Positive Human Health Effects of Wearing a Respirator in a Swine Barn(*).

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Issue: Sept, 2000

Study objectives: A study was conducted to evaluate the acute health effects of wearing an N-95 disposable respirator in a swine confinement facility.

Design: A crossover trial design was used in the study.

Setting: The study was carried out at the research facilities of the Centre for Agricultural Medicine, the Royal University Hospital, and the Prairie Swine Centre Inc, Saskatoon, Saskatchewan, Canada.

Participants: Twenty-one nonsmoking healthy male subjects with no previous swine barn exposure participated in the study.

Interventions: The subjects participated in a laboratory session (baseline day), a 4-h exposure in a traditional swine room wearing the respirator (intervention day), and a 4-hour exposure in a traditional swine room without a respirator (nonintervention day).

Measurements: Lung function, methacholine challenge tests, blood counts, nasal lavage, and cytokines in serum and nasal lavage fluid.

Results: Mean ([+ or -] SE) shift change in [FEV.sub.1], from preexposure to postexposure, was highest on nonintervention day (-8.1 [+ or -] 1.01%) and was significantly different from intervention day (0.32 [+ or -] 0.62%; p [is less than] 0.0001) and baseline day (1.57 [+ or -] 0.51%; p [is less than] 0.0001). Similar patterns were observed in the mean values of the provocative concentration of a substance (methacholine) causing a 20% fall in [FEV.sub.1] (nonintervention day, 130.4 [+ or -] 36.9 mg/mL; intervention day, 242.0 [+ or -] 38.0 mg/mL; and baseline day, 328.0 mg/mL [+ or -] 34.1 mg/mL). Significant increases in serum neutrophil levels and nasal cell counts were observed on the nonintervention day in comparison to the baseline and intervention days. Significant increases also were found in the levels of cytokines interleukin (IL)-6 and IL-8 in nasal lavage fluid and in the levels of IL-6 in serum for the nonintervention day in comparison to the other 2 days.

Conclusions: The results demonstrate that an N-95 disposable respirator can help to significantly reduce acute negative health effects in subjects not previously exposed to a swine barn environment. (CHEST 2000; 118:852-860)

Key words: blood counts; bronchial responsiveness; cytokines; intervention; lung function; naive subjects; nasal lavage; respirator; swine confinement

Abbreviations: EU = endotoxin units; IL = interleukin; [PC.sub.20] = provocative concentration of a substance (methacholine) causing a 20% fall in [FEV.sub.1] rpm = rotations per minute; WPF = work protection factor

Epidemiologic studies have shown that swine confinement workers are at increased risk of developing respiratory symptoms, reductions in expired flow rates, and increases in airways responsiveness.[1-7] Acute changes in lung function have been reported among swine confinement workers and healthy workers after a 4- to 8-h work shift.[8-10] In a longitudinal study, swine confinement workers had greater annual loss in lung function in comparison to nonfarming control subjects.[11] In a related study, the baseline shift change in [FEV.sub.1] was a significant predictor of the annual loss in [FEV.sub.1] in swine confinement workers.[12] In a longitudinal study of a selected number of swine confinement workers, there was an apparent trend toward the development of asthma.[13]

High levels of dusts and gases can be found in the indoor environment of swine confinement buildings.[14-16] Several cross-sectional studies have shown that dust and gases in the indoor environment are related to the respiratory health of the swine confinement workers.[17-19] Recent cross-sectional and longitudinal studies have shown that endotoxin is related to respiratory symptoms, lower lung function levels, and lung function decline in swine confinement workers.[20-21]

A crossover trial[22] was conducted to examine the human health effects of sprinkling canola oil in a swine barn to control dust. In this trial, 20 naive healthy subjects were exposed to a traditional swine confinement room and a room sprinkled with canola oil. The oil treatment significantly reduced dust levels and resulted in lower mean shift changes in pulmonary function, lower WBC counts, lower total cells in nasal lavage fluid, and increased mean provocative concentrations of a substance (methacholine) causing a 20% fall in [FEV.sub.1] ([PC.sub.20]).[22]

In a 1993 study,[23] only 30% of swine confinement workers reported the use of dust masks when working inside a barn. Attitudes toward wearing masks improved in an intervention study designed to examine the effects of improving knowledge, attitudes, and behaviors related to respiratory health in swine workers.[24] In an industrial hygiene experiment, the degree of dust protection offered by respiratory masks was assessed. Masks were mounted on glass funnels and dust was sampled with filters that were kept inside the funnel. Respiratory protection limited total dust exposures to [is less than] 25% of the nonmasked values with two-tie masks and to [is less than] 50% with one-tie masks. The number of respirable particles was reduced to [is less than] 58% by using two-tie masks.[25]

In this article, we report the results of a crossover trial conducted to examine the human health effects of wearing an N-95 disposable respirator in a swine barn. In addition to the technician-administered questionnaire, pulmonary function tests, nasal lavage, methacholine challenge tests, and blood sampling were conducted on 21 male, nonsmoking volunteers who were naive to the swine barn environment.

MATERIALS AND METHODS

The study was carried out over 12 days in March 1998, at the research facilities of the Centre for Agricultural Medicine, the Royal University Hospital, and the Prairie Swine Centre Inc, in Saskatoon, Saskatchewan, Canada. The University of Saskatchewan Advisory Committee on Ethics in Human Experimentation approved the study protocol and the consent form.

Recruitment

Through postings, lifetime nonsmoking male subjects, aged 18 to 35 years, were recruited for the study. Female subjects were not included in the study as a larger sample size would have then been required to control for sex in statistical analysis and to have adequate statistical power to detect differences in the outcomes between the 2 exposure days.

Prescreening

The prescreening included signing an informed consent form, a questionnaire to assess previous hog barn exposure, medical, smoking and allergy histories, as well as skin prick tests were performed for aeroallergens including the following: animals (cat, dog, cattle, horse, feathers, and hog dander); trees (box elder, birch, polar, willow, and mixed allergens); ragweed, mixed grasses, and mixed weeds; foods (eggs, milk, peanuts, and shell fish); dusts (house, grain, and wheat); house dust mites; molds (Aspergillus, Alternaria, Cladosporium, and Helmiathosporium species); and histamine. A positive result of a skin test was indicated by a wheal that was [is greater than or equal to] 3 mm. From this prescreening, 22 lifetime nonsmoking male subjects who were 18 to 35 years old were selected for the study.

Exclusions

Subjects with previous swine barn exposure, a history of smoking, a history of asthma, an adverse medical history, or a positive result of a skin prick test to any of the substances except histamine were excluded from the study.

Training Day

The 22 subjects selected for the study from the prescreening attended a training day prior to baseline assessment. A questionnaire that retrieved information on previous occupational exposures, respiratory symptoms, past illnesses including allergy, asthma, and other respiratory conditions, and an informed consent form were completed at that time. In an attempt to decrease the "learning effect" of performing repetitive pulmonary function tests,[26] nasal lavage, and mask donning, subjects practiced these procedures during the training session. Subjects also were educated on the appropriate protocol for barn entry procedures at the Prairie Swine Centre Inc.

Baseline Day

Baseline assessments were conducted at the Centre for Agricultural Medicine and the Royal University Hospital. Subjects arrived at 7:00 AM for pulmonary function tests and returned at 11:00 AM for repeat pulmonary function tests, nasal lavage, and blood samples. Subjects returned to the Royal University Hospital at 4:00 PM for methacholine challenge tests. After baseline assessment, one subject was excluded from the study, because the methacholine [PC.sub.20] was 32 mg/mL, whereas other subjects went up to the maximum methacholine concentration of 256 mg/mL. Twenty-one subjects participated in the remainder of the study. The minimum duration between training day, baseline day, and each of the exposure days was at least 7 days.

Crossover Design

Four subjects were assigned to the animal room each day. A randomization list was prepared for designating the subjects to intervention or nonintervention. Two subjects were randomly chosen to wear a respirator (intervention), whereas the other two subjects did not wear a respirator (nonintervention). After a minimum of at least 7 days, the subjects who wore respirators were assigned to the same animal room without a respirator. Similarly, the two subjects who did not wear a respirator were instructed to wear a respirator and were assigned to the same animal room. The days on which the subjects wore respirators hereafter will be referred to as intervention days, and the days on which the subjects did not wear respirators will be referred to as nonintervention days.

Exposure Day 1

Subjects arrived at the swine barn at 7:00 AM for pulmonary function measurements. Personal air samplers were attached to each subject, and subjects wearing respiratory protection had a quantitative fit test of the respirator prior to entering the barn. Subjects left the exposure room after 2 h for a 15-min period to perform pulmonary function tests and for those subjects wearing a respirator to have a fit test on a new respirator. These measurements were conducted in a room adjacent to the exposure room. To simulate the usual workload in a swine barn, subjects rode a stationary bike for 3 km at 18-km/h for each hour they spent in the barn. When subjects were not riding the bike, they were allowed to read quietly without disturbing the pigs. Subjects recorded severity of cough, nasal congestion, eye irritation, shortness of breath, chills, phlegm, headache, and chest tightness every hour (7 AM to 10 PM) using a Likert scale ranging from 0 to 5 (0, no symptoms; 5, severe symptoms). At the end of exposure (11:30 AM), pulmonary function was measured, nasal lavage performed, and blood was drawn. Subjects returned to the Royal University Hospital at 4:00 PM for methacholine challenge tests.

Exposure Day 2

After a minimum interval of at least 7 days after exposure day 1, subjects who wore respiratory protection on the first exposure day were assigned to the same animal room without respiratory protection on exposure day 2. Similarly, the subjects who did not wear respiratory protection on exposure day 1 wore respiratory protection on exposure day 2. Identical methods were used on exposure day 1 and exposure day 2.

Animal Facilities and Management

The exposure study was conducted in a swine grower/finisher room at the Prairie Swine Centre Inc. The room measured 14.3 x 11.0 x 3.0 m. The pen floor was partially slatted (30% of the pen area). A 0.6-m deep manure collection channel was located beneath the slatted portion of the floor. Interior walls had plywood sheathing on both sides of a stud wall frame. A bank of propeller fans (total air delivery capacity, 6,500 L/s at 20 Pa) exhausted air from one wall of the room. Unit block air inlets were located in the ceiling. Fresh air entered the attic through screened soffit openings. Heat was supplied by an unvented natural gas unit heater. An electronic controller regulated the sequencing and speed of exhaust fans, the opening area of supply inlet modules, and the operation of the heaters using a proportional control algorithm.

A total of 132 pigs was housed in the room. The average mass of the animals was 95 kg (SD, 12 kg) at the completion of the experiment. Pellet feed was filled daily to a single-space dry feeder in each of 12 pens. The management of the room and the production methods conformed to those commonly used in the swine industry in Saskatchewan. Over the course of the 2.5-week experiment, the alleyway floor of the room was not swept or cleaned.

Respiratory Protection and Fit Test

The National Institute for Occupational Safety and Health-approved N-95 disposable particulate respirators with two straps and metal nose clips (model 8210; 3M Canada Inc; London, ON, Canada) were utilized. Subjects were clean shaven for experiment days in the barn. A quantitative fit test was performed prior to subjects entering the barn and after 2 h in the barn environment. A new respirator was donned for each testing. The quantitative fit test was performed using a Porta-Count Plus (TSI Inc; St. Paul, MN), an N-95 Companion (TSI Inc), and a particle generator (TSI Inc) to assess particle levels inside and outside the respirator. A sampling probe (TSI Inc) was inserted in the respirator breathing zone prior to the subjects donning the respirator. During the quantitative fit test, subjects performed six exercises (normal breathing, deep breathing, head side to side, head up and down, talking out loud, and normal breathing) for 90 s each. A fit factor was calculated from all exercises and is an expression of the ratio of the mean concentration of ambient particles outside the respirators to the concentration of particles inside the respirator. A fit factor of [is greater than] 100 was required to assume that the respirator was well fit. After completing the fit test, a plastic Luer lock cap was applied to the open end of the probe on the subject's respirator to prevent any air leakage, and subjects then entered the barn environment. Respirators were not removed while in the barn environment.

Lung Function

A volume displacement spirometer (SensorMedics; Anaheim, CA) was used for pulmonary function measurements. Measurements were performed according to American Thoracic Society standards.[27] Each subject performed the pulmonary function tests in the sitting position. The variables, FVC, [FEV.sub.1], [FEV.sub.1]/FVC ratio, and maximal mid-expiratory flow rate were measured. The percentage changes in pulmonary function from the first measurement to the last measurement from each day were determined and were referred to as the shift change in pulmonary function for that day.

Methacholine Challenge Tests

Methacholine challenge studies were performed with the inhalation of a diluent followed by the inhalation of increasing doses of methacholine, starting at 1 mg/mL, with each increment representing a doubling of the dose to a maximum final concentration of 256 mg/mL.[28] Bronchial challenges were performed with a nebulizer (Bennett Twin Jet; Puritan Bennett Corp; Carlsbad, CA) at a driving pressure of 50 lb per square inch, which produced an output of 0.13 mg/mL. The subjects in sitting position inhaled the nebulized solution through a mask held close, but not tightly applied, to the face and breathed the mist quietly at tidal volume for 2 min. The [FEV.sub.1] was measured at 30 and 90 s after the 2-min inhalation of methacholine, with doses of methacholine administered at 5-min intervals. A clinical

pulmonary function spirometer (MCG; Medigraphics Corp; St. Paul, MN) was used to measure [FEV.sub.1] The [PC.sub.20] was interpolated from the log concentration-response curve or was extrapolated from the last two responses to 256 mg/mL. [PC.sub.20] was used as an indicator of airway responsiveness.

Nasal Lavage Procedure and Analysis

The nasal lavage procedure was adapted from Naclerio et al[29] The subjects extended their necks approximately 30 [degrees] from the horizontal while in sitting position. Five milliliters of room temperature normal saline solution (0.9%) was instilled into each nostril. Subjects did not breathe or swallow while obstructing the oropharynx with their tongue, and, after a minimum of 10 s and a maximum of 2 min, subjects flexed their necks forward, allowing the mixture of mucus and saline solution to be passively expelled into a sterile specimen container, which was stored on ice until analysis. For analysis, the total sample volume of the nasal lavage fluid was recorded. The sample then was centrifuged (RT600B Refrigerated Centrifuge; Sorvall; Newtown, CT) at 400 rotations per minute (rpm) for 10 min at 4 [degrees] C. The supernatant (2-mL aliquot) was removed and was stored in plastic tubes, which then were frozen at -70 [degrees] C for later cytokine analysis. The sediment was gently resuspended and washed once with phosphate-buffered saline solution, the supernatant was removed by vacuum suction, and the sediment was gently resuspended to a volume of 0.5 or 1 mL, depending on a visual estimation of cellularity. The cell count was performed on a Neubauer hemocytometer (Bright-Line; Americas Optical; Buffalo, NY). The cell count was calculated on the hemocytometer using the number of cells divided by the original fluid volume to give the number of cells per milliliter. A direct smear of the sediment was made for staining with Wright-Giemsa stain (Diff Quik; Jade Diagnostics; Aguada, Puerto Rico), and another direct smear of the sediment was made for esterase staining. A cytospin preparation (Cytospin 2; Shandon Southern Instruments; Sewickley, PA) of the sediment was performed at 500 rpm for 10 min at room temperature. The cytospin serves as a gentle centrifuge to concentrate cell-poor fluids for microscopic examination.[29]

WBC Methodology

The methodology for counting WBCs utilized the impotence principle with the use of a cell counter (Coulter Counter, model STKS; Coulter Electronics; Hialeah, FL). Analysis and classification of WBCs were based on the Coulter method of leukocyte differential counting using the following three measurements: individual cell volume, high frequency conductivity, and laser light scatter. The well-clotted blood sample was centrifuged at room temperature at a speed of 1,500 rpm for 10 min, which separated the serum from the cells. The serum then was divided into 1-mL aliquots and was placed into a polypropylene container. The sample was then frozen at -70 [degrees] C for later cytokine analysis.

Nasal and Serum Cytokines

Proinflammatory cytokines interleukin (IL)-6 and IL-8 were measured in cell-free nasal wash supernatant and in sera by commercially available immunoassay kits for IL-8 (Perseptive Diagnostics; Cambridge, MA) and (high-sensitivity) for IL-6 (R&D Systems; Minneapolis, MN). These cytokines were chosen to examine acute-phase

response and to confirm the previous finding that acute reactions to swine dust might be mediated by the cytokine IL-6.[22]

Environmental Dust Measurements

Dust mass was collected using personal aerosol samplers (Dupont Air Sampler; Canada Safety Supply; Saskatoon, SK, Canada) that were carried by the subjects. The samplers ran over the 4-h exposure period at a flow rate of 2.0 L/min with a preweighed, binder-free glass fiber filter (SKC; Edmonton, AB, Canada) inline. The cassette was attached at the shoulder near the subject's breathing zone. Filters were desiccated before and after sampling. Area samples for dust concentration were also collected (Aircon2; Gilian Instrument Corp; Caldwell, NJ). The sample was drawn through a 37-mm binder-free glass fiber filter (SKC). After weighing, filters were placed in 50-mL polypropylene centrifuge tubes and were stored at 4 [degrees] C until endotoxin analysis. Particle counts were performed using a laser particle counter (MetOne Inc; Grants Pass, OR), which was placed on a table that was 1.0 m above the floor and near the study subjects. The particle counter provided the following four particle-size (in optical diameter) ranges: 0.3 to 0.49 [micro]m (diminutive dust); 0.5 to 0.99 [micro]m; 1.0 to 4.99 gm (modified respirable dust); and [is greater than] 0.5 [micro]m (modified inhalable dust). Counts were taken four times per day and lasted 1 min per measurement. The mean of the four dust particle counts then were calculated.

Endotoxin Analysis

Endotoxin analysis was performed in laboratories of the Veterinary Infectious Disease Organization. The binder-free glass fiber filters with collected dust were extracted individually in the centrifuge tubes with 10 mL sterile nonpyrogenic water for injection USP (DIN 00624721; Astra Pharma Inc; Mississagua, ON, Canada) and were incubated for 1 h at room temperature in a sonicating water bath. The extracts were decanted, and serial twofold dilutions of the supernatant fluids were analyzed for Gram-negative bacterial endotoxin using an end-point assay (model QCL-1000; BioWhitaker; Walkersville, MD). The extracts were stored at 4 [degrees] C for [is less than] 24 h before being tested for endotoxin content. The endotoxin standard that was supplied with the assay (Escherichia coli O111:B4, lot No. 6 L2110; BioWhitaker) in duplicate at four concentrations from 0.1 to 1.0 endotoxin units (EU)/mL was assayed simultaneously to generate the standard curve. Linear regression determined the formula for the calculation of EU in the extracted dust samples from optical density readings that were within the range that resulted from the assay of the endotoxin standard. Hence, the lower detection limit is 0.1 EU/mL, which is equivalent to 1.0 EU per filter. The sampling time and flow rate were used to calculate the concentration of endotoxin in air (EU/[m.sup.3]).

Ammonia and Carbon Dioxide Measurements

Gas levels were measured during each exposure day. An air sample was collected continuously into a Tedlar bag (Cole-Parmer; Anjou, Quebec, Canada), and diffusion tubes were used to measure the daily mean ammonia (Matheson Gas Products; Edmonton, AB, Canada) and carbon dioxide (Matheson Gas Products) levels. Three tubes were used for each air sample, and a mean value was obtained from the three readings.

Temperature Measurements

Room temperature and relative humidity were measured and recorded four times per day using a wet-bulb psychrometer (Cole-Parmer). Outdoor temperature was monitored once per day at 10:30 AM using a probe connected to the barn's communications and ventilation control system (OMNI 4000; Phasou; Winnipeg, MB, Canada).

Statistical Methods

Paired t tests were used to test the significant differences in dust and endotoxin concentrations, and symptom scores were used to test differences between intervention and nonintervention days. Overall differences between the baseline day and two experimental days in pulmonary function measurements, methacholine challenge results, WBC counts and differential, nasal lavage and serum cytokine levels were tested using an F statistic based on Pillai test for multivariate repeated-measures analysis of variance.[30] If the Pillai tests indicated a significant overall difference, paired t tests then were used to test the differences between any 2 days.[31] Since the pair-wise comparisons were preplanned, p values were not corrected for multiple comparisons.

RESULTS

Demography

All 21 participants were men with a mean age of 22.4 years (SD, 0.92 years). The subjects had a mean height of 177.8 cm (SD, 5.54 cm) and a mean weight of 81.1 kg (SD, 11.6 kg).

Dust, Gas, and Endotoxin Concentrations

Mean particle counts and measurements of ammonia and carbon dioxide concentrations over the 12-day study period are shown in Table 1. Table 2 outlines the results of dust and endotoxin measurements, and personal sampler assessments. These results indicate that no significant differences were observed for mean dust and endotoxin concentrations during the 4-h swine barn exposure between intervention and nonintervention days.

Table 1--Dust and Gas Concentrations in the Barn Indoor Environment Over the 12-Day Study Period(*)

Area Sampler Measurements	Data
Diminutive dust, counts/mL	21.6 [+ or -] 2.5
Modified respirable dust, counts/mL	32.5 [+ or -] 1.8
Modified inhalable dust, counts/mL	49.1 [+ or -] 2.6
[NH.sub.3], ppm	17.6 [+ or -] 0.9
[CO.sub.2], ppm	2,302.8 [+ or -] 138.4

(*) Values given as mean [+ or -] SE.

Table 2--Dust and Endotoxin Concentrations From Personal Sampler Assessments During Intervention and Nonintervention(*)

Personal Sampler	Intervention		
Dust concentration, mg/[m.sup.3]	4.53 [+ or -] 0.33		
Airborne endotoxin, EU/[m.sup.3]	4,916.5 [+ or -] 510.6		
Endotoxin concentration, EU/mg	1,168.9 [+ or -] 121.5		
Personal Sampler	**Nonintervention**	**p Value**	

Dust concentration, mg/[m.sup.3]	4.58 [+ or -] 0.38	0.91
Airborne endotoxin, EU/[m.sup.3]	4,035.3 [+ or -] 516.0	0.30
Endotoxin concentration, EU/mg	958.6 [+ or -] 149.0	0.34

(*) Values given as mean [+ or -] SE.

Respirator Fit

Respirator fit tests were quantitatively assessed and were conducted on the subject's first entry into the barn and then again after 2 h of exposure at which time the used respirator was replaced with a new respirator. The mean quantitative fit factors at the two occasions were 191.0 (SD, 23.0) and 195.4 (SD, 11.9), respectively. These means are above the minimum required fit factor of 100, indicating a good fit for the respirators.

Symptom Scores

The mean self-reported symptom scores on intervention and nonintervention days are shown in Figure 1. The mean scores related to cough, chest tightness, and phlegm were significantly greater on the intervention day than those on the nonintervention day. No significant differences were observed in scores related to headache and nasal irritation.

[Figure 1 ILLUSTRATION OMITTED]

Pulmonary Function Test Values

Across-shift changes in pulmonary function for all parameters were significantly greater on the nonintervention day than on the intervention day and baseline day (Table 3). No significant differences were observed between baseline and intervention days in any of the pulmonary function measurements. On nonintervention days, a mean reduction of 8.12% was observed in [FEV.sub.1] over the 4-h exposure in comparison to the slight improvements in [FEV.sub.1] on baseline and intervention days (Fig 2).

[Figure 2 ILLUSTRATION OMITTED]

Table 3--Shift Change in Pulmonary Function Measurements on Baseline, Intervention, and Nonintervention Days(*)

Measurements	Baseline Day
[FEV.sub.1], % change	1.57 [+ or -] 0.51
FVC, % change	-0.02 [+ or -] 0.51
[FEF.sub.25-75%], % change	4.21 [+ or -] 1.62
[FEV.sub.1]/FVC ratio, % change	1.45 [+ or -] 0.51
Measurements	**Intervention Day**
[FEV.sub.1], % change	0.32 [+ or -] 0.62
FVC, % change	0.12 [+ or -] 0.47
[FEF.sub.25-75%], % change	0.53 [+ or -] 1.66
[FEV.sub.1]/FVC ratio, % change	0.21 [+ or -] 0.42
Measurements	**Nonintervention Day**
[FEV.sub.1], % change	-8.12 [+ or -] 1.01([dagger]) ([double dagger])
FVC, % change	-2.24 [+ or -] 0.79([sections]) ([parallel])
[FEF.sub.25-75%], % change	-19.51 [+ or -] 1.89([dagger]) ([double dagger])
[FEV.sub.1]/FVC ratio, % change	-5.96 [+ or -] 0.70([dagger])

Measurements	p Value ([double dagger])
[FEV.sub.1], % change	< 0.001
FVC, % change	0.08
[FEF.sub.25-75%], % change	< 0.001
[FEV.sub.1]/FVC ratio, % change	< 0.001

(*) Values given mean [+ or -] SE. [FEF.sub.25-75%] = midexpiratory phase of forced expiratory flow.

([dagger]) p < 0.001 vs baseline day.

([double dagger]) P < 0.001 vs intervention day.

([sections]) p = 0.05 vs baseline day.

([parallel]) p = 0.03 vs intervention day using paired t tests.

Bronchial Responsiveness

Mean methacholine [PC.sub.20] was significantly lower on nonintervention days than on baseline and intervention days (Fig 3). Interestingly, the mean [PC.sub.20] observed on the intervention day was significantly lower than that observed on the baseline day.

[Figure 3 ILLUSTRATION OMITTED]

WBC Counts

Mean WBC counts and differentials are shown in Table 4 for baseline, intervention, and nonintervention days. No significant differences were observed in the mean eosinophil, monocyte, and lymphocyte counts among these three occasions. The mean neutrophil and total WBC counts were significantly elevated on nonintervention day compared to the baseline and intervention days. No significant differences were observed in any of the mean blood count measurements between baseline and intervention days.

Table 4--WBC Counts and Differentials on Baseline, Intervention, and Nonintervention Days(*)

Cell Counts	Baseline Day, cells/[micro]L
WBCs	6,390 [+ or -] 196
Neutrophils	3,767 [+ or -] 193
Eosinophils	114 [+ or -] 16
Monocytes	557 [+ or -] 39
Lymphocytes	1,929 [+ or -] 108

Cell Counts	Intervention Day, cells/[micro]l
WBCs	6,590 [+ or -] 272
Neutrophils	3,686 [+ or -] 195
Eosinophils	110 [+ or -] 26
Monocytes	552 [+ or -] 62
Lymphocytes	2,214 [+ or -] 190

Cell Counts	Nonintervention Day, cells/[micro]L
WBCs	7,890 [+ or -] 386([dagger])([double dagger])
Neutrophils	5,005 [+ or -] 397([double dagger])([sections])
Eosinophils	105 [+ or -] 20
Monocytes	548 [+ or -] 35
Lymphocytes	2,100 [+ or -] 156

Cell Counts	p Value

WBCs	0.002
Neutrophils	< 0.002
Eosinophils	0.89
Monocytes	0.98
Lymphocytes	0.29

(*) Values given as mean [+ or -] SE.
([dagger]) p = 0.001 vs baseline day.
([double dagger]) p = 0.001 vs intervention day.
([sections]) p = 0.006 vs baseline day using paired t tests.

Nasal Lavage Cell Counts

The mean for the total number of cells measured in nasal lavage fluid on nonintervention days was 122,590 cells/mL (SE, 39,205 cells/mL), and significantly fewer cells were measured on intervention days (mean, 39,052 cells/mL; SE, 10,147 cells/mL; p = 0.03) and baseline days (mean, 16,514 cells/mL; SE, 4,388 cells/ mL; p = 0.012). The difference in the mean total number of cells between baseline and intervention days was statistically significant (p = 0.024).

Proinflammatory Cytokines

In comparison to the baseline day, significant increases were observed in the proinflammatory cytokines IL-8 and IL-6 in nasal lavage fluid on intervention and nonintervention days (Table 5). The mean values of IL-8 and IL-6 on nonintervention day were three to six times greater than those observed on intervention day. Only IL-6 was detectable in the blood serum on all three occasions, and the mean IL-6 concentration was significantly greater on nonintervention day than those observed on intervention and baseline days (Table 5). The difference in levels of IL-6 between intervention and baseline days was not statistically significant.

Table 5--Levels of Nasal Lavage and Serum Cytokines on Baseline, Intervention, and Nonintervention Days(*)

Cytokines	Baseline Day, pg/mL
Nasal lavage fluid	
IL-8	437.0 [+ or -] 59.2
IL-6	6.1 [+ or -] 3.0
Serum	
IL-6	1.0 [+ or -] 0.1

Cytokines	Intervention Day, pg/mL
Nasal lavage fluid	
IL-8	553.7 [+ or -] 71.6
IL-6	24.1 [+ or -] 13.0
Serum	
IL-6	1.8 [+ or -] 0.7

Cytokines	Nonintervention Day, pg/mL
Nasal lavage fluid	
IL-8	1,450.7 [+ or -] 92.6([dagger]) ([double dagger])
IL-6	147.8 [+ or -] 30.1([dagger]) ([sections])
Serum	
IL-6	9.2 [+ or -] 0.9([dagger]) ([double dagger])

Cytokines	p Value
Nasal lavage fluid	
IL-8	< 0.001
IL-6	< 0.001
Serum	
IL-6	< 0.001

(*) Values given as mean [+ or -] SE.
([dagger]) p < 0.001 vs baseline day.
([double dagger]) p < 0.001 vs intervention day.
([sections]) p = 0.001 vs intervention day.

DISCUSSION

These results indicate that the use of well-fit, disposable N-95 particulate respirators (with two-straps and metal nose-clips) over a 4-h exposure period in a swine confinement facility by naive volunteers virtually eliminates acute respiratory

symptoms, shift changes in [FEV.sub.1] and serum IL-6 responses, and nasal lavage fluid IL-6 and IL-8 responses and considerably ameliorates the exposure-related response to inhaled methacholine.
In our study, we detected IL-6 and IL-8 in nasal lavage fluid and IL-6 in serum. The inability to detect IL-8 in serum might be related to interference of the IL-1 receptor antagonist in the acute reaction.[32,33] These findings indicate that IL-6 may be an important regulatory cytokine in the inflammatory response to a swine barn environment. Although there was a significant decrease in the mean [PC.sub.20] on the intervention day compared to the baseline day, the dose levels were 242.0 and 328.0 mg/mL, respectively, indicating that neither day produced any clinically important bronchial responsiveness. Whereas on the nonintervention day, a mean [PC.sub.20] of 130.4 mg/mL indicates that the wearing of a respirator reduced bronchial responsiveness.
In describing these findings, we have confirmed and extended our previous observations that environmental control measures in swine facilities using sprinkled canola oil result in reductions in acute shift changes in [FEV.sub.1] that are similar to those that we herein reported with the use of disposable respirators.[22] We also have extended previous work by ourselves and others on the efficacy of respiratory personal protection in swine confinement facilities. In our previous work, we reported that swine producers who used respirators for preventive purposes had better lung function than did those who did not use respirators or those who used respirators because of respiratory symptoms.[23] Further, it has been demonstrated that educational intervention can increase the use of respiratory personal protection.[24]

Industrial hygiene experiments have indicated the potential capability of paper masks to reduce particulate concentrations.[25] Popendorf et al[34] measured work protection factors (WPFs) for three classes of respirators (fully disposable, reusable half-mask with valve, and powered air-purifying helmet) by measuring dust and endotoxin levels collected inside and outside these masks during agricultural exposures (swine, poultry, and grains).[34] They demonstrated that, while the disposable paper mask had a WPF of only 16, vs 19 and 30 for the reusable half-mask and powered air-purifying helmets, respectively, the disposable paper masks were favored by workers for weight and convenience.[34] While we did not evaluate the WPF, we did show that a properly fitted disposable half-mask (metal nose clip and two straps) can afford apparent extensive protection, at least in naive, previously unexposed, nonallergic volunteers.

Our previous work,[12,20] and that of others,[21,35,36] has shown that of the various exposures inside animal confinement facilities, including dusts, endotoxins and ammonia are the principal substances associated with acute changes. We have previously demonstrated that by simultaneously reducing dust and endotoxin concentrations in swine confinement facilities by sprinkling canola oil, we could effect marked reductions in both the respiratory and systemic effects of exposure.[22] As the use of a disposable respirator in these experiments achieved reductions in both respiratory and systemic effects of exposure in the naive volunteers that were similar to those seen with dust and endotoxin control with sprinkled canola oil, it seems reasonable to assume that reductions of within-mask concentrations of the substances occurs, and that endotoxins, which are present on dust particles, can be controlled with either dust control with canola oil or with filtering by means of a respiratory personal protective device.

What are the mechanisms of the dramatic reductions in response to exposures in these naive volunteers? Previous work clearly has demonstrated that swine barn exposures in naive volunteers are associated with short-term shift changes,[22] increases in airways responsiveness,[22] evidence of inflammatory response,[7] and production of immunologic mediators tumor necrosis factor-[Alpha], IL-6, and IL-8,[22,37,38] whether by mouth or nose breathing.[39] All of the foregoing effects of exposures in naive, previously unexposed volunteers could be evidence of a nonspecific response to acute exposures that may or may not be relevant in the genesis of suspected dysfunction that has been described previously in chronically exposed workers in the swine industry.[1-5,35,36]

Our previous work has demonstrated that reductions in contaminant concentrations result in marked amelioration of the effects in volunteers.[22] The work reported herein demonstrates that use of personal protection has similar effects. Although unproven, it seems reasonable to suggest that both the reduction of exposures through dust control and the use of personal protection should result in similar beneficial long-term effects, at least in most exposed workers. While personal protection is useful to assist workers in short-term high-dose exposures, we believe that long-term prevention of dysfunction requires the development of control technologies and production technologies that allow workers to function within a healthful environment. In the meantime, many workers, especially those with asthma or other symptoms, who are exposed may benefit from appropriate respiratory protection,[40] as would workers exposed to short-term high-dose exposures that may be difficult to control by currently available technologies. Further work to develop economically and technologically feasible control technologies that would allow for appropriate advice for these workers and their employers is required.

ACKNOWLEDGMENTS: We thank Dr. Charles Rhodes for his scientific contribution and Ms. Denise Bono for her technical assistance to the project. We are grateful to 3M Canada Inc for supplying all respirators necessary for the training and testing of subjects for this project, to Levitt Instruments, Edmonton division, for supplying the Porta-Count and N-95 Companion and for training personnel for this project, and to the volunteers who participated in the project.

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Manuscript received November 4, 1999; revision accepted February 8, 2000.

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