Predictors of longitudinal changes in pulmonary function among swine confinement workers

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OBJECTIVE: To determine predictors of longitudinal changes in pulmonary function in swine confinement workers.

DESIGN: Longitudinal study conducted from November 1989 to June 1991 and January 1994 to May 1995.

SETTING: Swine confinement workers in Saskatchewan.

PARTICIPANTS: Forty-two swine confinement workers who were studied in 1989/90 and studied again in 1994/95.

RESULTS: Of 98 male swine confinement workers (mean age ± SD 36.3±11.1 years) studied at baseline, 42 were studied again five years following. Complete information on baseline across-shift pulmonary function (preshift forced expiratory volume in 1 s [FEV₁], forced vital capacity [FVC], and every 2 h FEV₁ and FVC during the shift), and five-year follow-up pulmonary function (with FEV₁ and FVC) were available on all 42 subjects. Mean across-shift changes (preshift measurement to last measurement of the day) at baseline were –159.8±61.7 mL in FEV₁ and –35.3±65.6 mL in FVC. Mean annual rate change between baseline and follow-up for FEV₁ was –53.9±61.7 mL/year and for FVC –48.9±71.6 mL/year. After adjusting for age, height, smoking and hours spent in the barn, the baseline across-shift change in FEV₁ and FVC was a significant predictor of annual rate change in FEV₁ (P=0.01) and FVC (P=0.02), respectively. To determine the effects of indoor air quality on longitudinal lung function decline, indoor air environmental measurements were analysed. Complete information on respiratory health and indoor air quality was available on 34 of the 42 subjects. Assessment of indoor environment of swine barns included a summer and winter measurement for airborne dust, gases and endotoxin levels. After adjusting for age, height, smoking, ammonia and hours spent in the barn, the endotoxin level (Eu/mg) was a significant predictor of annual rate change for FEV₁ but not FVC.

CONCLUSIONS: These results suggest that shift change is an important predictor of longitudinal changes in lung function in swine confinement workers and that endotoxin exposures may mediate annual decline in FEV₁ in these workers.

Key Words: Across-shift change, Endotoxin, Indoor air quality, Longitudinal decline, Pulmonary function, Swine confinement workers
Prédicteurs des modifications longitudinales dans la fonction pulmonaire chez les personnes travaillant dans les porcheries

OBJECTIF : Déterminer les prédicteurs des modifications longitudinales dans la fonction pulmonaire chez les personnes travaillant dans les porcheries.

MODÈLE : Étude longitudinale menée en 1989/1990 et en 1994/1995.

CONTEXTE : Personnes travaillant dans les porcheries en Saskatchewan.

PARTICIPANTS : Quarante-deux sujets travaillant dans des porcheries, étudiés en 1989/1990, puis réétudiés en 1994/1995.

RÉSULTATS : Du groupe des 98 sujets, étudiés aux valeurs de référence, de sexe masculin (âge moyen ± ET 36,3 ± 11,1 ans) travaillant dans les porcheries, 42 ont été réétudiés cinq ans après. Des données complètes sur la fonction pulmonaire de référence tout au long de la journée de travail (volume expiratoire maximum/seconde [VEMS] avant la prise de service, la capacité vitale forcée [CVF], le VEMS et la CVF mesurés toutes les deux heures pendant le travail), et un suivi de la fonction pulmonaire sur une période de cinq ans (avec les mesures du VEMS et de la CVF) étaient disponibles pour l’ensemble des 42 sujets. Les modifications moyennes à travers la journée de travail (mesure avant la prise de service jusqu’à la dernière mesure de la journée) aux valeurs de référence étaient de 159,8±61,7 mL dans le VEMS et de 35,3±65,6 mL dans la CVF. Le taux moyen annuel de changement entre les valeurs de référence et le suivi était pour ce qui est du VEMS de 53,9±61,7 mL/année et pour la CVF de 48,9±71,6 mL/année. Après correction pour l’âge, la taille, les habitudes tabagiques et les heures passées dans la porcherie, le changement des valeurs de référence du VEMS et de la CVF était à travers les périodes de la journée un prédicteur significatif du taux de changement annuel du VEMS (P=0,01) et de la CVF (P=0,02). Pour déterminer les effets de la qualité de l’air intérieur sur l’abaissement longitudinal de la fonction pulmonaire, des mesures environnementales de la qualité de l’air intérieur ont été analysées. Des données complètes sur la santé respiratoire et la qualité de l’air intérieur étaient disponibles pour 34 sujets sur 42. L’analyse de l’environnement intérieur des porcheries comprenait des mesures, pratiquées en hiver et en été, de la concentration de poussières transportées dans l’air, des gaz et des endotoxines. Après correction pour l’âge, la taille, les habitudes tabagiques, l’ammoniaque et les heures passées dans la porcherie, la concentration d’endotoxines était un prédicteur significatif du taux de changement annuel du VEMS mais pas de la CVF.

CONCLUSIONS : Ces résultats laissent à penser que le changement de la fonction pulmonaire au cours de la journée est un prédicteur important des modifications longitudinales de la fonction pulmonaire chez les personnes travaillant dans les porcheries et que les expositions aux endotoxines pourraient médier la chute annuelle du VEMS observée chez ces travailleurs.

Swine confinement workers have an increased prevalence of respiratory symptoms and reduced pulmonary function test values compared with grain farmers and nonfarmers (1-5). An increase in airways responsiveness (6-8) and across-shift decrements in pulmonary function (9-11) have been reported in swine workers. Associations between longitudinal decline in lung function and air contaminants have been observed among swine confinement workers (12). In a recent longitudinal study, we found accelerated annual decline in forced expired volume in 1 s (FEV1) and forced vital capacity (FVC) among swine confinement workers versus nonswine farming subjects (13). There have been reports relating these airways responses to the indoor air environment of swine confinement units. The ambient air in these units includes varying levels of dusts, microbes, ammonia and endotoxins (14,15). A recent study reported a dose-response relationship between across-shift changes in lung function in swine farmers, and endotoxin and ammonia levels in the confinement units (16). Across-shift changes in FEV1 and levels of indoor airborne environmental contaminants have been significantly associated with longitudinal changes in FEV1 (17). We report the results of our investigations on the relationship between shift change and longitudinal decline in lung function measurements, and between environmental exposure to air contaminants and longitudinal decline in lung function measurements among swine confinement workers in Canada.
standardized questionnaire, was used to ascertain respiratory symptoms. The same questionnaire was used in 1994/95 (5,15) as was used in 1989/90 with the inclusion of questions regarding current employment in the swine industry and improvements or changes to ventilation management in the confinement facilities in the interval since the initial measurements.

Environmental measurements: In 1989/90, environmental measurements were carried out in a total of 50 swine confinement buildings, and were matched with respiratory health data obtained from subjects. In 1994/95, environmental measurements were carried out in 37 swine confinement buildings, with 42 subjects available for restudy. Of these 42, only 34 subjects were matched for complete environmental measurements for the 1994/95 period. The disparity in number of environmental measures available was the consequence of barn closures between the study periods, improvement of barn management status to that of a ‘high health’ barn with limited access and refusal to allow follow-up measurements of the barn environment.

Environmental measurements were carried out according to methods as previously described (15). Measurements were carried out simultaneously with pulmonary function measurements in 1989/90, and most subjects had pulmonary function measurements obtained on the same day as environmental measurements in 1994/95. In each barn, environmental measurements were obtained in all work sites (rooms) representing the four typical production stages: farrowing, weaning, growing and finishing. No environmental measurements were obtained that were below the level of detection. The most significant change in environmental assessment from the across-shift study in 1989/90 to the follow-up study in 1994/95 was the addition of personal samplers for respirable dust measurements. In the follow-up study, subjects were fitted with a personal sampler before entering the barn in the morning. A York Respirable Dust Sampler, model IU 3799 (Ametek, Florida), containing a preweighed 37 mm type A/E glass fibre filter (VWR, Alberta) was hung from the shirt collar of the workers, and connected with tubing to a Gilian Gil-Air Personal Sampler (Gilian Instruments Corporation, New Jersey), which hung on a washable belt at the waist. The air pump was set to run at a rate of 1.7 L/min. The subject wore the personal sampler for the entire time spent working in the barn. On completion of the barn work, the subject was asked to estimate the time spent at each of the four production stages and the time spent on each activity. The most common activities were feeding, cleaning, breeding and pig treatments such as injections and processing of piglets. Dust sample collection for respirable and total dust occurred over an 8 h period.

For both across-shift and follow-up, arithmetic means were calculated to estimate average exposure in the barn. To estimate the average annual exposure, the arithmetic mean for the number of zones in the barn was calculated, and then the arithmetic mean of the means for summer and winter measurements was calculated. Because there was no significant association with 1989/90 environmental measurements, the environmental measurements obtained in 1994/95 were used in the statistical analysis.

Endotoxin analysis: Respirable dust samples measured from each of the barns were sent to the National Institute for Occupational Safety and Health (NIOSH), Morgantown, West Virginia in 50 mL centrifuge tubes for endotoxin analysis. Kinetic-QCL plate reader with Kinetic-QCL software (BioWhittaker, Maryland) was used for analysis. Filters with the collected dust were extracted individually in 10 mL of sterile, nonpyrogenic water (LAL Reagent water, BioWhittaker) in the original 50 mL centrifuge tube by rocking at room temperature for 60 minutes (Labquake shaker, Labinator). Endotoxin analysis was performed using the chromogenic modification of the Limulus amebocyte lysate (Kinetic-QCL, BioWhittaker) in the original 50 mL centrifuge tube by rocking at room temperature for 60 minutes (Labquake shaker, Labinator). The extracts were then centrifuged at 1000 rpm for 10 mins, and dilutions of the supernatant fluids were analyzed in duplicate for endotoxins by the kinetic chromogenic modification of the Limulus amebocyte lysate assay (Kinetic-QCL, BioWhittaker). If the supernatant fluids could not be analyzed immediately, they were frozen at −80°C. The procedure described in the commercial endotoxin kit (LAL Testing Made Easy, BioWhittaker) was followed, and inhibition or enhancement assays were used as required. Results are reported in endotoxin units (EU) per milligram or cubic meter of air.

Lung function measurements: Lung function measurements were performed using an SMI spirometrics volume displacement spirometer (Sensormedics Inc, California) for

| Variable                  | Retested n=42 (mean ± SD) | Unavailable for follow-up n=32 (mean ± SD) | P   |
|---------------------------|---------------------------|-------------------------------------------|-----|
| Age (years)               | 37.5±10.8                 | 33.3±12.3                                 | 0.13|
| Height (cm)               | 180.6±5.6                 | 176.4±7.2                                 | 0.009|
| Weight (kg)               | 84.8±12.7                 | 83.8±15.0                                 | 0.76|
| Work (frequency)          |                           |                                          |     |
| 2 hours/day               | 2                         | 4                                         | 0.80|
| 2 to 4 hours/days         | 13                        | 8                                         |     |
| 4 to 6 hours/days         | 13                        | 8                                         |     |
| 6 to 8 hours/days         | 10                        | 6                                         |     |
| More than 8 hours/day     | 4                         | 3                                         |     |
| Smocking status           |                           |                                          |     |
| Nonsmoker                 | 27 (64.3%)                | 19 (59.4%)                                | 0.83|
| Current smoker            | 7 (16.7%)                 | 5 (15.6%)                                 | −    |
| Exsmoker                  | 8 (19.0%)                 | 8 (25.0%)                                 | −    |
| Pulmonary function at baseline |                  |                                          |     |
| FEV1 (L)                  | 4.4±0.7                   | 4.3±0.7                                   | 0.47|
| PVC (L)                   | 5.6±0.9                   | 5.3±0.8                                   | 0.13|
| Shift change in FEV1 (%)  | −3.8±5.1                  | −3.1±7.6                                  | 0.63|
| Shift change in PVC (%)   | −0.6±1.2                  | −0.5±1.6                                  | 0.69|

FEV1, Forced expiratory volume in 1 s; PVC Forced vital capacity
both baseline across-shift and follow-up evaluations (5,11,15). Techniques followed the standards set by the American Thoracic Society (18). During the 1989/90 period, lung function was measured on-site in the barn before entering the work environment, every 2 h during the work shift, and at the end of the work shift. The difference between the first measurement of the day and the last measurement of the day was considered the across-shift change.

During the follow-up in 1994/95, lung function measurement was conducted at a time during the work day at the subject’s home or at a clinic location near the swine confinement facility. Lung function indexes measured during both shift change and follow-up were FEV₁, FVC, FEV₁/FVC×100, and maximal midexpiratory flow rate (FEF₂₅-₇₅). Predicted values were obtained using the regression equation of Crapo et al (19).

Smoking habits: Based on smoking habits reported in 1989/90 and at follow-up in 1994/95, subjects were allocated into the categories of ‘nonsmoker’, ‘current smoker’ and ‘exsmoker’. Subjects were assigned a nonsmoker status if they denied smoking at both time points. Subjects who reported smoking in 1994/95 were assigned to the current smoker category. Those who reported smoking in 1989/90...
and denied smoking in 1994/95, those who were exsmokers at both times and those who were exsmokers only in 1994/95 were assigned to the exsmoker category.

Statistical analysis: Across-shift change in pulmonary function was calculated by taking the difference between preshift measurement and the last measurement measured on the same day. There was at least a 2 h difference between the two readings. In addition to the absolute difference, the shift change was also expressed as the percentage change from the preshift measurement. Annual rate change in pulmonary function was obtained by dividing the difference in the 1989/90 and 1994/95 pulmonary function values by the time between the two values. Means and standard deviations were calculated for continuous variables. Categorical variables were described by frequencies and percentages. Pearson correlation coefficients were used to quantify the association between the annual rate change and the shift change in pulmonary function measurements. Multiple regression analyses were used to examine the relationship between the annual rate change and across-shift change in pulmonary function measurements after adjusting for confounding variables.

RESULTS

Mean values for lung function test variables at baseline and follow-up evaluations are shown in Table 2. The absolute mean across-shift reductions (± SD) in FEV₁ and FVC were –159.8±204.2 mL and –35.3±65.6 mL, respectively. When expressed as the percentage change of baseline evaluations, the changes were –3.8±5.1% and –0.6±1.2% for FEV₁ and FVC, respectively. Over the study period, mean annual rate changes in FEV₁ and FVC were –53.9±61.7 mL/year and –48.9±71.6 mL/year, respectively. Environmental measurements for both study periods in the participating confinement facilities are shown in Table 3.

Relationships between the percentage shift change and annual rate change are shown for FEV₁ in Figure 1 and for FVC in Figure 2. Correlation coefficients between the percentage shift change and annual rate change for FEV₁ and FVC were 0.34 (P=0.03) and 0.38 (P=0.01), respectively.

The results of multiple regression analysis of independent variables and annual rate change in FEV₁ and FVC are outlined in Table 4. These analyses show that significant determinants of annual rate change in FEV₁ are age, exsmoking status and percentage shift change in FEV₁ on baseline evaluation. The major determinant of annual rate change in FVC is percentage shift in FVC (P=0.02). Exsmoking status (P<0.11) and work hours per day (P<0.06) are marginally significant for the annual rate change in FVC.

Relationships between the environmental variables and annual rate change in FEV₁ and FVC are shown in Table 5. In this model, age, exsmoking status, across-shift change and endotoxin concentration were significant predictors of FEV₁. Across-shift change and to a lesser extent, exsmoking status were predictors of annual rate change in FVC. Endo-
toxin units per cubic metre was not a significant determinant for FVC or FEV₁. After log-transforming endotoxin levels, the determinants retained significance, and Eu/m³ was significant for annual rate change in FVC (P=0.05). The correlation between environmental results and study periods showed a significance between endotoxin units per milligram (P=0.05) for summer 1989/90 and winter 1994/95, and for respirable dust concentration (P=0.01) between winter 1989/90 and summer 1989/90.

**DISCUSSION**

These data confirm and extend the previous results of Schwartz et al (12), Reynolds et al (17) and Senthilselvan et al (13) regarding the longitudinal decline in lung function test variables in exposed workers in swine confinement facilities. Schwartz et al (12) demonstrated a relationship between longitudinal decline in lung function test variables and environmental contaminants. Reynolds et al (17) demonstrated a dose-response relationship between longitudinal decline and environmental exposures. Senthilselvan et al (13) demonstrated that the workers in swine confinement facilities suffered an excess yearly decline in FEV₁ and FVC of 26.1 and 33.5 mL/year, respectively, over men who lived in rural areas but did not experience farming or other potentially detrimental occupational or environmental contaminant inhalation exposures. Thus, it seems relatively well established that swine confinement workers suffer yearly reductions in lung function test variables that are in excess of those observed in non-exposed, nonfarming control subjects. Both previous smoking status (ex-smoking) and concentrations of ambient air contaminants are potential determinants in annual decline in both FEV₁ and FVC, while age is an important predictor of annual loss in FEV₁; shift change at baseline evaluation is the predictor of the annual rate change in both FEV₁ and FVC that emerges as the most powerful in both models.

These findings raise the possibility that, if shift change at one point in time could be used to predict longitudinal decline in excess of that seen in nonexposed control subjects (13), then shift change could be used to predict which workers might be prone to development of future losses in lung function and possibly airflow limitation (20). If this is the case, other tests, such as tests of airways responsiveness that have been shown sensitive in swine producers (6), might be used to evaluate and possibly follow individual workers at risk.

It has recently been demonstrated that shift change observations in FEV₁ and FVC are reasonably reproducible in naive subjects exposed to a swine barn environment (21) and that shift change measurements in exposed subjects may be used to evaluate the effectiveness of environmental control measures in the swine confinement facilities (11). Therefore, the test of shift change in FEV₁ may be a useful tool in assessing the effectiveness of environmental control measures in these facilities. That such might be the case is supported by the recent work of Senthilselvan et al (11) that demonstrated directionally similar reductions in shift changes in the lung function indexes FEV₁ and FVC, cellular response of nasal mucosa as measured by nasal lavage, inflammatory response as measured by cytokines, and evidence for bone marrow response as measured by peripheral white blood cell counts, following the initiation of environmental control measures.

What are the pitfalls? Although the evidence for shift changes predicting longitudinal decline in exposed swine confinement workers is reasonable, it is not certain whether the same substances in the complex environmental exposure inside swine confinement buildings are responsible for both the acute process (as observed by shift changes) and chronic change (as observed by annual decline), although endotoxins appear important. Second, the methodology of obtaining the follow-up evaluations in 1994/95 was different than that of 1989/90, in that the first observations were obtained on-site in the swine facilities, while the follow-up observations were obtained in a nearby town or village, which required a period of absence from exposure (estimated at between 1 and 2 h). However, this circumstance would likely mitigate toward an underestimation of the annual rate change because the FEV₁ and FVC measurements conducted on the first occasion on-site might be more likely to include acute changes as a result of exposure at the time.

Third, there was only minimal correlation between the 1989/90 and the 1994/95 environmental measurements. This minimal correlation could be due to changes in management practices over the study period that may cause variability in environmental conditions. Changes to manure handling procedures, feed types, cleaning methods and ventilation systems can affect the levels of contamination. Because no relationship was seen with the 1989/90 environmental data, further investigation of the association between environmental and changes in lung function is required to elucidate the role of changes in facility management.

Taken together, our interpretation of the evidence is that shift-change measurements in FEV₁ and FVC are reasonable predictors of longitudinal decline in exposed swine workers and can be conducted with sufficient reproducibility to assess the effectiveness of environmental control or personal protection in these facilities.

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