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Lung function and bronchial reactivity in farmers

MARTIN IVERSEN, RONALD DAHL, ERIK JUEL JENSEN, JENS KORSGAARD, THORKIL HALLAS

From the Department of Respiratory Diseases, University Hospital, Aarhus, and the Danish Pest Infestation Laboratory, Copenhagen, Denmark

ABSTRACT The purpose of this study was to evaluate the prevalence and type of lung function disorders in Danish farmers. Three samples of farmers were drawn from a group of unselected farmers who had participated in an epidemiological study. Group I (47 persons) was a sample of the 8% of all farmers who had reported that they had asthma; group II (63 persons) was a sample of the 28% of farmers who had had wheezing, shortness of breath, or cough without phlegm; and group III (34 persons) a sample of the farmers (64% of the total) who had no asthma and no respiratory symptoms. The farmers with symptoms (groups I and II) had low mean levels of FEV_1 and high values for residual volume, whereas the symptomless farmers had normal lung function and no airways obstruction. The proportion of farmers with an FEV_1 below the 95% confidence limit for predicted values was 43% in group I and 23% in group II; there were none in group III. Bronchial hyperreactivity to histamine occurred in 96% of asthmatic farmers, 67% of farmers with wheezing or shortness of breath, and 59% of symptomless farmers. A low level of FEV_1 was associated with the number of years in pig farming and bronchial hyperreactivity in group II but not group I or III. Most of the bronchial hyperreactivity was explained in the multiple regression analysis by a low FEV_1, though this was significant only for farmers in group II. Thus farmers who reported asthma, wheezing, shortness of breath, or a dry cough in general had airways obstruction with an increased residual volume, whereas symptomless farmers had normal lung function. Severe bronchial hyperreactivity was mostly explained by a diagnosis of asthma and poor lung function, though some farmers with normal lung function and no respiratory symptoms had increased bronchial reactivity.

Introduction

Occupational exposure to dust and fumes has been associated with chronic respiratory symptoms and chronic obstructive lung disease in cross sectional studies.[1] Longitudinal studies[2] have shown that workers exposed to inorganic and organic dust have increased annual loss of forced expiratory volume in one second (FEV_1). Farmers are exposed to various respiratory hazards, including organic dust; cross sectional studies in farmers[3-6] have shown a high prevalence of chronic respiratory symptoms, chronic obstructive lung disease, and asthma. Some studies[7-11] point to pig farming as a special risk factor for the development of respiratory symptoms in farmers.

The present study was undertaken to assess the prevalence and type of respiratory disease in a farming population and to look for risk factors for the loss of lung function in farmers.

Address for reprint requests: Dr Martin Iversen, Lungeklinikken, Aarhus Kommunehospital, 8000 Aarhus C, Denmark.

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Methods

SELECTION OF STUDY POPULATION

A total of 1175 male farmers participated in a cross sectional study in the county of Aarhus, Denmark.[11] From this population of unselected farmers three samples were drawn for a clinical investigation of farmers who had exclusively farmed for their living. In the original population of 808 such farmers the mean age was 53 years ($\leqslant$30 years 7%, 31–50 years 37%, 51–70 years 49%, >70 years 6·6%), 35% were current smokers, 27% had daily cough and phlegm, 8% reported that they had asthma, and 3·3% had had treatment for asthma; 15% had shortness of breath, 18% wheezing, 23% dry cough, and 14% respiratory symptoms during work in the animal house. Sixty nine per cent were pig farmers, 36% exclusively so.

The samples we took for the present study were 47 (group I) of 63 farmers (75%) who said that they had asthma, 63 of the 228 farmers (28%) who had reported one or more respiratory symptom such as wheezing, shortness of breath or cough without phlegm, and 34 (group III) of the 517 persons (64%) who considered themselves to be healthy and without respiratory symptoms. All subjects in the three groups had a supplementary history taken, with special reference to symptoms during work and to allergic disease. The age distribution in the three groups is shown in table 1.

LUNG FUNCTION MEASUREMENTS

Lung function studies were done in the sitting position with a nose clip. A Pulmonet III water filled spirometer with helium dilution (Godart, Bilthoven, The Netherlands) was used for measurement of residual volume (RV), functional residual capacity (FRC), and total lung capacity (TLC). Forced expiratory volume in one second and forced vital capacity (FVC) were measured by dry wedge spirometer (Vitalograph, S-model 20600, Buckingham). Predicted values were from the European working party on standardisation of lung function tests.[12] Histamine challenge was performed according to a method modified by Cockroft *et al*,[13] a PARI nebuliser (Paul Ritzan, Pariwerk, Stanberg am See, West Germany) being used for aerosol generation. The nebuliser was filled with 2 ml of test solution and driven by compressed air (5 l/min). This gave a mean output of 0·57 ml/min. Aerosol was inhaled during two minutes of tidal breathing. Peak expiratory flow rate (PEF) was measured 30 and 90 seconds after each inhalation. The challenge started with inhalation of isotonic saline, followed by increasing doses of inhaled histamine chloride in doubling concentrations, beginning with 0·03 mg/ml. The study continued until PEF had fallen 20% from baseline or a concentration of 8 mg/ml had been reached. Medication in the form of beta agonists or anticholinergic drugs were not allowed on the test day and sustained release preparations of beta agonist or theophylline were not allowed for 24 hours before the challenge. The 12 subjects with an FEV_1 below 1 litre did not undergo histamine challenge. The provocative concentration of histamine causing a 20% fall in PEF (PC_{20})—that is, from the post-saline PEF—was determined by linear interpolation. Bronchial hyperreactivity in this study means a PC_{20} histamine value of 8 mg/ml or less. Our technique using a PARI nebuliser has been shown to give a PC_{20} that is 2·5 doubling concentrations lower than that seen with a standard Wright nebuliser calibrated to an output of 0·14 ml/min (M Iversen and H Harving, unpublished observations).

Table 1 *Personal characteristics of the three groups of farmers (number (%) unless otherwise specified)*

	*Group**: I (n = 47)	II (n = 63)	III (n = 34)
Age (mean, years)	61	53	55
Age distribution (%):			
≤30	0	2	3
31–50	15	37	41
51–70	74	56	47
>70	11	5	9
Years in farming (mean)	48	38	42
Years with lung symptoms (mean)	19	13	0
Pig farming	33 (70)	45 (71)	20 (59)
Exclusively pig farming	22 (46)	21 (34)	11 (33)
Current smokers	18 (38)	32 (51)	10 (29)
Daily cough and phlegm	34 (73)	33 (53)	3 (8)
Shortness of breath	33 (70)	20 (31)	0
Wheezing	36 (76)	25 (40)	0
Cough without phlegm	25 (54)	43 (69)	0
Respiratory symptoms during work in animal house	28 (60)	21 (33)	1 (4)
Medical treatment for asthma	24 (50)	3 (5)	0

*Group I reported that they had asthma; group II consisted of subjects with wheezing, shortness of breath or cough without phlegm; group III consisted of subjects with no asthma or respiratory symptoms.

STATISTICAL ANALYSIS

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS).[14] The significance level is $p = 0.05$ unless otherwise specified. Relationships between discrete variables were evaluated by the χ^2 test and comparison of means of parametric variables by one sided analysis of variance. Multiple regression analysis was used to evaluate which factors were related to FEV_1 and PC_{20}. In the analysis of lung function measurements standardised residuals (SR) were obtained by dividing the absolute residual (observed minus predicted in litres) by the residual standard deviation (RSD), taken from the regression equation used to predict lung function.[12] Standardised residuals have the same scale for all lung function indices and are normally distributed around the mean, hence avoiding the age and height bias introduced by the use of percentages of predicted values.[15]

Results

PERSONAL CHARACTERISTICS

The age distribution differed for the groups, subjects in group I being older on average than those in groups II and III (table 1); 85% were over 50. The number of years in farming, number of years in pig farming, and number of years with lung symptoms could therefore not be compared directly. Though subjects in group III were selected as having no respiratory symptoms, one person said that he had experienced certain symptoms during work in the animal house. Daily cough and phlegm had a high prevalence (34/47, 73%)

in farmers with asthma (group I) and in subjects (33/63, 53%) with wheezing or shortness of breath (group II), whereas the prevalence was low in group III (3/34, 8%). The prevalence of smoking was low in group III (10/34, 29%) and high in group II (32/63, 53%). Most were pig farmers and 22/47 (46%) in group I, 21/63 (34%) in group II, and 11/34 (33%) in group III were exclusively pig farmers.

LUNG FUNCTION MEASUREMENTS

Farmers with asthma (group I) and those with shortness of breath, wheezing, or dry cough (group II) had significantly lower FEV_1 and VC values than predicted and significantly larger RV and FRC (both groups) and TLC (group I) than predicted (table 2)—that is, loss of lung function of the obstructive type. Symptomless farmers (group III) had higher than predicted values of FEV_1, FVC, RV, and FRC. The differences in FEV_1 and VC were pronounced when analysed with respect to standardised residuals. The mean SR for VC was −0·82 in group I and −1·13 in group II, whereas farmers in group III had a positive mean SR of 0·59 for FEV_1. When observed values of FEV_1 were compared with predicted values, 20 (43%) in group I and 14 (23%) in group II but none in group III had an FEV_1 below the lower 95% confidence limit of predicted values. Extrapolation of these frequencies to the total population of farmers suggested that 10% of farmers had an FEV_1 below the 95% confidence limit of predicted values.

Table 2 *Lung function measurements in the three groups of farmers*: observed mean values with predicted means[12] in square brackets and 95% confidence intervals (CI) for the observed mean standardised residuals (SR)*

	Group: I (n = 47)	II (n = 63)	III (n = 34)
VC (l)	3·37 [3·84]	3·97 [4·61]	4·33 [4·31]
95% CI	3·01–3·74	3·69–4·25	4·01–4·66
SR	−0·82	−1·13	0·04
FRC (l)	4·15 [3·37]	4·07 [3·50]	3·81 [3·43]
95% CI	3·80–4·49	3·80–4·34	3·54–4·08
SR	1·15	0·95	0·63
RV (l)	3·48 [2·30]	3·06 [2·23]	2·70 [2·22]
95% CI	3·13–3·83	2·78–3·35	2·47–2·92
SR	2·88	2·03	1·15
TLC (l)	6·86 [6·27]	7·03 [6·97]	7·03 [6·66]
95% CI	6·39–7·32	6·70–7·36	6·63–7·43
SR	0·83	0·09	0·52
FEV_1 (l)	2·19 [2·93]	3·27 [3·55]	3·62 [3·32]
95% CI	1·84–2·55	2·97–3·58	3·28–3·96
SR	−1·43	−0·54	0·59

*See table 1.
VC—vital capacity; FRC—functional residual capacity; RV—residual volume; TLC—total lung capacity; FEV_1—forced expiratory volume in one second.

LOSS OF FEV_1

The standardised residual of FEV_1 ($SFEV_1$) was used as the measure of loss of lung function in a multiple regression analysis for each group, with $SFEV_1$ as the dependent variable, and age, number of years in pig farming, $logPC_{20}$, and smoking (yes/no) as predictor variables. The use of age as a predictor variable would indicate if there was a decrease in FEV_1 in excess of that predicted by the regression equation for the predicted values. In group I (asthmatic subjects) loss of FEV_1 showed no significant relation to any of the predictor variables. In group II $logPC_{20}$ and number of years in pig farming were significant predictors for $SFEV_1$ whereas age in itself was not. There was a tendency for smoking to decrease $SFEV_1$ (table 3). In group III there were no significant predictor variables in the regression equation for loss of FEV_1. Thus in the 28% of farmers with wheezing, shortness of breath, or dry cough (group II) bronchial hyperreactivity, number of years in pig farming, and possibly smoking were predictors for a larger than expected loss of FEV_1.

BRONCHIAL HYPERREACTIVITY

A high prevalence of bronchial hyperreactivity was found in all three groups of farmers (figure): 36/38 (95%) in group I, 40/61 (66%) in group II, and 20/34 (59%) in group III. Extrapolation to the total population of farmers suggests that 64% of farmers have some degree of bronchial hyperreactivity. The median values of PC_{20} in groups I, II and III were 0·3, 1·9 and 3·8 mg/ml histamine. To evaluate which factors were related to the presence of bronchial hyperreactivity a multiple regression analysis was performed for each group with $logPC_{20}$ as the dependent variable and age, $SFEV_1$, years in pig farming, and current smoking as predictor variables. None of these variables was a significant predictor of $logPC_{20}$ in group I (asthmatic) or group III (symptomless). In farmers with wheezing, shortness of breath, or dry cough (group II) FEV_1 was the most important predictor of $logPC_{20}$, and age was another significant predictor. Smoking and number of

Table 3 *Multiple regression analysis with standardised residual of FEV_1 ($SFEV_1$) as dependent variable and age, bronchial reactivity ($logPC_{20}$), years in pig farming, and being a smoker or non-smoker as predictor variables, with the regression coefficients and their standard errors (SE), and the significance of the coefficients, based on data from farmers in group II*

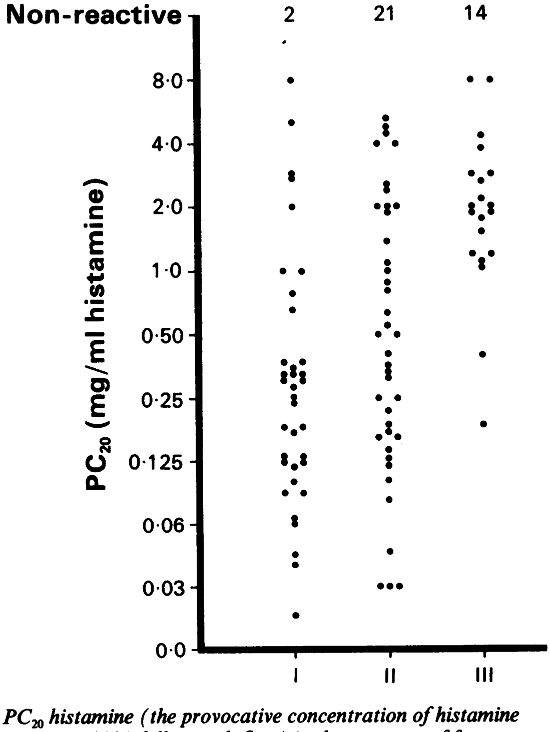
Dependent variable	Predictor variable	Coefficient	SE of coefficient	p
$SFEV_1$	Age	−0·0125	0·0141	0·376
	$LogPC_{20}$	1·3012	0·2096	0·000
	Years in pig farming	−0·0186	0·0090	0·044
	Smoker or non-smoker	−0·4793	0·2837	0·097

years in pig farming were not significant predictors (table 4).

Discussion

This study has extended a previous epidemiological study[11] in farmers by measurement of lung function and bronchial reactivity. The epidemiological study clearly showed an association between pig farming and respiratory symptoms and indicated that pig farming was a risk factor for self reported asthma. Previous cross sectional studies have also shown that pig farming is associated with a high prevalence of respiratory symptoms such as wheezing and cough and that the prevalence of these symptoms is higher than in other farming occupations.[8 10 16]

A special sampling technique was used in this study. A random sample of non-selected farmers would yield only a small number of farmers with symptoms; we therefore sampled from farmers both with and without symptoms to obtain a higher proportion of farmers with symptoms in the study group so that we could characterise lung function disorders in such farmers.



PC_{20} histamine (the provocative concentration of histamine causing a 20% fall in peak flow) in three groups of farmers. Group I (n = 47)—farmers who had reported asthma; group II (n = 63)—farmers who had reported shortness of breath, wheezing, or dry cough; group III (n = 34)—farmers who had no respiratory symptoms.

Table 4 *Multiple regression analysis with bronchial reactivity (logPC_{20}) as the dependent variable and age, standardised residual of FEV_1 ($SFEV_1$), years in pig farming, and being a smoker or non-smoker as predictor variables, with the regression coefficients and their standard errors (SE), and the significance of the coefficients, based on data from farmers in group II*

Dependent variable	*Predictor variable*	*Coefficient*	*SE of coefficient*	*p*
LogPC_{20}	Age	−0·0198	0·0064	0·003
	$SFEV_1$	0·3166	0·0510	0·000
	Years in pig farming	0·0005	0·0046	0·922
	Smoker or non-smoker	−1·1914	0·1420	0·181

The stratified sampling technique may, however, obscure a relation between lung function and environmental variables, such as smoking and pig farming, and this may explain why a positive association between pig farming, bronchial hyperreactivity, and FEV_1 was found only in farmers with shortness of breath, wheezing, or a dry cough (group II). Because there was a strong relation between age and respiratory symptoms in the random sample of farmers,[11] the farmers obtained by stratified sampling were older than the farmers in the random sample, and this may have influenced the results. Recently studies with lung function measurements in farmers suggest that chronic airways obstruction may be considered an occupational disease in farmers. The results of lung function measurement in this study agree with those of previous studies,[3 4] where a high prevalence of chronic airways obstruction was found in farmers. An English study[6] showed that dairy farming and silage work was associated with a low FEV_1 and a Dutch study[17] of pig farmers showed that certain feeding and manure handling systems were associated with a low FEV_1. This study is the first to show that the number of years in pig farming is associated with a low FEV_1. It is also the first study to measure bronchial reactivity in farmers, and to suggest that farmers have increased levels of bronchial reactivity. In 26 subjects (personal series) with no asthma or respiratory symptoms (median age 37 years, 31% smokers) only 4 (15%) had bronchial hyperreactivity ($PC_{20} \leqslant 8$ mg/ml histamine), compared with 59% of the symptomless farmers in this study.

Working in farming is characterised by exposure to high levels of organic dust,[18] especially in pig farming.[16 19] Population based cross sectional studies[1] have shown that exposure to dust and gases is associated with respiratory symptoms such as wheezing. A longitudinal study of industrial workers[2] showed that loss of FEV_1 was related to exposure to organic and inorganic dust, and a dose-effect relation was found. Grain elevator workers, like farmers, are exposed to high levels of organic dust and prolonged exposure to grain dust has been shown to be associated with cough, sputum, wheezing, airflow obstruction,[20] and an increase in non-specific bronchial reactivity.[21] An acute decrease in FEV_1 during the working day has been found in grain workers[22] and a longitudinal study[23] showed a rapid decline in FEV_1 in some workers that was linearly related to dust exposure. Cross sectional, population based studies have shown a relation between non-specific bronchial hyperreactivity and low levels of FEV_1 and respiratory symptoms such as wheezing and shortness of breath.[24 25]

The results in this study are thus in accordance with the findings of other studies of individuals with occupational dust exposure. In this study heavy dust exposure (that is, work in pig rearing units) was associated with low levels of FEV_1 and respiratory symptoms. Because this was a cross sectional study it could not determine whether non-specific bronchial hyperreactivity was causally or non-causally associated with low levels of FEV_1. Dust exposure might induce an increase in non-specific bronchial reactivity and the development of symptoms at a later stage or individuals with bronchial hyperreactivity might constitute a group especially susceptible to the effects of dust exposure. The first explanation seems more likely as significantly more of the symptomless farmers than of a control group of symptomless non-farmers had bronchial hyperreactivity. A longitudinal study in farmers of lung function, bronchial reactivity, and dust exposure, analogous to the study in grain workers,[24] has not yet been performed. Future longitudinal studies in farmers should consider decline in lung function, bronchial reactivity, and their relation to occupational exposure.

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