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Lung function and chronic respiratory symptoms of pig farmers: focus on exposure to endotoxins and ammonia and use of disinfectants

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Abstract

***Objectives*—The prevalence of chronic respiratory symptoms among pig farmers is known to be high, but the aetiology of these symptoms is not yet unravelled. Long term average exposure to dust was evaluated, endotoxins and ammonia and use of disinfectants were compared with chronic respiratory symptoms and depressed base line lung function.**

***Methods*—A cross sectional study was performed among 194 Dutch pig farmers, of whom 100 had not and 94 had chronic respiratory symptoms. Exposure-response relations were evaluated with multiple logistic and linear regression analysis. Estimates of long term average exposure were based on two personal exposure measurements, taken on one day in summer and one day in winter. Information on use of disinfectants and disinfection procedures was assessed by a walk through survey and interview by telephone.**

***Results*—Exposure to dust, endotoxins, and ammonia were not related to chronic respiratory symptoms. Duration of the disinfection procedure and pressure used at disinfection were strongly and positively related to chronic respiratory symptoms. A significant inverse association between base line lung function and endotoxin exposure was found only among asymptomatic farmers. Ammonia exposure and duration of the disinfection procedure were significantly associated with base line lung function in the entire population.**

***Conclusion*—Results suggest that use of disinfectants is an important aetiological factor in chronic respiratory health effects of pig farmers. This factor has not been studied before. Results also suggest an aetiological role for exposure to endotoxins and ammonia in development of chronic respiratory health effects, but longitudinal studies with detailed exposure assessment strategies are required to assess their roles.**

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Studies performed since 1977 in countries in north America and Europe showed high prevalences of acute and chronic respiratory symptoms among pig farmers. The same studies suggested that major base line lung function variables (forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1)) seem not to differ largely from expected values.[1-5] The aetiology of these respiratory health effects remains until now indistinct. Pig farmers are exposed to a variety of health hazards such as organic dusts and their constituents, gases, chemicals used for disinfection of buildings, and climatic conditions. Recent epidemiological studies were focused on the potential health hazard of exposure to high levels of endotoxins, and to a lesser extent to other components of organic dusts. Reported relations between measured exposures and chronic respiratory health effects are sparse. Heederik *et al*[6] and Zejda *et al*[7] reported associations between base line lung function and exposure to endotoxins. In their studies exposure was based on static measurements in swine confinement buildings over one or two days.

In our study we assessed personal exposure of inhalable dust, endotoxins, and ammonia and evaluated their association with base line lung function and chronic respiratory symptoms. In this study we also investigated disinfectants as potential aetiological factors. Several case studies have been described with respiratory symptoms, including asthma, induced by disinfectants.[8-14] These agents have, however, been overlooked as possible causes of respiratory health effects in pig farmers. The questionnaire based evaluation that preceded this study, showed that farmers reported more asthma like symptoms with more frequent disinfection (unpublished data). This study describes associations between chronic respiratory symptoms and base line lung function and determinants of exposure already mentioned.

Material and methods

POPULATION AND HEALTH DATA

The population consisted of 194 pig farmers who lived in the two south eastern provinces of The Netherlands; 94 with two or more chronic respiratory symptoms (chronic cough, chronic phlegm, ever wheezing, frequent wheezing, shortness of breath, and chest tightness (asthma)) and 100 without these symptoms. The population was derived from a group of 1133 male owners of pig farms who had completed a self administered questionnaire and who worked at least five hours a day in pig farming. Presence of chronic respiratory symptoms was investigated with the Dutch shortened version of the British MRC questionnaire,[15] as part of a self administered questionnaire. This was subsequently checked in a medical survey held in the winter of 1990-1. All 94 farmers who had reported two or more chronic respiratory symptoms were included in the study. The 100 symptomless farmers who were taken as controls were randomly selected out of the group of the 145 farmers with confirmed absence of symptoms, who were randomly selected from the farmers who had reported no chronic respiratory symptoms in the questionnaire. In the medical survey, forced expiratory lung function measurements were conducted with a Vicatest-V spirometer (Mijnhardt, Bunnik, The Netherlands). The procedure of testing and selecting of variables was carried out according to standards of the European Community of Coal and Steel.[16] Lung function tests were taken between 08 30 and 15 15. Variables included in the study were: forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), maximum mid-expiratory flow (MMEF: forced expiratory flow between 25% and 75% of FVC), and peak expiratory flow (PEF).

EXPOSURE DATA AND DISINFECTION

Personal inhalable dust and personal ammonia samples were taken during one work shift in summer and one in winter. Measurements took on average 8·3 (SD 0·6, range 5·2–10·4) hours. Ammonia exposure was assessed in duplicate with a passive monitoring method.[17] Basically, GF-A glass fibre filters (diameter 2·4 cm) were coated with a saturated solution of tartaric acid in diethylether and placed in a badge. A Teflon filter was used for an entrance membrane. After sampling, 20 ml of demineralised water was added to the glass fibre filters, which were placed in an ultrasonic bath for 15 minutes. Samples were further analysed according to a modified indophenol detection method,[18] and the concentration was assessed by spectrophotometry. The exposure concentration was expressed as time weighted average exposure. For 159 farmers exposure could be assessed on two days. For them, the geometric mean of both exposure concentrations was used as a measure of exposure in epidemiological analyses. The procedures for measurement of dust exposure and analysis of endotoxins in dust samples have been described elsewhere.[19 20] A mathematical modelling technique with regression equations reported elsewhere[21] was used to estimate long term average exposure. Basically, associations were measured between exposure level as a dependent variable and farm characteristics and time spent on activities during sampling as independent variables. Subsequently, regression equations, data on farm characteristics and time spent on activities in pig farming in two full weeks, were used to estimate long term average exposure to dust and endotoxins. For 161 farmers data were available on long term average dust and endotoxin exposure.

Pig farms in the study comprised on average 19 compartments. Compartments in the farrowing and finishing section, and in the section with weaned piglets, are small. After emptying a compartment, when animals are brought to another section, compartments are cleaned. Most of the 1133 farmers who completed the questionnaire regularly disinfect after cleaning. For the 194 subjects who were included in this study, information on use, type, and quantity of disinfectant was obtained during a visit to the farm. All visits were done by the same trained interviewer. Type of disinfectant was classified as chloramine-T, quaternary ammonium compounds, quaternary ammonium compounds combined with aldehydes (glutaraldehyde, glyoxal, formaldehyde), a combination of these compounds, and other compounds. Thirty out of 194 farmers did not use disinfectants. As preliminary analyses suggested associations between disinfection and respiratory health, additional information on disinfection procedures was obtained in an interview by telephone. Information was obtained on: frequency of disinfection on the farm, frequency of disinfection by the farmer, means of application, pressure used, duration of procedure, time until re-entering compartments after disinfection, and use of personal protection equipment during mixing and application of disinfectants. Out of the 164 farmers with disinfectants 150 participated in the interview.

DATA ANALYSIS

Associations between respiratory health and determinants of exposure were evaluated in multiple linear regression analysis (PROC REG) for lung function and multiple logistic regression analysis (PROC LOGISTIC) for chronic respiratory symptoms. Associations with lung function were adjusted for age, standing height and smoking (pack-years). Associations with respiratory symptoms were adjusted for age and smoking (current smoking). All exposure variables and aspects of the disinfection procedure were evaluated and retained in the models if they were associated with health outcomes. Excluded variables were evaluated for confounding effects. In all models, log transformed values were used for exposure to endotoxins, dust, and ammonia. Statistical analyses were performed with SAS/PC version 6·04.

Results

Table 1 shows characteristics of the entire population and of the groups with two or more and without chronic respiratory symptoms (chronic cough, chronic phlegm, ever wheezing, frequent wheezing, shortness of breath, and chest tightness (asthma)). In the entire population, average FVC and PEF exceeded predicted values, FEV_1 was about equal to the control value, and other lung function variables were below control values. The largest difference from the control value was found for MMEF, which was on average

*Table 1 Characteristics of entire population of pig farmers, and of farmers with and without chronic respiratory symptoms**

	All (n = 194)	Asymptomatic (n = 100)	Symptomatic (n = 94)
Age (y (SD))	38 (10)	36 (9)	40 (9)
Time in pig farming (y (SD))	15 (8)	13 (8)	16 (8)
Standing height (cm (SD))	177 (6)	178 (6)	177 (6)
Smoking (%):			
Current	32	18	47
Ex-smoker	31	33	30
Never-smoker	37	49	23
Baseline lung function (% predicted† (SD)):			
FVC (l)	108 (13)	111 (13)	105 (13)‡
FEV_1 (l)	101 (17)	106 (15)	95 (15)‡
PEF (l/s)	107 (24)	113 (23)	101 (23)‡
MMEF (l/s)	82 (31)	91 (29)	72 (29)‡

*Chronic cough, chronic phlegm, ever wheezing, frequent wheezing, shortness of breath, and chest tightness (asthma): no *v* one or more.
†According to Quanjer.[16]
‡Lower than in asymptomatic farmers (*t* test, P < 0.01).

*Table 2 Disinfection procedures in entire population of pig farmers, and in farmers with and without chronic respiratory symptoms**

	All (n=150) n (%)	Asymptomatic (n=74) n (%)	Symptomatic (n=76) n (%)
Frequency on farm†:			
2 Times/week	44 (29·5)	21 (28·8)	23 (30·3)
1 Time/week	60 (40·3)	29 (39·7)	31 (40·8)
1 Time/2 weeks	23 (15·4)	9 (12·3)	14 (18·4)
Less often	22 (14·8)	14 (19·2)	8 (10·5)
Pressure:			
No pressure	21 (14·0)	13 (17·6)	8 (10·5)
Low (< 20 bar)	99 (66·0)	52 (70·3)	47 (61·8)
Medium (20-50 bar)	20 (13·3)	8 (10·8)	12 (15·8)
High (> 50 bar)	10 (6·7)	1 (1·4)	9 (11·8)
Type of application†:			
Pressure washer	118 (79·2)	53 (72·6)	65 (85·5)
Foam washer	14 (9·4)	10 (13·7)	4 (5·3)
Watering can	10 (6·7)	6 (8·1)	4 (5·3)
Spray washer	7 (4·7)	4 (5·5)	3 (3·9)
Time to re-entry after disinfection†:			
< Half a day	37 (25·0)	22 (29·7)	15 (20·3)
Half a day	25 (16·9)	11 (14·9)	14 (18·4)
One day	86 (58·1)	41 (55·4)	45 (60·8)
Protection during disinfection†:			
No	83 (55·3)	41 (55·4)	42 (55·3)
Yes	66 (44·0)	33 (44·6)	33 (43·4)
Protection during mixing of disinfectants†:			
No	102 (68·0)	51 (68·9)	51 (67·1)
Yes	46 (30·7)	22 (29·7)	24 (31·6)
Duration of disinfection procedure:			
< 5 min	68 (45·3)	38 (51·4)	30 (39·5)
5-10 min	58 (38·7)	30 (40·5)	28 (36·8)
> 10 min	24 (16·0)	6 (8·1)	18 (23·7)

*Chronic cough, chronic phlegm, ever wheezing, frequent wheezing, shortness of breath, and chest tightness (asthma): no *v* one or more.
†Total not equal to 100%, some observations not classifiable.

82% of the predicted value. All lung function variables expressed as percentage of predicted were lower in symptomatic than in asymptomatic farmers (*t* test, P < 0·01). The largest difference was nearly 20% and was found for MMEF. Average age, years in pig farming, and prevalence of current smoking were higher among cases. Differences in lung function between symptomatic and asymptomatic farmers, as a percentage of predicted value, remained after adjustment for smoking in the multiple linear regression analysis.

Of the 150 farmers interviewed on disinfection procedures, only one asymptomatic farmer (1·4%) *v* nine symptomatic farmers (11·8%) used high pressure for disinfection (table 2). Six (8·1%) asymptomatic farmers spent more than 10 minutes on disinfection each time, compared with 18 (23·7%) symptomatic farmers. For other aspects of disinfection the distribution was similar in both groups. Average exposure to dust was 2·7 mg/m^3, to endotoxins 112 ng/m^3, and to ammonia 1·7 mg/m^3 (table 3). Exposures did not differ between symptomatic and asymptomatic farmers.

In multiple logistic regression analysis, medium pressure or high pressure, and spending more than 10 minutes on disinfection each time were significantly and positively associated with respiratory symptoms (table 4), with estimated odds ratios (ORs) of 7·1 and 4·2, respectively. Medium and high pressure were combined in the analysis because the distribution would yield a very large confidence interval (CI) for the high pressure group. In the analysis, no difference was found between disinfection for less than five minutes and five to 10 minutes. These two categories were taken together in the analysis. Level of exposure to dust, endotoxins, and ammonia, quantity of disinfectants used in one year, and type of disinfectant were not associated with respiratory symptoms. These variables did not affect estimates of other variables, and were therefore not included in the model.

For 106 farmers a complete data set was available to test associations between lung function and exposure to endotoxins and ammonia and disinfection procedures. Log

*Table 3 Exposure to endotoxins and ammonia in entire population of pig farmers, and in farmers with and without chronic respiratory symptoms**

	n	Arithmetic mean	Geometric mean	Geometric SD	(Range)
Dust (mg/m^3):					
All	161	2·7	2·6	1·3	(0·9 –5·9)
Asymptomatic	83	2·7	2·7	1·3	(1·5–4·5)
Symptomatic	78	2·6	2·5	1·3	(0·9–5·9)
Endotoxins (ng/m^3):					
All	161	112	105	1·4	(41·4–316)
Asymptomatic	83	111	104	1·4	(41·4–216)
Symptomatic	78	113	106	1·5	(43·7–316)
Ammonia (mg/m^3):					
All	159	1·7	1·6	1·6	(0·3–4·2)
Asymptomatic	79	1·8	1·6	1·7	(0·4–4·2)
Symptomatic	80	1·6	1·5	1·6	(0·3–3·7)

*Chronic cough, chronic phlegm, ever wheezing, frequent wheezing, shortness of breath, and chest tightness (asthma): no *v* one or more.

Table 4 Multiple logistic regression analysis on chronic respiratory symptoms and disinfection procedure among 150 pig farmers (n = 74 without symptoms, n = 76 with symptoms)*

	OR (95% CI)	P value
Age (per 10 y)	1·7 (1·1–2·4)	0·012
Current smoking (yes/no)	3·3 (1·5–7·1)	0·003
Pressure:		
Low *v* no	2·1 (0·7–6·1)	0·194
Medium/high *v* no	7·1 (1·9 27·1)	0·004
Duration:		
> 10 min *v* < 10 min	4·2 (1·4–12·7)	0·010

*Chronic cough, chronic phlegm, ever wheezing, frequent wheezing, shortness of breath, and chest tightness (asthma): no *v* one or more.

Table 5 Multiple regression analysis of lung function on endotoxin exposure, ammonia exposure and disinfection procedure in the total population and stratified for chronic respiratory symptoms (adjusted for age, standing height, and smoking habits (pack-years))*

	All (n = 106)			*Asymptomatic farmers (n = 51)*			*Symptomatic farmers (n = 55)*		
	b	*(SEM)*	*P value*	*b*	*(SEM)*	*P value*	*b*	*(SEM)*	*P value*
FVC (l):									
No *v* low/medium pressure	0·05	0·18	0·399	−0·19	0·26	0·232	0·17	0·27	0·263
High *v* low/medium pressure	−0·26	0·27	0·168	—	—	—	−0·17	0·27	0·270
> 10 *v* < 10 minutes	−0·48	0·18	0·004	−0·90	0·39	0·012	−0·28	0·21	0·095
Endotoxin exposure†	−0·25	0·18	0·083	−0·72	0·28	0·008	0·10	0·25	0·352
Ammonia exposure†	−0·05	0·13	0·364	0·01	0·20	0·490	−0·01	0·19	0·474
FEV_1 (l):									
No *v* low/medium pressure	−0·10	0·18	0·303	−0·36	0·22	0·057	−0·02	0·29	0·476
High *v* low/medium pressure	−0·31	0·27	0·127	—	—	—	−0·10	0·30	0·373
> 10 *v* < 10 minutes	−0·44	0·18	0·008	−0·68	0·33	0·025	−0·19	0·23	0·201
Endotoxin exposure†	−0·26	0·18	0·080	−0·64	0·24	0·006	−0·05	0·27	0·431
Ammonia exposure†	−0·27	0·13	0·022	−0·11	0·17	0·254	−0·35	0·20	0·043
MMEF (l/s):									
No *v* low/medium pressure	−0·44	0·32	0·086	−0·86	0·44	0·027	−0·29	0·47	0·271
High *v* low/medium pressure	−0·54	0·47	0·126	—	—	—	−0·14	0·48	0·387
> 10 *v* < 10 minutes	−0·53	0·31	0·046	−0·59	0·66	0·187	−0·20	0·37	0·290
Endotoxin exposure†	−0·36	0·32	0·129	−0·70	0·48	0·078	−0·33	0·44	0·233
Ammonia exposure†	−0·68	0·23	0·002	−0·37	0·33	0·135	−0·98	0·33	0·002
PEF (l/s):									
No *v* low/medium pressure	0·24	0·61	0·350	−0·45	0·81	0·290	0·34	0·89	0·353
High *v* low/medium pressure	−0·85	0·88	0·169	—	—	—	−0·19	0·91	0·417
> 10 *v* < 10 minutes	−1·20	0·59	0·023	−1·76	1·23	0·080	−0·37	0·69	0·296
Endotoxin exposure†	−0·47	0·60	0·220	−1·24	0·90	0·088	0·00	0·84	0·498
Ammonia exposure†	−0·77	0·43	0·039	−0·30	0·62	0·318	−1·00	0·62	0·056

*Tested one sided; †log transformed exposure concentration; b = regression coefficient.

transformed endotoxin and ammonia exposure was used in the analysis, which means that one unit change stands for an increase in exposure by a factor of 2·72. Such an increase in exposure to endotoxins was weakly associated with a decrease in FVC and FEV_1 of about 250 ml in the entire group (table 5, P < 0·10). Over the range of exposures in our population (5–95 percentile: 54 to 196 ng/m^3), the estimated decrease was about 320 ml. The exposure-response relations were much stronger in asymptomatic farmers, with estimated decreases of more than 900 ml and 800 ml, respectively, over the range of exposures in our population. Exposures to ammonia were strongly and inversely related to all lung function variables except FVC. For example, an increase in exposure to ammonia by a factor of 2·72 was related to a decrease of 270 ml in FEV_1. The decrease in FEV_1 over the exposures in our population (5–95 percentile: 0·6 to 3·2 mg/m^3) was 450 ml. Relations between lung function and ammonia were for different variables 25% to 40% steeper in the group of symptomatic farmers than in the entire group. In the group of asymptomatic farmers negative but non-significant associations were found.

A disinfection procedure taking more than 10 minutes was significantly associated with lower values of most lung function variables (table 5). For example, FVC and FEV_1 were estimated to be 480 and 440 ml less, respectively, in farmers disinfecting for more than 10 minutes. Associations with disinfection procedures were not significant in symptomatic farmers. Overall, the best lung function was found if low or medium pressure was applied and the worst when high pressure was used. Low and medium pressures were taken together in the analysis as their association with lung function was similar. A significant decrease of about 20% was found for MMEF among asymptomatic workers. Dust exposure and type of disinfectant were not related to lung function, and did not influence other exposure-response estimates and were not included in the model. In similar models (table 5) with quantity of specific disinfectant used in one year added as an explanatory variable, quantity was inversely but not significantly associated with lung function in the entire group. In contrast, the associations with MMEF and PEF were highly significant among asymptomatic farmers. This effect was independent of duration and frequency of procedure. For each type of disinfectant, use of median quantity was associated with a similar decrease in lung function, which ranged on average from about 30% for PEF, to 40% for MMEF.

The associations between respiratory symptoms and lung function and determinants of exposure were adjusted for all other variables in the models (tables 4 and 5). The different determinants of exposure were independent of each other but associated with respiratory health. The associations between lung function or chronic respiratory symptoms and other aspects of disinfection (table 2), were also evaluated. Of those, only type of application was more or less consistently related to lung function, but this effect is probably the same as that found with pressure as both variables were correlated.

Discussion

In our population of 1432 male pig farmers, including 299 working daily less than five hours in pig farming, 32·9% reported at least one chronic respiratory symptom. The prevalence of these symptoms has been shown to be invariably high in other studies of pig farmers in countries in Europe and north America.[1-6 22] In our study a disinfection procedure of 10 minutes or more was much more prevalent among farmers with two or more than in farmers without chronic respiratory symptoms. Use of higher pressures (20 bar or more) during disinfection was positively related to chronic respiratory symptoms as well. Associations with duration and pressure were independent from each other. We are not aware of any other study that reported use of disinfectants as a potential respiratory health hazard for pig farmers. Exposures to ammonia, inhalable dust, and endotoxins were not associated with chronic respiratory symptoms.

Characteristics of the disinfection procedure (longer duration, no or high pressure, larger quantity of disinfectants) and exposure of endotoxins and ammonia were associated with lower base line lung function in pig farmers. Associations were most clearly present in asymptomatic farmers for disinfection procedure and endotoxin exposure. In this group the estimated effect of increase in endotoxin exposure by a factor of 2·72 and a disinfection procedure of more than 10 minutes were each associated with a decrease of about 15% in the different variables. The magnitude of the significant relations with ammonia exposure differed, and ranged from about 5% for FEV_1 to 18% for MMEF in the entire population, but associations were 25% to 40% steeper in symptomatic farmers.

Symptomatic farmers were oversampled in our study. Data on lung function and associations with exposure as presented for the entire population are therefore not representative for the base population. Exposure-response relations for a representative sample of the base population are expected to be closer to those reported for asymptomatic than for symptomatic farmers. When the results for the asymptomatic farmers are being compared with other studies we can make the following observations. Similar patterns of lung function variables were found, with FVC, FEV_1, and PEF in the same range as control values, and MMEF lower than the control value.[1-5 7 23] A decrease in MMEF may be regarded as an early change associated with flow limitation, even if the initial part of the spirogramme is unaffected.[24]

Duration of the disinfection procedure was consistently associated with lung function and respiratory symptoms. Multiple regression analyses showed that this could not be attributed to use of larger quantities of disinfectant in one year, type of disinfectant, other evaluated aspects of the disinfection procedure, or differences in exposures to dust, endotoxins, or ammonia. Potentially, this relation found for duration of disinfection reflected an association with level of ambient exposure concentration or critical time of exposure.

Most commonly used disinfectants contain quaternary ammonium compounds with or without aldehydes (glutaraldehyde, glyoxal, formaldehyde), or chloramine-T. In the scientific literature, several effects of exposure to chloramine-T have been reported. These include respiratory symptoms such as cough, wheezing and dyspnoea, and immediate and late asthmatic reactions. Effects on eyes and upper respiratory system are reported either together with or without symptoms of the lower respiratory system.[8 9 11 25] Recently, two cases have been reported with occupational asthma due to exposure to disinfectants containing quaternary ammonium compounds.[13 14] Glutaraldehyde has been shown to be able to induce occupational asthma by means of serial PEF measurements.[10 12] Norbäck *et al*[26] performed a cross sectional study on 39 workers in medical services exposed to glutaraldehyde concentrations below the Swedish occupational exposure limits, and 68 unexposed controls. They reported differences in symptom prevalence of the upper respiratory tract, but not of symptom prevalence of the lower respiratory tract. To our knowledge their study is the only one reporting prevalences of respiratory health effects in an occupational group exposed to either quaternary ammonium compounds, glutaraldehyde, or chloramine-T. Respiratory effects of exposure to formaldehyde, mostly from sources other than disinfectants, have frequently been reported. These include occupational asthma, effects on base line lung function and associations with respiratory symptoms in some occupational groups, although other studies fail to show such associations.[27-30]

In the entire group, the estimated decrease in FVC and FEV_1 of about 250 ml with an increase in exposure to endotoxins by a factor of 2·72 was of borderline significance. In asymptomatic farmers the associations were significant, and estimated decreases in lung function were 2·5–3 times larger (about 15% of median lung function values). The decrease in the entire population was similar to that reported by Heederik *et al*[6] in a group of 62 farmers. Concentrations of endotoxins in swine confinement buildings and variation in exposure between people in that study were in the same range as in our study. They reported a decrease in FVC of 263 ml ($P < 0{\cdot}10$) and in FEV_1 of 208 ml ($P < 0{\cdot}05$)/100 ng/m^3 increase in endotoxin concentration. Such an increase is similar to the difference between the 10th and 90th percentile of the exposure distribution in our study, which corresponds to an increase by a factor of nearly 2·72. Taking oversampling of symptomatic farmers into account, the exposure-response relation is expected to be about a factor of two steeper in our study. Zejda *et al*[7] reported in a group of 46 pig farmers a borderline significant decrease in FVC, of 145 ml with an increase by a factor of 2·72 in endotoxin concentration in swine buildings, about 40% less than in our study. In their study FEV_1 was not related to endotoxin concentration. They reported an endotoxin exposure that was five times higher than in our study, despite similar dust exposures. Endotoxin concentration multiplied by number of hours working in swine buildings, as an approximation of personal exposure, was strongly related to FVC (P = 0·02), and weakly related to FEV_1 (P = 0·06). It is not clear whether this finding can be attributed to number of hours alone, which might be related to any type of exposure. No detailed comparison can be made between our study and those of Heederik *et al*[6] and Zejda *et al*,[7] as exposure was not based on personal exposure measurements in their studies. Generally there is poor correlation between static air measurements and personal sampling.[19 31] It is unlikely that static measurements induced only systematic bias, as exposures largely depend on the activity of pigs caused by disturbance by the farmer, and by the farmer's own activity.[21 32]

The inverse association between lung function and exposure to ammonia was not expected, as ammonia is hygroscopic and therefore the dose is generally expected to be low. In free form it will be captured in the upper part of the respiratory tract. It has been suggested that dust particles can act as carriers that bring ammonia into smaller airways,[33 34] which may explain our results. In the epidemiological studies mentioned earlier[6 7] reported exposures were three to seven times higher than in our study. Associations adjusted for confounding factors between exposure to ammonia and either base line lung function or chronic respiratory symptoms were not found or reported in these and other studies. Reports on effects of chronic exposure to ammonia at any level of exposure are sparse. Holness *et al*[35] studied 58 workers exposed to on average 9·2 mg/m^3 ammonia in the soda ash industry, but did not find differences in symptoms and lung function between exposure categories, or with control workers.

Exposure-response relations differed for respiratory symptoms and lung function. Also other studies in pig farming and the animal feed industry, with the same questionnaire and lung function test, showed this phenomenon.[6 36] In addition, associations with lung function differed between symptomatic and asymptomatic farmers. There may be different reasons for these inconsistencies. Firstly, different biological mechanisms may be underlying these discrepancies. Secondly, symptomatic farmers may adjust their working practice to limit inhaled doses of pollutants, which they associate with symptoms. This may be done by avoiding activities with high (dust related) exposure, by using dust masks, and more subtle behavioural changes. Thirdly, symptomatic farmers may be more sensitive to normal ammonia exposure encountered in pig farming, whereas at these exposures ammonia does not cause respiratory symptoms in symptom free farmers.

There was no indication that discrepancies in relations between exposure and lung function could be attributed to acute effects of exposure before lung function testing in either asymptomatic or symptomatic farmers.

In conclusion, our results suggest that the aetiology of chronic respiratory health effects in pig farmers is multifactorial. Disinfectants were, until this study, not regarded as potential health hazards. In our study, exposure to disinfectants was only based on qualitative information and quantity used. The relations need to be substantiated by actual exposure measurements. Associations with endotoxin exposures support the hypothesis that endotoxins are causally related to chronic respiratory health effects. Inconsistency in relations between reported symptoms and tested lung function, and in lung function between symptomatic and asymptomatic farmers requires more attention. It is expected that cross sectional studies can add little more to the insight into the aetiology of respiratory symptoms of pig farmers than has already been obtained from our study. Our study involved very labour intensive and costly field work campaigns. Small variations in exposure between people in the presence of relatively large variations within people, changing exposures over a longer period of time, the multifactorial aetiology of symptoms, and combined exposures require preferably prospective study designs, with an even more detailed measurement of exposure and investigation of health effects.

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