.3) | 13.4 (9.5) | NS |
| Passive smoking, n (%) | 22 (13.7) | 12 (20.7) | NS |
| <i>Alcohol†</i> | | | |
| <10 g, n (%) | 116 (55.5) | 70 (67.3) | |
| 10–50 g, n (%) | 88 (42.1) | 33 (31.7) | NS |
| >50 g, n (%) | 5 (2.4) | 1 (1.0) | |

* χ^2 tests for qualitative variables; Student's *t* tests for quantitative variables.

†n = 209 for dairy farmers; n = 104 for controls.

Table 3 Sp_o₂ and pulse rate in dairy farmers and controls in 1999

| Available data | Dairy farmers (n = 192) | Control subjects (n = 101) | p value |
|------------------------------|-------------------------|----------------------------|---------|
| Sp _o ₂ | | | |
| Mean (SD) | 96.9 (1.4) | 97.6 (1.2) | <0.01* |
| Pulse rate | | | |
| Mean (SD) | 71.2 (11.0) | 74.4 (13.8) | NS* |

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

Table 3 presents results of Sp_o₂ evaluation at T2. Sp_o₂ could not be measured in 32 subjects for the following reasons: failure of the pulse oximeter during an evaluation session (26 subjects) and impossible measure (six subjects). Comparisons of these 32 subjects with the other reevaluated subjects showed that they tended to be older ($p = 0.08$), lived at higher altitudes ($p = 0.05$), and had more chronic bronchitis ($p = 0.01$), but that they were not significantly different with regard to spirometric values nor exposure (the fact of being or not a farmer). Sp_o₂ was slightly but significantly lower in dairy farmers than in controls with a mean difference of 0.7%. Distribution of Sp_o₂ was similar in both groups; the difference was not explained by low values in a few farmers.

In a multiple linear regression model, dairy farming, age, and pack-years were inversely correlated with Sp_o₂. Conversely the FEV₁/VC ratio was positively correlated with Sp_o₂ (table 4).

Longitudinal analyses

The longitudinal analysis of respiratory function tests could be performed in 301 subjects whose explorations were considered as being of good quality at both T1 and T2. Table 5 presents mean annual changes in respiratory function parameters between T1 and T2. VC was not found to decline. On the whole cohort, the mean annual decline in FEV₁ and FEV₁/VC was -13.4 ml per year and -0.30% per year, respectively. Farming was associated with an accelerated decline in FEV₁/VC ($p < 0.025$) after adjustment for age, smoking, sex, height, log(IgE), altitude, and initial respiratory function values. Other factors associated with an accelerated decline in respiratory function were age, smoking in pack-years (for FEV₁/VC only, $p < 0.001$), height (for VC and FEV₁), and initial lung function values. When the three indicators of allergy were separately tested in the model, the only significant relation was between total IgE and FEF₂₅₋₇₅.

Table 4 Multiple regression model for blood oxygen saturation (Sp_o₂)

| Independent variables | Sp _o ₂ | | |
|-----------------------|------------------------------|------|---------|
| | Coeff. | SE | p value |
| Exposure | -0.46 | 0.18 | <0.01 |
| Male | -0.17 | 0.17 | NS |
| Age | -0.02 | 0.07 | <0.001 |
| Smoking | -0.03 | 0.08 | <0.001 |
| Altitude | -0.12 | 0.15 | NS |
| FEV ₁ /VC | 0.03 | 0.01 | <0.01 |
| log(IgE) | -0.19 | 0.14 | NS |
| Intercept | 96.75 | | |
| r ² | 0.25 | | |

Regression coefficients (coeff.) with negative values indicate a negative relation. All variables listed were included simultaneously in the model; each coefficient and p value is controlled for all other covariates. Age, smoking, log(IgE), and FEV₁/VC are continuous variables. Exposure: controls = 0, farmers = 1; altitude: plain = 0, tableland = 1. SE, standard error.

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

| | Farmers (n = 196) | Controls (n = 105) |
|-----------------------------------|-------------------|--------------------|
| Time between the two surveys (y) | 5.83 (0.27) | 5.62 (0.43) |
| ΔVC, ml/y (SD) | 0.05 (75.1) | 3.53 (69.9) |
| ΔFEV ₁ , ml/y (SD) | -16.58 (48.9) | -7.37 (54.7) |
| ΔFEV ₁ /VC, %/y (SD) | -0.36 (1.2) | -0.19 (1.1) |
| ΔFEF ₂₅₋₇₅ , ml/y (SD) | 11.38 (116.7) | -6.69 (116.7) |

Except for total IgE, analysis of variance with repeated measures showed the same results as those presented in table 6 with, overall, more significant relations. In contrary to what was observed using the multiple linear regression model, total IgE were significantly correlated with the decline in FEV₁ ($p < 0.05$).

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.^{15, 16} 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 Sp_o₂ 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 Sp_o₂ measures allowed the use of a pulse oximeter for epidemiological studies.²³ Our results showed that Sp_o₂ was significantly lower in dairy farmers. The fact that Sp_o₂ 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 Sp_o₂. This suggests that other mechanisms than bronchial obstruction are involved. Exposure to organic dusts, including endotoxins, may induce inflammatory pulmonary reactions,^{10, 24, 25} and therefore explain at least part of the decrease in Sp_o₂. Finally it cannot be totally excluded that more callous hands in farmers play a role in the observed results.

Table 6 Regression models for annual changes in lung function

| Independent variables | VC | | FEV ₁ | | FEV ₁ /VC | | FEF ₂₅₋₇₅ | |
|-----------------------|--------|---------|------------------|---------|----------------------|-------|----------------------|-------|
| | Coeff. | SE | Coeff. | SE | Coeff. | SE | Coeff. | SE |
| Exposure | 7.94 | 9.23 | -3.80 | 6.54 | -0.30† | 0.13 | -21.50 | 14.22 |
| Age | -1.79§ | 0.43 | -1.46§ | 0.32 | -0.03§ | 0.01 | -2.01‡ | 0.66 |
| Smoking | 0.02 | 0.43 | -0.49 | 0.31 | -0.02§ | 0.01 | -1.53† | 0.65 |
| Male | 50.42§ | 14.35 | 20.78* | 10.16 | -0.06 | 0.18 | 42.85* | 20.79 |
| Height | 2.98§ | 0.80 | 1.80‡ | 0.54 | -0.01 | 0.01 | 2.00 | 1.10 |
| Altitude | 7.63 | 8.15 | 4.48 | 5.80 | 0.04 | 0.10 | -5.91 | 12.69 |
| log(IgE) | -6.72 | 7.71 | -9.30 | 5.48 | -0.19 | 0.10 | -31.87‡ | 11.88 |
| Initial value | -0.05§ | 0.01 | -0.04§ | 0.01 | -0.10§ | 0.01 | -0.06§ | 0.01 |
| Intercept | | -236.67 | | -127.20 | | 11.81 | | 7.28 |
| r ² | | 0.18 | | 0.14 | | 0.40 | | 0.22 |

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.

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 5). 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.³ 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 reviewed¹¹⁻¹² 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, studies²⁹⁻³⁰ 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 associated with an accelerated decline in the FEV₁/VC ratio.²⁰ 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.

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