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Respiratory Dysfunction in Swine Production Facility Workers: Dose–Response Relationships of Environmental Exposures and Pulmonary Function

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Human respiratory health hazards for people working in livestock confinement buildings have been recognized since 1974. However, before comprehensive control programs can be implemented, more knowledge is needed of specific hazardous substances present in the air of these buildings, and at what concentrations they are harmful. Therefore, a medical epidemiological and exposure–response study was conducted on 207 swine producers using intensive housing systems (108 farms).

Dose–response relationships between pulmonary function and exposures are reported here. Positive correlations were seen between change in pulmonary function over a work period and exposure to total dust, respirable dust, ammonia, respirable endotoxin, and the interactions of age-of-producer and dust exposure and years-of-working-in-the-facility and dust exposure. Relationships between baseline pulmonary function and exposures were not strong and therefore, not pursued in this study.

The correlations between exposure and response were stronger after 6 years of exposure. Multiple regression models were used to identify total dust and ammonia as the two primary environmental predictors of pulmonary function decrements over a work period. The regression models were then used to determine exposure concentrations related to pulmonary function decrements suggestive of a health hazard. Total dust concentrations ≥ 2.8 mg/m^3 were predictive of a work period decrement of $\geq 10\%$ in FEV_1. Ammonia concentrations of ≥ 7.5 ppm were predictive of a $\geq 3\%$ work period decrement in FEV_1. These predictive concentrations were similar to a previous dose–response study, which suggested 2.5 mg/m^3 of total dust and 7 ppm of NH_3 were associated with significant work period decrements. Therefore, dust ≥ 2.8 mg/m^3 and ammonia ≥ 7.5 ppm should be considered reasonable evidence for guidelines regarding hazardous exposure concentrations in this work environment.

Key words: swine confinement workers, pulmonary function, occupational hazards, ammonia, total dust exposures

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INTRODUCTION

Respiratory health hazards for persons working in enclosed swine production facilities were first recognized in 1974 [Donham et al., 1977]. Since that time, numerous epidemiological studies have been conducted in the United States, Canada, and Western Europe, documenting this occupational hazard [Donham et al., 1982, 1984a,b, 1989; Attwood, 1987; Cormier, 1991; Bongers, 1987; Haglind, 1987; Holness, 1987; Dosman, 1988; Zuskin, 1991; Wilhelmsson, 1989]. Several review articles have been published summarizing these epidemiological and environmental findings [Donham, 1990, 1992, 1993; Rylander, 1989].

Although there have been many studies documenting the widespread nature of the hazard, there have been only a few articles published regarding prevention. Therefore, in 1985, we initiated a 5-year prospective study to identify methods to prevent respiratory disorders among swine producers and workers. This study was a combined clinical and environmental epidemiological study, as well as an intervention study. The study methods and early epidemiological results are published elsewhere [Donham et al., 1990]. Intervention results are also published [Gjerde et al., 1991; Ferguson et al., 1989].

During the planning phase for the previously cited study, there was very little information available on the relationship between exposure dose and health effects of workers. This lack of information has created difficulties in establishing effective industrial hygiene controls, because a knowledge of dose–response relationships is essential to the understanding of safe concentrations and therefore, the design of control methods to meet these concentrations. The first attempt at studying exposure response in this environment was published in 1982 [Donham et al., 1982]. This research found associations between respiratory symptoms and length of time working in buildings. Symptoms were more prevalent in those who worked two or more hours per day, and six or more years in these buildings. A later study suggested 10 or more years of exposure as related to development of symptoms [Donham et al., 1989]. Studies in the Netherlands and Canada demonstrated relationships between dust and ammonia exposure and pulmonary function and symptoms [Attwood et al., 1987; Cormier, 1991]. A second Canadian study [Zejda et al., 1992] also revealed association between exposures, respiratory symptoms, and pulmonary function. Chronic bronchitis, FEV_1, and FVC decrements were associated with hours of work. A related study demonstrated associations of pulmonary function decrements to exposure to total dust, endotoxin, number of swine on the farm and years in swine production [Zhou et al., 1992].

These studies demonstrated the suspected relationships, but did not provide data to estimate maximum safe exposure concentrations. Some pork producer education publications have suggested the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLV) be used as guidelines; e.g., ammonia = 25 ppm, and dust 10 mg/m^3. These recommended levels are intuitively too high because they are recommendations for single exposure environments. In the livestock environment, many different hazardous substances may be synergistic or additive with respect to health effects. Additionally, the dust in this environment is a bioaerosol, containing several bioactive substances [Donham et al., 1985]. The ACGIH recommendations of 10 mg/m^3 assume a nuisance dust. Therefore, the appropriate recommended dust exposure limit logically would be less than the 10 mg/m^3 ACGIH recommendation.

A study conducted in 1985 [Donham et al., 1989] in the swine facility environments sought to define maximum safe exposure concentrations while taking into account multiple simultaneous exposures and bioactive aerosols. The study was conducted with 54 swine-producing farms. Concentrations of ammonia, endotoxin, and dust in relationship to respiratory symptoms and pulmonary function of workers were examined. Analyses were based on correlation and multiple regression analysis of exposures to pulmonary function and symptoms. Based on these results, recommended maximum exposure limits were developed. These recommendations included total dust at 2.4 mg/m^3, respirable dust at 0.23 mg/m^3, endotoxin (EC_5 standard) at 0.1 μg/m^3, and ammonia at 7 ppm. A companion study, conducted on the same farms, looked at relationships of environmental exposures relative to production parameters and health of the swine. Recommended maximum concentrations for swine health were defined as 3.4 mg/m^3 total dust, 11 ppm ammonia, and 0.1 μg/m^3 endotoxin [Donham et al., 1991].

The previous study (which involved 54 swine farms in Sweden) has been the only dose–response study to date in which exposure guidelines were recommended. This work needed to be repeated under different environmental and management conditions to expand the data base on this issue. Therefore, the present study was conducted as part of the larger intervention study previously described [Donham, 1990], in an attempt to further define dose–response relationships.

METHODS

Epidemiological and Environmental Study Design

Details of the study design are published in the previously cited publication [Donham et al., 1990]. However, the essentials of the study design most relevant to this dose-response study follow. One hundred-and-eight swine farmers (207 males $\geq$18 years) were selected in a stratified random sample from 2,000 swine farms in Eastern Iowa. A farm comparison group was also studied, in which subjects were matched for age ($\pm$5 years), sex, and smoking status. The comparison group was randomly selected from working farms (nonconfinement production) within a radius of five miles from the subject; assessments were made at the same time as those for the subjects. Standardized questionnaires were administered by trained interviewers to subjects and the comparison groups, assessing chronic symptoms [Ferris, 1978] and acute, or work-related, symptoms [Rylander et al., 1990b]. Pulmonary function testing was performed at the worksite before (baseline) and after a minimum work exposure of two hours (range 2–6 hours). The pulmonary function testing was performed on both subjects and the comparison groups according to procedures described previously [Donham et al., 1990]. Pulmonary function measurements were made on a computer driven rolling-seal spirometer (Spirotec model S-100) using ATS guidelines [Ferris, 1978]. The demographic description of the subjects, and results of health assessments are reported elsewhere [Donham et al., 1990].

Environmental assessment for gases (ammonia, carbon dioxide, hydrogen sulfide and carbon monoxide) was completed by both passive dosimeters (Sensidyne) and colorimetric pull tubes (Gas Tech). Total and respirable dust were assessed by both area and personal sampling. At least two representative areas of the building where the worker spent most of his or her time on the study were sampled. Total and respirable dust were determined gravimetrically by collection of samples on preweighed, cellulose acetate filters (Gelman) in 35-mm cassettes, using personal vacuum pumps (Gillian). Total dust was collected using a flow rate of 2 L/min, and respiratory dust was collected at a rate of 1.7 L/min using cyclone separators (MSA) to selectively collect particles smaller than 10 μm. Endotoxin content of both total and respirable dust was determined by the limulus amebocyte lysate assay, using the chromogenic assay (Whitaker Bioproducts QCL1000, with EC_5 standard). Environmental and medical data were collected in spring, autumn and winter with about equal numbers of subjects in all seasons.

Statistical Methods

Statistical analysis was performed using SAS software. Exposure–response relationships were examined for change over the workshift of the following pulmonary function parameters: FEV_1, FVC, FEV_1/FVC, FEF25, FEF50, FEF75, and FEF25–75. The effects of age, sex, and height were controlled by calculating the percentage of predicted pulmonary function using the normal population described by Crapo et al. [1981]. Descriptive statistics were used to estimate measures of central tendency and distribution for pulmonary function and environmental parameters. Arithmetic means were calculated for measures such as pulmonary function, age, and years of employment that could be described by a normal distribution. Geometric means were calculated for environmental measures, such as dust, endotoxins, and ammonia, that could best be described by a log-normal distribution. Differences between means were evaluated using *t*-tests and analysis of variance (ANOVA). Relationships between pulmonary function changes and environmental parameters were calculated using Pearson correlation coefficients. Dependent and independent variables, where statistically significant correlations were found, were selected for further study using various regression techniques. Stepwise multiple regression was used to develop models for prediction of pulmonary function changes from independent variables. Workshift change in each pulmonary function variable was treated individually as the dependent variable. Independent variables tested in the regression models included baseline pulmonary function data, age, years of employment in the industry, smoking, and personal sampling results for concentrations of total dust, respirable dust, total endotoxin, and ammonia. The predictive power of the regression models was assessed using the square of the multiple correlation coefficient (R^2). Assumptions of the models were evaluated using scattergram plots and univariate tests of normality. Selected polynomial models were used to estimate the concentration of environmental agents that could be associated with a specified workshift change in pulmonary function.

Exposure thresholds* were predicted using the results of the multiple linear regression models with the following parameters. We specified values for the dependent variables in the model in order to predict threshold levels of the independent variable of total dust and ammonia, as follows: (1) workshift decline in percentage predicted pulmonary function specified at either 0%, 3%, or 10%; (2) baseline pul-

*Threshold is used here to define a level of exposure related to a pulmonary function change that would generally be accepted as an indicator of an adverse physiological change.

monary function specified at 100% of predicted; and (3) smoking status specified as 1 for smokers and 0 for nonsmokers.

The concentrations of environmental contaminants associated with the specified pulmonary function changes were then predicted using the multiple linear regression model developed from the data set.

RESULTS

Although little previous work had been done on pulmonary function dose–response relationships in this environment, the reported studies have related to workshift changes rather than baseline pulmonary function [Donham et al., 1989; Attwood et al., 1987]. Assessment of cross-shift changes in lung function have also proved useful in other organic dust exposures. Preliminary assessment of data in this study indicated little relationship between baseline pulmonary function and environmental exposures. Therefore, the present efforts and all analyses reported here relate to the relationships between environmental parameters and pulmonary function changes over the workshift.

Correlation of pulmonary function with the area measurements of environmental parameters was weak, and in most cases not statistically significant. However, total dust levels were positively correlated with percentage decrease in FEV_1 ($r = 0.12$), FEV_1/FVC ($r = 0.13$), FEF25–75 ($r = 0.13$), FEF25 ($r = 0.20$), and FEF75 ($r = 0.11$).

Personal samples were more strongly correlated with pulmonary function, and therefore further analyses considered only personal samples as the independent variables. For all subjects combined, total dust, respirable dust, ammonia, respirable endotoxin, the age-total dust interaction and the years-total dust interaction were all positively correlated with a decrease in pulmonary function over the workshift. Age was negatively associated with pulmonary function decrements over the workshift.

Multiple linear regression models were fit using the stepwise procedure with personal sampling data for all subjects. In some cases, no significant independent variables could be identified. In general the regression models were weak ($R^2 \leq 0.08$), but statistically significant ($p \leq 0.05$). Independent variables that were retained in the models included respirable endotoxin, total dust, smoking, baseline pulmonary function, years of exposure, interaction between years of exposure, and dust. If respirable endotoxins were included in the model predicting FEV_1, no other environmental variables added significantly to the model. However, many (85) individuals were missing data for endotoxins. If endotoxins were removed from the consideration, to increase the total number of data points ($n = 201$), total dust and smoking were the predictive variables retained. All independent variables (total dust, respirable endotoxin, smoking) retained in the regression models were positively correlated with a decrease in pulmonary function over the workshift.

The exposure thresholds for total dust and respirable endotoxin estimated using the linear regression models were typically extremely low (e.g., 0.009 mg/m^3 for total dust at 0% change in FEV_1 for smokers) or extremely high (e.g., 440 mg/m^3 for 10% change). It is noteworthy the models predicted that smokers have much lower exposure thresholds compared to nonsmokers.

As review of scattergrams and univariate analysis of distributions indicated that assumptions of linearity for these multiple linear regression models were not valid,

TABLE I. Exposure Variable Means (Personal Samples) by Quartiles According to Years Worked in Swine Confinement Buildings

Factors	Years of work in swine confinement buildings 0–6	7–9	10–13	>14	All subjects
N	54	47	57	43	201
Variable					
Age	26.3	36.2	40.2	44.6	36.0
Mean years of employment in swine confinement buildings	3.3	7.7	11.4	17.0	9.6
Total dust[a] (mg/m^3)	3.90	5.00	5.64	5.37	4.53
Respirable dust[a] (mg/m^3)	0.19	0.19	0.23	0.28	0.23
Total endotoxin[a] (EU/m^3)	135.64	244.69	340.36	170.72	202.35
Respirable endotoxin[a] (EU/m^3)	18.51 (21)[b]	18.15 (31)	17.89 (40)	13.03 (24)	16.59 (117)
Ammonia[a] (ppm)	5.21	5.53	5.70	6.69	5.64

[a]Geometric mean.
[b]Data points (N) available for respirable endotoxins.

multiple regression models with polynomial terms were subsequently investigated. In addition, the data were evaluated within groups by years of exposure in order to evaluate the latency of respiratory effects based on duration of work in intensive swine buildings. Means, correlations, and multiple polynomial regressions were calculated for two groups, defined by the median (<9 years and >9 years) and for four groups defined by quartiles (0–6 years, 7–9 years, 10–13 years, ≥14 years).

Mean values for pulmonary function tests and environmental variables, overall and by quartile, are presented in Table I. The only statistically significant differences between groups included age and years of employment in the industry.

Table II presents Pearson correlation coefficients by quartile. Analysis by quartiles resulted in increased significance and strength of correlations between environmental parameters and pulmonary function changes. Generally, correlation coefficients for the 6–14 years-exposed groups were statistically significant compared to the other quartiles. Specifically, the correlations for FEF25 and FEF50 were strongest in the 7–9 years quartile. Age was predominantly negatively correlated with decreased baseline and with a workshift decrease in pulmonary function for all four quartiles. Total dust, respirable dust, age-total dust interaction, years-total dust interaction, and smoking were positively correlated with decrease in pulmonary function. The positive correlations between pulmonary function decline and ammonia and total endotoxin were less consistent than with the previously listed environmental parameters.

Use of multiple regression models with polynomial terms improved the fit (R^2) of the models (Table III). In these regressions, baseline pulmonary function was forced into the models because the capacity for change in pulmonary function in a similar previous study [Donham et al., 1989] was dependent on the baseline. When subjects were divided into groups based on years of employment, the fit (R^2) increased tremendously for the groups working longer than 6 years (R^2 = 0.05–0.66). The group with 0–6 years of experience had much lower R^2 values (0.00–0.20). In addition to baseline pulmonary function, independent variables that were retained in these models included total dust, total dust squared, total endotoxin, total endotoxin

TABLE II. Swine Confinement Workers' Change in Pulmonary Function Over a Work Period Relative to Environmental Exposures. Pearson Correlation Coefficients for Change in Pulmonary Function vs. Personal Samples by Quartiles, According to Years of Work in the Buildings

Percent change (decrease)in pulmonary function over workshift	Total dust	Respirable dust	Ammonia	Total endotoxin	Age	Years of work	Age–dust interaction	Years–dust interaction	Current smoker
All subjects									
FEV_1	$0.21^{\dagger}$	—	0.12*	—	—	—	0.15*	0.14**	—
FVC^b	0.13*	—	—	—	−0.16**	$-0.17^{\dagger}$	—	—	—
FEV_1/FVC	0.16**	0.16**	—	—	—	0.12*	$0.18^{\dagger}$	$0.21^{\dagger}$	—
FEF_{25-75}	0.15**	—	—	—	—	—	0.16**	0.15**	—
0–6 years[a]									
FEV	—	—	—	0.27*	—	—	—	0.25*	—
FVC	—	—	—	0.28**	—	—	—	—	—
FEV_1/FVC	—	—	−0.24*	—	—	—	—	—	—
FEF_{25-75}	—	—	—	—	—	—	—	0.24*	—
7–9 years									
FEV_1	—	0.30*	$0.52^{\dagger}$	0.27*	—	—	—	—	—
FVC	—	—	0.28*	—	−0.34**	—	—	—	—
FEV_1/FVC	0.30**	$0.43^{\dagger}$	$0.37^{\dagger}$	—	—	—	0.30**	0.32**	—
FEF_{25-75}	$0.38^{\dagger}$	$0.41^{\dagger}$	$0.44^{\dagger}$	$0.37^{\dagger}$	—	—	$0.42^{\dagger}$	$0.38^{\dagger}$	—
10–13 years									
FEV_1	0.29**	—	—	—	—	—	0.29**	0.26*	—
FVC	0.25*	—	—	—	—	—	0.33**	—	—
FEV_1/FVC	—	—	—	—	—	—	—	—	—
FEF_{25-75}	—	—	—	—	—	—	—	—	—
14 years and over									
FEV_1	—	—	—	—	$-0.43^{\dagger}$	$-0.30^{\dagger}$	—	—	$0.44^{\dagger}$
FVC	—	—	—	—	$-0.42^{\dagger}$	—	—	—	—
FEV_1/FVC	—	—	—	—	—	—	—	—	—
FEF_{25-75}	—	—	—	—	—	—	—	—	—

[a]Quartile by years of work in swine buildings.
[b]FVC for all subjects correlated with respirable endotoxin ($r=0.18$, $p<0.05$).
*Statistically significant at $p \leq 0.10$.
**Statistically significant at $p \leq 0.05$.
†Statistically significant at $p \leq 0.01$.

squared, ammonia, ammonia squared, respirable dust, age, age–dust interaction, smoking, and years of employment–dust interaction. Total dust, ammonia, and smoking were consistently associated with decreased pulmonary function over the workshift. Contrary to expectations, age and total endotoxin were consistently negatively associated with pulmonary function decrease.

Exposure thresholds were calculated using the multiple polynomial regression models for the quartile strategy since this approach yielded the highest multiple correlation coefficients. The method of calculation was as described above with the dependent variables specified at either 0%, 3%, or 10%. A regression model was developed for each quartile and each PFT variable. Total dust and ammonia were the most consistent variables where threshold values could be estimated. Tables IV and V present the results of threshold estimations for total dust and ammonia. Figures 1

TABLE III. Workshift Decrement in Pulmonary Function of Pork Producers: Summary of Regression Models for Prediction of Pulmonary Function (R^2)

Dependent variable	Model tested[a] 1[b] Multiple regression: all subjects	2 Polynomial terms: all subjects	3 Polynominal terms: 2 group <9 yr	>9 yr	4 Polynominal terms: 4 group 0–6 yr	7–9 yr	10–13 yr	14+ yr	5 Polynomial terms >6 yr
N	202	170	102	100	54	47	57	43	147
PCHFEV$_1$[c]	0.08**	0.12*	0.13*	0.24	0.08*	0.40*	0.32†	0.42*	0.18**
PCHFVC	0.08**	0.08**	0.30*	0.19	0.09**	0.30**	0.35†	0.23*	0.12*
PCHFEV$_1$/FVC	0.04†	0.06*	0.09†	0.04	0.01	0.19†	0.16**	0.05	0.10**
PCHFEF$_{25}$	—	0.14†	0.06*	0.32*	—	0.25†	0.07*	0.66†	0.21**
PCHFEF$_{50}$	—	0.11**	0.21*	0.07*	0.20†	0.27†	0.07*	0.27†	0.09*
PCHFEF$_{25-75}$	0.07**	0.10†	0.18**	0.15	0.02	0.40**	0.18†	0.20**	0.11**

[a]Independent variables that were retained in these models included total dust, respirable dust, total endotoxin, ammonia, baseline pulmonary function values, age, age–dust interaction, years–dust interaction, smoking and the squares of total dust, respirable dust, total endotoxin, and ammonia. Environmental variables were transformed by taking the natural logarithm before performing statistical analysis.
[b]Baseline PFTs included in model, but not forced as they were in all polynominal models.
[c]PCHPFT, percentage change (decrease) over the workshift in pulmonary function.
*Statistically significant at $p \leq 0.10$.
**Statistically significant at $p \leq 0.05$.
†Statistically significant at $p \leq 0.01$.

and 2 present examples of the regression plots for these models. Models for FEV$_1$ and FEF are presented since FEV$_1$ is exemplary for cross-shift changes and is usually less variable than flow rates. The exposure thresholds estimated for dust and ammonia using these polynomial terms appear to be much more reasonable (within the range of values detected in the environment and closer to current PELs/TLVs) than those estimated without the addition of polynomial terms.

It should be noted that regression models predictive of change in pulmonary function could not necessarily be computed for all quartiles or all PFT variables. For example, no statistically significant models were produced for FVC for the 14+ year quartile. Valid models which were developed also did not retain dust or ammonia as independent variables in all cases and therefore, no threshold could be calculated for certain PFT values, such as FEV$_1$/FVC. The other environmental variable retained in some regression models was endotoxin; however, thresholds for endotoxin could not be calculated because of mathematical limitations (e.g., a square root of a negative number).

Exposure threshold estimates for total dust when specifying cross-shift decrements at 0%, 3%, and 10% ranged respectively as follows: (1) 0.02 mg/m^3 (FEV$_1$, smokers with >6 years exposure) to 10.9 mg/m^3 (FEV$_1$, 10–13 years exposure); (2) 0.1 mg/m^3 (FEV$_1$, smokers) to 20.9 mg/m^3 (FEV$_1$, 10–13 years exposure); and (3) 1.3 mg/m^3 (FEV$_1$, smokers) to 2,860 mg/m^3 (FEF25–75, >6 years exposure). Less dust exposure was required for a response in smokers compared to nonsmokers for cross-shift changes in FEV$_1$.

Regression models for the group with 7–9 years of exposure were used to estimate thresholds for ammonia. Estimates for ammonia range from 2.9 ppm (for

TABLE IV. Exposure Threshold Estimations Calculated for Total Dust (mg/m^3) in Intensive Swine Buildings, Considering Years of Exposure

	Percentage change in FEV_1		
Years of exposure	0	−3	−10
	Total dust concentration (mg/m^3)		
FEV_1			
>6 smokers	0.02	0.1	1.3
>6 nonsmokers	0.04	0.1	2.8
0–6		Dust not included in model	
7–9		Dust not included in model	
10–13	10.9	20.9	93.7
14+		Dust not included in model	
FEF_{25}			
>6	6.4	13.6	79.1
FEF_{50}			
>6	1.7	2.5	6.6
FEF_{25-75}			
>6	2.3	19.6	2,860.3

FEF25–75) to 3.7 ppm (for FEV_1) for no cross-shift change in pulmonary functions relative to controls. When assigning a 3% decrease in PFT, the estimated exposure thresholds were 4.1 ppm (FEF25–75) and 7.5 (FEV_1). With a 10% assigned decrease in PFT, the estimated exposure thresholds were 9.2 ppm (FEF25–75) and 40.9 ppm (FEV_1).

DISCUSSION

Table III presents the results of the regression analyses to examine threshold levels. If one examines the data overall regarding exposure-response, there are some important characteristics to note. There was a much higher correlation of exposure with response after 6 years of exposure (Tables III–V). The cumulative effects of exposure over a 6-year period are significantly associated with these objective signs of PFT decline over a work period. This suggests that these acute responses are influenced by chronic exposure, an observation that has been noted in previous studies [Donham et al., 1982, 1989].

On the other hand, there was less positive correlation of pulmonary function (both change over work exposure and baseline) with length of exposure beyond 10 years. Also, age was negatively correlated with PFT change over exposure. This may be explained by the selection effects; i.e., the healthy or tolerant workers stay in the job, while the affected ones drop out.

A third characteristic of the data was that the predicted levels of exposure increased as lung function deficit was increased, which indicates a dose–response relationship. The levels of decrement chosen were based on epidemiologic relevant values of 0%, 3%, or 10% decrements.

An important criterion in considerations involved in estimating exposure threshold recommendations included consistency of relationship. For example, total dust was a variable that had a statistically significant relationship to most dependent variables examined. Ammonia, however, only appeared for three dependent vari-

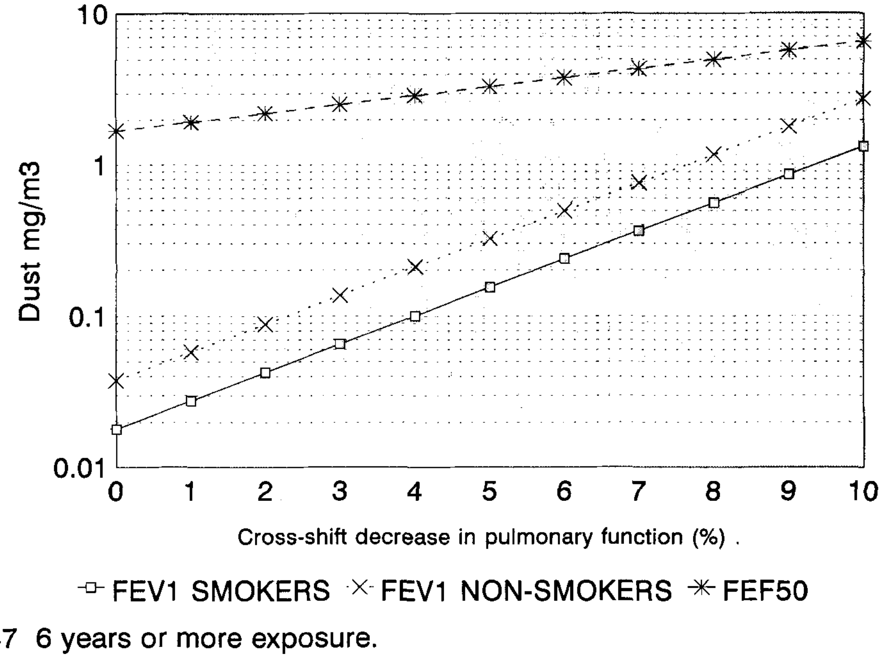

Fig. 1. Regression models used to estimate dust thresholds.

ables. Therefore, the weight of evidence for ammonia as an agent is not as strong as total dust. A second consideration in recommending estimated exposure thresholds was the plausibility of control of predicted concentrations. For example, some of the levels that were computed from the regression models are not attainable in this work environment without radical control measures, and thus were not considered. Also, concentrations consistent with previous studies were considered. These results were compared to the only previous study where specific maximum environmental concentrations were recommended [Donham et al., 1989]. Also, concentrations were considered relevant that were reasonably similar to threshold limit values published by the American Conference of Governmental Industrial Hygienists. Finally, FEV_1 was considered a more important dependent variable than others for calculating threshold concentrations, as it has often been relied on in other exposure response studies as a more reliable measure of acute exposure. Flow rates are known to be more variable than FEV_1 or FVC.

Based on the data presented here, and the previously cited data presented in the study [Donham et al., 1989], we think there is a reasonable basis for exposure guidelines for producers for total dust and ammonia. We suggest a maximum time-weighted concentration of total dust of between 1.3 and 2.8 mg/m^3, based on personal sampling. These concentrations are predictors for a 10% decrease in FEV_1 with two or more hours of exposure during a work period, and six total exposure years. The 1.3 mg/m^3 is for smoking workers, while the 2.8 mg/m^3 level is for nonsmoking workers. Since it is not ethical to eliminate consideration for smokers in the workplace, it is difficult to overlook this lower threshold level. However, achieving a 1.3-mg/m^3 dust

TABLE V. Exposure Threshold Calculations for Ammonia (ppm) in Intensive Swine Buildings, Considering Years of Exposure

	Percentage change in FEV_1		
Years of exposure	0	−3	−10
FEV_1			
0–6	Ammonia not included in model		
7–9	3.7	7.5	40.9
10–13	Ammonia not included in model		
14+	Concentrations could not be computed		
>6	Ammonia not in model		
FEF_{25-75}			
7–9	2.9	4.1	9.2

concentration within these buildings, particularly in the winter, would be extremely difficult and costly. Achieving concentrations of 2–3 mg/m^3 is technically and economically feasible. This latter fact, similar to smoking workers, raises an ethical consideration of how much should economics and current control technology be considered in recommending exposure limits? Another important factor for considering recommended threshold exposure concentrations is the agreement with previous studies. The only previous dose–response study recommended 2.4 mg/m^3 (area sampling) and 3.8 mg/m^3 (personal sampling) [Donham et al., 1989]. However, in the later study, all workers were entered in the regression equation, regardless of years of exposure, whereas in the present study, only the group with 6 years or more exposure were included. This would have the potential effect of lowering the exposure recommendation, relative to the current study.

It is more difficult to recommend maximum concentrations for exposure to ammonia. First of all, correlations of ammonia to pulmonary function were not as consistent as were the correlations of pulmonary functions to total dust. Considering all ages and smoking status, there was only one statistically significant, but weak, correlation, which was to FEV_1 ($R=0.12$; $p=0.10$). However, when looking at length of exposure, the 7–9 years exposed group had high correlations of ammonia exposure to both volume and flow decrements. Ammonia was included as a significant dependent variable in the step wise regression in three instances, i.e., FEV_1, FVC, and FEF25–75. The level of 7.5 ppm seen for a 3% decline in FEV_1 seems reasonable to set as a recommended threshold level. A reasonable and achievable concentration with current technology is 7 or 8 ppm. Furthermore, this is consistent with the previously cited recommended level for ammonia in this environment of 7 ppm [Donham et al., 1989].

As the dependent variable in this dose–response study is cross-shift change in pulmonary function, it is valid to question the relationship to long-term health efforts. A nested case-control study was conducted on this same population, where workers with pulmonary function changes or symptoms were brought into the hospital for extensive clinical studies. These "cases" were found to have hypercellularity of bronchoalveolar lavage fluids and evidence of air entrapment in the lungs [Schwartz et al., 1992]. Additionally, other studies have shown swine producers have lower thresholds to methacholine challenge relative to comparison groups [Rylander et al., 1990a]. Although no long-term prospective studies have been reported linking work-

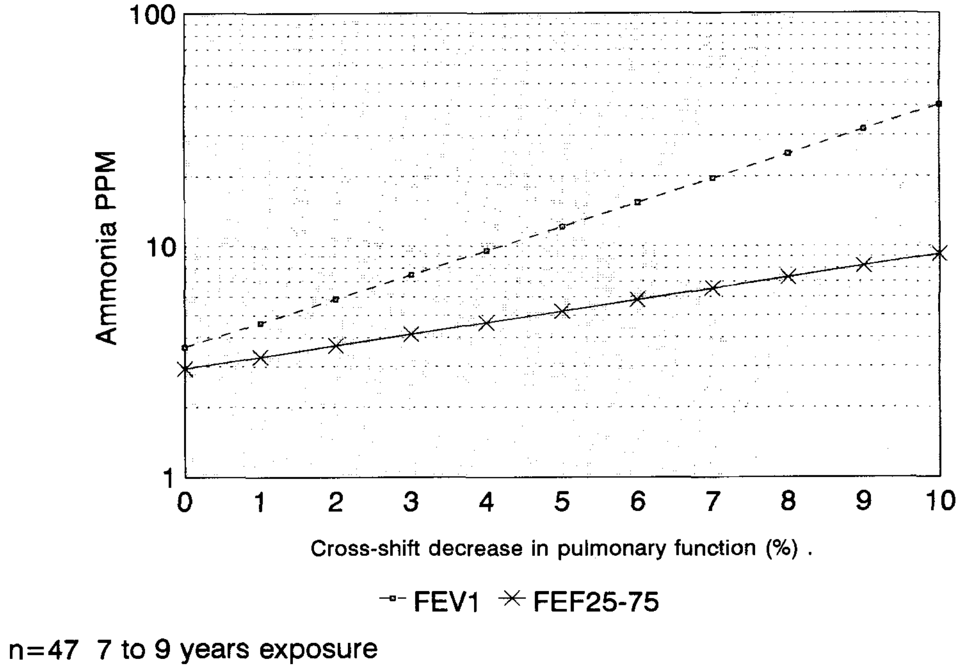

Fig. 2. Regression models used to estimate ammonia thresholds.

shift PFT decline and chronic illness, the available data suggest a relationship to hyperreactive airways and chronic obstructive disease.

CONCLUSIONS

These data have verified dust, ammonia, and respirable endotoxin exposures as related to work period pulmonary function decrements in swine confinement workers. Also, it is quite evident these relationships do not become manifest until exposed for more than 6 years. When using multiple repression models, only total dust and ammonia remain in the equation.

Threshold estimates for respirable endotoxin could not be calculated because the number of assessments were too few, leading to mathematical complication. Dose–response relationships for these exposures are relatively consistent. In attempting to compute maximum exposure concentrations for the substances, we found good agreement with a previous study. Based on these data (using FEV_1 as the dependent variable), we suggest reasonable guidelines for worker health should include total dust exposure be no greater than 2.8 mg/m^3 and ammonia no greater than 7.5 ppm. Certainly the data are not complete enough to set threshold limit values. However, these levels seem reasonable guidelines based on previous studies, are achievable, and make biological sense.

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