Longitudinal Changes in Bronchial Responsiveness Associated With Swine Confinement Dust Exposure

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Longitudinal Changes in Bronchial Responsiveness Associated With Swine Confinement Dust Exposure*

Peter F. J. Vogelzang, MD, PhD; Joost W. J. van der Gulden, MD, PhD; Hans Folgering, MD, PhD; Dick Heederik, PhD; Martin J. M. Tielen, PhD; and Constant P. van Schayck, PhD

Study objectives: Acute exposure to the air in swine confinement units causes bronchial hyperresponsiveness and inflammation of the airways. This study was performed to assess the longitudinal development of bronchial responsiveness in pig farmers and to establish exposure-response relationships.

Methods: A cohort of 171 pig farmers was followed over a 3-year period. Bronchial responsiveness was assessed by a histamine provocation test. Long-term average exposure to inhalable dust and endotoxin was determined by personal monitoring in summer and winter, using data on farm characteristics and activities. Time-weighted average (TWA) personal exposure to ammonia was measured. Data on farm characteristics were gathered in the same period.

Results: Mean increase in responsiveness was 2.52 doubling concentrations of histamine for a 10% decrease in FEV1 and 1.36 doubling concentrations for a 20% decrease in FEV1. Long-term average exposure to dust was 2.63 mg/m³ and to endotoxin was 105 ng/m³. TWA exposure to ammonia was 1.60 mg/m³. After adjusting for age and smoking behavior, long-term average exposure to inhalable dust was associated with increases in bronchial responsiveness expressed as steps for provocative concentration causing 10% fall in FEV1. TWA exposure to ammonia, use of wood shavings as bedding, and automated dry feeding were associated with increases in responsiveness expressed as steps for provocative concentration causing a 20% fall in FEV1.

Conclusions: Exposure to dust and ammonia in pig farms contributes to chronic inflammation of the airways and should be reduced.

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Key words: ammonia; occupational epidemiology; occupational exposure; organic dust; pig farmer

Abbreviations: PC₁₀ = provocative concentration causing a 10% fall in FEV₁; PC₂₀ = provocative concentration causing a 20% fall in FEV₁; TWA = time-weighted average

Work in the closed environment of pig confinement buildings will bring about a high exposure to dust and gases of organic origin. Constituents such as bacterial endotoxin1–2 and ammonia3 feature prominently as etiologic factors in the development of respiratory disease in pig farmers. The prevalence of bronchial hyperresponsiveness in cross-sectional studies was usually higher in pig farmers than in nonfarming control subjects,4–9 with one exception,10 but not higher than in other farmers.4–7–8 Nonfarming subjects experimentally exposed to high levels of dust through working in a pig confinement building displayed sharp and reproducible increases in bronchial responsiveness.11,12 No longitudinal information is available on the development of responsiveness in pig farmers. We reported an association between the number of years worked as pig farmer and the prevalence of mild bronchial responsiveness.13 Bronchial responsiveness was shown to be associated cross-sectionally with certain specific character-
tistics of the pig farm (quaternary ammonium compounds, wood shavings, automated dry feeding), but not with measured personal exposure of the farmer.13 Bias from various sources makes it difficult to interpret cross-sectional studies reporting associations between exposure and bronchial responsiveness.11–13 To assess the effect of exposure, longitudinal studies that suffer less from such bias are required.

The present study evaluates longitudinal changes in bronchial responsiveness in a 3-year follow-up in a cohort of 171 pig farmers. Associations with exposure to inhalable dust, endotoxin, ammonia, and farm characteristics determining exposure are shown to exist.

**Materials and Methods**

**Study Population**

In 1990, a questionnaire survey was administered to 1,504 pig farmers.14 To be able to study exposure-response relations, a study population was formed with sufficient contrast in respiratory morbidity, and therefore presumably also in exposure. In 1991, 200 randomly selected subjects from among the respondents with one or more chronic respiratory symptoms (chronic cough, chronic phlegm, shortness of breath, ever wheezing, frequent wheezing, chest tightness/asthma) and 190 randomly selected subjects without such symptoms were invited for a medical examination that included an extensive interview. Of the 200 farmers who reported one or more chronic symptoms in the postal questionnaire, 115 qualified for the category of suffering from COPD and/or asthma on the basis of further information obtained in the interviews at the medical examinations. They were considered to be consistently symptomatic. Of the 199 farmers without chronic symptoms reported in the postal questionnaire, 145 revealed no chronic symptoms either in the more extensive interviews. They were considered to be consistently asymptomatic. Ninety-eight of the consistently symptomatic subjects and 100 of the consistently asymptomatic subjects were randomly selected for a follow-up program that included measurements of environmental and personal exposure in their own confinement units. All worked at least 5 h/d in pig farming. This cohort was invited in June of 199213 and June of 1995 for medical examinations that included an extensive interview. Of the 199 participants, 140 participants, respectively.

Bronchial responsiveness was assessed by a shortened procedure as described by Hargreave et al.18 Participants inhaled aerosolized histamine for 2 min, starting with saline solution control, and then with doubling concentrations from 0.03 to 16 mg/mL. Histamine. The nebulizer was calibrated for an output of 0.13 mL/min. The provocative concentration causing a 10% fall in FEV1 (PC10) and the provocative concentration causing a 20% fall in FEV1 (PC20) were assessed by linear intrapolation in a log-dose-response plot. In case a 10% decrease was reached after inhaling saline solution control, PC10 was arbitrarily set at 0.01. If a 10% decrease in FEV1 was not reached at 16 mg/mL, PC10 was arbitrarily set at 32 mg/mL. This is similar to the approach used by Preller et al.18

The study was approved by the Committee for Ethical Research of the University of Nijmegen.

**Validation**

To validate the comparison of data from 1992 and 1995, a short validation experiment was carried out. The experimental setups were reconstructed, and five volunteers were tested between 2 days and 5 days apart using the actual nebulizers of 1992 and 1995 (which were both still available) and the same study protocol. As the pig farmers in the study did not have severely obstructed airways, healthy volunteers were chosen for this validation as well.

**Exposure and Farm Characteristics**

Measurements of exposure were carried out on the farms of all participants during full work shifts of on average 8.3 h on 2 days in summer 1991 and winter 1992. Personal exposure to inhalable dust (50% cutoff diameter of 30 μm, meeting requirements for total dust sampling) was determined using a dust sampler with a 6-mm diameter inlet opening and an airflow of 2 L/min. Teflon filters with a pore size of 1 μm (Millipore; Bedford, MA) were used. Endotoxin in the inhalable dust samples was analyzed with a modified kinetic Limulus amoebocyte lysate test.18 Methods for measurement of dust and endotoxin are described in detail elsewhere.19–20 Because the day-to-day variations of exposure to dust in individual participants were considerable compared with the variations of exposure in the entire group, the long-term average exposure was predicted by a mathematic modeling technique. Long-term average exposure to dust and endotoxin of each individual farmer was estimated using data on farm characteristics and time spent on activities in pig farming of all cohort members combined. A separate article on this approach illustrated that the exposure predicted with the modeling approach correlates well with the average exposure measured over more than eight occasions, and that error is reduced and remains random.21

Personal ammonia exposure was determined in duplicate by using a passive monitoring method.22 Samples were analyzed according to a modified indophenol detection method, and concentration was assessed by spectrophotometry. Results were expressed as time-weighted average (TWA) exposure. From the total number of 171 cohort members, complete data on exposure to dust, endotoxin, or ammonia were available for 146, 146, and 140 participants, respectively.

In the winter of 1992, an inventory of farm characteristics was made by walk-through surveys on the farms of participants. In the summer as well as in the winter, the farmers completed a diary on time spent on activities in pig farming, thus covering two 7-day periods. Based on the information from the surveys and the diaries, the average time a farmer was exposed to a particular characteristic was arrived at. The methods used to estimate exposure to these farm characteristics are fully described by Preller et al.18
Analysis

Changes in bronchial responsiveness between 1992 and 1995 were calculated by taking the log of base 2 of the ratio of the two concentrations causing a fall of 10% or 20%, respectively, in FEV1:

\[ \Delta PC_{10} = \log_2 \left( \frac{PC_{10\, 1995}}{PC_{10\, 1992}} \right) \]

In this way, the changes were expressed in terms of doubling concentrations of histamine.

As exposure was log-normally distributed, log-transformed values with base 2 were used in the analyses of associations with health effects. Bronchial responsiveness can show fluctuations over short periods, especially following occasional heavy exposure.\(^{11–12}\) Pig farmers experiencing heavy exposure on one of the days with a histamine responsiveness test, therefore, may show very large increases or decreases during the follow-up. This may seriously distort estimates of longitudinal decline and consequently hamper exposure-response analysis. Therefore, trimmed means were used in exposure-response analyses, by excluding 12 pig farmers prior to analyses with concentration steps PC10, and 6 prior to analyses with concentration steps PC20.\(^{23}\) Mean values of the exposure variables were not affected by this procedure.

Most pig farmers were not hyperreactive, at least at the start of the follow-up. Room for decreases in responsiveness was limited, as we used no concentration of histamine > 16 mg/mL. Consequently, more farmers with very large increases in responsiveness were excluded from exposure-response analysis than farmers with very large decreases in responsiveness.

Associations between exposure and increases in responsiveness were tested with linear regression analysis, adjusting for age and smoking behavior, the latter defined as pack-years of cigarettes. For current and past cigarette smokers, the numbers of pack-years were calculated by the number of cigarettes smoked per day multiplied by the number of years smoked, divided by 25. Initial small caliber is associated with greater responsiveness, as any further contraction of obstructed airways inevitably leads to a more rapid decline in diameter. Entering baseline FEV1 into multivariate analysis is done to adjust for a confounding effect from initial caliber. However, prevalence of small caliber was low in this group of basically healthy, working men, and consequently the geometrical effect on responsiveness could not play a major role. As baseline FEV1 was itself associated with exposure,\(^{22}\) associations between exposure and increases in responsiveness were not adjusted for baseline FEV1. As baseline atopy (IgE to common allergens measured in sera) had little effect on the associations tested,\(^{10}\) it was left out of the final models as well.

In the regression analysis with farm characteristics, the farmers who used a certain characteristic were compared to those without. For every characteristic, the group not using it formed the reference category. Our previous reports had provided ample evidence that these characteristics are detrimental, both to respiratory health of pig farmers in general and also to responsiveness cross-sectionally.\(^{13–14,22}\) Considering the a priori evidence, a one-sided test was chosen. By using a multivariate regression, the results could be adjusted for confounders and the other farm characteristics.
Computations were completed with Statistix for Windows (Analytical Software; Tallahassee, FL) for personal computer.

Results

Personal Characteristics

Mean age of the 171 farmers was 39.6 years at the start of the observation period (Table 1). Mean number of years worked in pig farming was 16.7. There were small differences in age (41.6 vs 37.6) and number of years worked as pig farmer (18.1 vs 15.4) between symptomatic and asymptomatic farmers at the start of the observation period. Five participants were no longer active as pig farmers in 1995; three of them stopped partly because of respiratory problems. Percentage of cigarette smokers was 25 (35 for symptomatic vs 15 for asymptomatic farmers).

Histamine Responsiveness

Mean decline in lung function was 73 mL/yr for FEV$_1$ and 55 mL/yr for FVC. This was not different for symptomatic or asymptomatic farmers. Histamine responsiveness sharply increased in 3 years in this group of pig farmers. Mean increase in responsiveness was 2.52 doubling concentrations of histamine for a 10% decrease in FEV$_1$ (p < 0.001) and 1.36 doubling concentrations for a 20% decrease in FEV$_1$ (p < 0.001). The changes in histamine responsiveness are shown as concentration steps for PC$_{10}$ and PC$_{20}$ in Figures 1, 2. In these figures, the pig farmers excluded from exposure-response analyses are indicated by asterisks.

If the pig farmers with a baseline FEV$_1$ ≤ 80% predicted at the start of the follow-up (n = 16) were excluded, the temporal trend in responsiveness is largely unaffected (2.44 concentration steps for PC$_{10}$ and 1.16 for PC$_{20}$). The temporal trend in responsiveness was seen in both the highest- and lowest-exposed pig farmers.

Responsiveness in 1995 correlated with the number of years worked as pig farmer (Spearman R$^2$ for PC$_{10}$ = 0.23, p < 0.05; for PC$_{20}$, = 0.26, p < 0.05), which we observed already in 1992.$^{13}$

Validation

The individual results for PC$_{20}$ were within the two- to threefold reproducibility required by European Respiratory Society standards.$^{15}$ The mean results from the five volunteers, however, showed a nonsignificant tendency toward greater responsiveness when using the 1995 nebulizer (1.3 concentration steps for PC$_{10}$ and 1.1 concentration steps for PC$_{20}$), suggesting that the histamine yield of the 1992 nebulizer may have been smaller than that of the 1995 nebulizer. We cannot exclude, therefore, that the increase in responsiveness was overestimated to some extent, despite the use of the same protocol, setup, and type of nebulizer at the two measurements. If the differences found at the validation experiment were applied as a correction factor to the measured increases in responsiveness, the corrected mean increase in responsiveness was 1.48 doubling concentrations for a 10% decrease in FEV$_1$ (p < 0.001) and 0.72 doubling concentrations for a 20% decrease in FEV$_1$ (p < 0.001).

![Figure 1. Changes in bronchial responsiveness from 1992 to 1995 among 171 pig farmers. Increases presented as concentration steps for a 10% decrease in FEV$_1$. * = farmers excluded before exposure-related analysis.](image)
Exposure and Associations With Respiratory Effects

Estimated long-term average exposure to inhalable dust was 2.63 mg/m$^3$ (geometric mean) and to endotoxin was 105 ng/m$^3$. TWA exposure to ammonia was 1.60 mg/m$^3$ (Table 1).

Increases in bronchial responsiveness in the 3-year period, measured as doubling concentration steps for PC$_{10}$, were significantly associated with exposure to inhalable dust, but not with exposure to endotoxin and not significantly to ammonia (Table 2). The associations with exposure were stronger for the consistently symptomatic farmers than for those without symptoms. The association between dust exposure and increases in responsiveness, based on these data, is represented in Figure 3.

Increases in bronchial responsiveness measured as doubling concentrations for PC$_{20}$ were associated with exposure to ammonia, but not to dust or endotoxin (Table 2). Again, the associations with exposure were stronger for the consistently symptomatic farmers alone. There was a correlation with dust exposure among the symptomatic farmers alone. There was no correlation with dust exposure among the symptomatic farmers, but that was no longer significant when adjusting for confounders in a multivariate analysis. The association between ammonia exposure and increases in responsiveness, based on these data, is represented in Figure 4.

If baseline FEV$_1$ or baseline responsiveness were included in the models, results for associations with dust and with farm characteristics are unchanged. Results for associations with ammonia are a third lower and not statistically significant. Analysis after exclusion of obstructed pig farmers (n = 16) yielded the same results.

Table 2—Associations Between $^2$Log-Transformed Exposure to Dust and Endotoxin (Long-term Average) and Ammonia (TWA) and Increases in Bronchial Responsiveness in Concentration Steps for PC$_{10}$ and PC$_{20}$, of 171 Pig Farmers During the 3-Year Follow-up Between 1992 and 1995. Adjusted for Age and Smoking (Pack-Years of Cigarettes)

<table>
<thead>
<tr>
<th>Variables</th>
<th>n*</th>
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<th>p Value†</th>
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<td></td>
</tr>
<tr>
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<tr>
<td>Endotoxin</td>
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<tr>
<td>PC$_{20}$</td>
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<tr>
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</tr>
<tr>
<td>Endotoxin</td>
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<tr>
<td>Ammonia</td>
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<td>0.33</td>
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<td>Ammonia</td>
<td>66</td>
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<td>0.18</td>
<td>0.34</td>
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</table>

*No. of pig farmers in the final regression model.
†Tested one sided.
If the associations with exposure were reanalyzed with differences corrected for the results of the validation experiment, the strength of associations was of the same order and remained statistically significant.

Farm Characteristics and Associations With Respiratory Effects

Both the use of wood shavings as bedding material and the use of an automated dry feeding system were associated with a larger increase in bronchial responsiveness, expressed as concentration steps for PC$_{20}$ (Table 3). The use of quaternary ammonium compounds as active substance in disinfectants was not associated with increases in responsiveness, though it was cross-sectionally associated with hyperresponsiveness both in 1992 and in 1995 (not shown). As was the case with exposure to dust and ammonia, associations tended to be stronger for the group of symptomatic pig farmers. Associations were weaker for responsiveness when expressed as concentration steps PC$_{10}$, but pointed in the same direction.

Table 3—Multivariate Associations Between Farm Characteristics and Increases in Bronchial Responsiveness in Concentration Steps for PC$_{20}$ of 171 Pig Farmers During the 3-Year Follow-up Between 1992 and 1995. Adjusted for Age and Smoking (Pack-Years of Cigarettes)

<table>
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<tr>
<td>Others</td>
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<td>Automated dry feeding</td>
<td>23</td>
<td>0.92</td>
<td>0.34</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*No. of pig farmers exposed to the characteristic. The numbers of the unexposed reference categories were not included in the Table. The total number of pig farmers in the final regression model was 157. †Tested one sided. ‡Quaternary ammonium compounds (QACs) as active substance.

Discussion

In this 3-year follow-up of 171 pig farmers, we found a sharp increase in bronchial responsiveness. Long-term average exposure to inhalable dust was associated with increases in bronchial responsiveness expressed as concentration steps for PC$_{10}$. TWA exposure to ammonia, use of wood shavings as bedding, and automated dry feeding were associated with increases in responsiveness expressed as concentration steps for PC$_{20}$.

Log-transformed exposure with base 2 was used in analysis. This means that the regression coefficients in Table 2 represent the effect of an increase in exposure with a factor 2. For instance a doubling of long-term average exposure to inhalable dust was associated with an extra increase in responsiveness of 0.59 concentration steps for PC$_{10}$ during follow-up. For the farm characteristics in Table 3, the regression coefficients represent the effect of using the characteristic. For instance, the farmers using wood shavings as bedding ($n = 5$) had an extra increase in responsiveness of 1.54 concentration steps for PC$_{20}$ during follow-up, when compared to the farmers who used no bedding ($n = 130$).

The increase in responsiveness over the 3-year period was very large. At this rate of increase, all farmers should have been hyperresponsive by now considering the average of 16.7 years experience in pig farming. So, the actual increase in responsiveness in this group of pig farmers must have been smaller than the measured results. That the pig farmers did indeed increase in responsiveness, though at a smaller rate, is supported by the following arguments:

1. If the results of the validation experiment are subtracted from the measured results, a more plausible rate of increase remains.
2. There was a statistically significant association between PC<sub>10</sub> and PC<sub>20</sub> values and the number of years worked as pig farmer both at the start<sup>13</sup> and the end of this study, a finding reported also by Rylander and coauthors.<sup>24</sup>

3. The increases in responsiveness in this study were associated with exposure.

4. In experimental studies, subjects increase substantially in responsiveness after exposure to swine dust.<sup>11–12</sup>

The associations with exposure were not affected by the potential bias in the results. This could have occurred if the magnitude of bias was determined by exposure. However, the trend in responsiveness was seen in both higher and lower exposed farmers and was unaffected when obstructed pig farmers were excluded. Such differential bias is, therefore, highly unlikely. This supports the notion that the exposure in pig farming leads to prolonged inflammation of the airways.

Some of the observed increase in bronchial responsiveness may have been due to the reduction in FEV<sub>1</sub>. As shown in Table 1, the symptomatic farmers had a lower FEV<sub>1</sub> at the start than the asymptomatic ones and had a larger increase in responsiveness. This could lead to overestimation of the direct effect of exposure on responsiveness. However, exclusion of pig farmers with a baseline FEV<sub>1</sub> < 80% predicted left the temporal trend in responsiveness unaffected. Furthermore, inclusion of baseline FEV<sub>1</sub> in the analyses of associations with exposure yielded lower results for ammonia exposure only, demonstrating that this factor had a limited influence on the results.

Large changes in exposure during the observation period are a potential explanation for a rapid increase in responsiveness. However, at the second medical examination, questions on farming methods were asked and the results suggested no major shifts in exposure.

The effect of endotoxin on lung function in pig farmers is very clear.<sup>1–2</sup> A possible role of other dust components is less established. In the present study, we found no association between endotoxin exposure and increases in responsiveness, but we did for dust exposure, though not consistently for PC<sub>10</sub> and PC<sub>20</sub>. Earlier, we have shown that besides endotoxin, inhalable dust has an effect on lung function as well.<sup>2</sup> This supports the hypothesis that more substances in organic dust than endotoxin alone, for instance β(1–3)-D-glucan from fungi<sup>25</sup> and peptidoglycan from Gram-positive bacteria,<sup>26</sup> contribute to the development of respiratory disease in exposed workers. This is further corroborated by the observation that the use of automated dry feeding systems, known to be associated with higher exposure to dust<sup>18,27</sup> and with health effects,<sup>13–14,28</sup> contributed to increases in responsiveness. In many countries, occupational threshold exposure levels for exposure to dust are as high as 10 mg/m<sup>3</sup>. The threshold limit value for grain dust in the United States is 4 mg/m<sup>3</sup>. Recently, a lower threshold of 2.8 mg/m<sup>3</sup> for organic dust was proposed.<sup>3</sup> The health effects demonstrated in this study, at an average exposure level to dust of 2.6 mg/m<sup>3</sup>, suggest that such a threshold level for organic dust exposure should certainly not be higher.

Associations between TWA exposure to ammonia and increases in responsiveness were significant for concentration steps PC<sub>20</sub>. Earlier, we demonstrated an inverse association between ammonia exposure and baseline lung function in the cross-sectional part of our studies. This was strongest for the symptomatic farmers as well.<sup>22</sup> Based on associations between ammonia exposure and FEV<sub>1</sub> decrements over a work shift, a threshold of 5.4 mg/m<sup>3</sup> for ammonia in confinement farming was recommended.<sup>3,29</sup> The present study provides additional evidence that a threshold of 18 mg/m<sup>3</sup> currently valid in many countries is too high for this multiexposure environment.

Analyses of associations with exposure were performed after exclusion of subjects with increases in responsiveness deemed unreliable. If these subjects were included in the analyses, associations were weaker, though in the same direction, for all exposure variables.

In conclusion, we find evidence for increases in responsiveness in pig farmers associated with exposure to dust and ammonia. This stresses the need for reduction of exposure, for which measures are proposed in an earlier publication.<sup>18</sup> Few pig farmers leave their job due to health reasons alone. Earlier, we demonstrated it is likely that self-selection out of this industry due to asthma occurs in an early stage.<sup>30</sup> Such a self-selection would attenuate observed exposure-response associations. This group with an average 16.7 years of pig farming, therefore, forms a relatively insensitive group. That clear effects of exposure are shown in such a group emphasizes the need for prevention.

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REFERENCES


2 Vogelzang PFJ, van der Gulden JWJ, Folgering H, et al. Endotoxin exposure as a major determinant of lung function...


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