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Acute Respiratory Effects and Endotoxin Exposure During Wheat Harvest in Northeastern Colorado

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Acute cross-shift respiratory changes were evaluated for workers at 25 farms in northeastern Colorado during the summer of 1994 wheat harvest. Information on workers' respiratory health, past occupational exposures, and smoking status was obtained. Each worker was asked to rank eight acute symptoms before he or she began harvest work for the day. Spirometry was also performed before work began. Each participant wore a high-flow personal air sampling pump for the full shift. At the end of the workshift, spirometry and ranking of the eight acute symptoms were conducted again. Total dust exposure was determined gravimetrically. Total endotoxin was measured by the Limulus amoebocyte lysate (LAL) assay. The 98 harvest workers included in the study ranged in age from 18 to 80. Ten percent of the workers had moderate airway obstruction, as indicated by the pre-shift spirometry test results. Fifty percent of the workers were current or ex-smokers. Despite an unusually poor harvest, total dust exposures ranged from 0.09 to 15.33 mg/m^3 (geometric mean 0.83 mg/m^3), with 8 percent of workers exposed above the American Conference of Government Industrial Hygienists® (ACGIH®) threshold limit value® (TLV®) of 4 mg/m^3. Total endotoxin exposures ranged from 4.4 to 744.4 EU/m^3 (geometric mean 54.2 EU/m^3), with 33 percent of workers exposed above 90 EU/m^3, the level suggested as a threshold for acute mucous membrane irritation and pulmonary change among cotton workers. Sixty percent of workers experienced a cross-shift change in at least one respiratory symptom. The respiratory index (sum of cross-shift changes in the eight acute respiratory symptoms) was significantly correlated with both total dust and endotoxin exposure. Cross-shift changes in the spirometric variables were associated with smoking status, age, presence of airway obstruction, and history of chronic respiratory symptoms, but not with dust or endotoxin exposure. Peak expiratory flow rate was found to decrease over the workshift in a manner similar to that experienced by cotton workers.

Keywords Agricultural Health and Safety, Grain Dust, Endotoxin, Respiratory Symptoms, Pulmonary Function

A number of studies have demonstrated the association between both acute and chronic pulmonary and non-pulmonary effects and exposure to grain dusts.[(1–4)] Acute effects associated with present-day grain dust exposures include occupational asthma, dyspnea, chest tightness, dry cough, wheezing, expectoration, conjunctivitis, rhinitis, dermatitis, headache, fever and chills, flushed face, and pain in joints and muscles.[(4–5)] If fever accompanies acute symptoms, the diagnosis has historically been called "grain fever," or more recently "organic dust toxic syndrome" (ODTS).[(6)] Chronic health effects associated with grain dust exposure include asthma, chronic bronchitis, farmer's lung or hypersensitivity pneumonitis (HP), non-specific chronic obstructive pulmonary disease (COPD), and long-term reduction in lung function.[(1,7)] Chronic adverse effects are likely to result from repetitive acute inflammatory responses to grain dust exposure.

Studies of U.S. and Canadian cohorts have shown that grain workers generally have a significantly higher prevalence of respiratory symptoms and disease and reduced lung function as compared to unexposed workers from the same region of similar age, height, and smoking habits.[(1–2,8–9)] These investigations have clarified the contributions of smoking, ethnicity, layoff, duration of employment, and allergic status to the prevalence of respiratory symptoms and disease among grain workers.[(8,10)] It has also been shown that workers who leave the grain industry have higher prevalence of symptoms as compared to those who remain employed.[(10)] This "healthy worker" effect has undoubtedly led to an underestimate of the adverse effects of grain dust exposure.

Studies of grain dust exposures have mostly been performed on grain elevator workers who have regular exposure to grain dust. Other exposed worker groups, in particular farmers, have not been as well studied. The majority of farms across the United States are small family operations or employ less than 10 workers, and are exempt from Occuptional Safety and Health Administration (OSHA) regulations and general duty inspections.[11] Thus, exposure levels have not been measured for farm workers on a regular or systematic basis.

Farmers may be exposed to grain dust during harvesting and storage, feeding of livestock, or during cleaning and maintenance of silos or bins. While their exposure has been estimated at only 40 to 60 days per year, farm worker exposure has been estimated to range from half that of grain elevator workers to as high or higher than grain elevator workers.[12−15] It has been suggested that modern agricultural practices, such as confined feeding operations, may result in further increased exposures.[11] In addition, farmers have multiple hazardous exposures, including toxic gases from animal confinement buildings and manure pits, fertilizers, pesticides, animal dander and feces, infectious agents, and moldy hay and grain dusts.[11,16−18] The cumulative effect of multiple exposures and varied intensity on farmers is unknown.

Few studies have developed dose-response relationships between an individual's quantitative exposure to grain dust and health effects. In those that have, only acute effects have been examined and only total or respirable dust has been monitored.[19−20] Even fewer studies have looked at dose-response by specific component of grain dust. Grain dust is a heterogeneous mixture of organic and inorganic constituents, including plant matter, insects, mites, hair, feathers, excreta, bacterial endotoxins, fungal mycotoxins, pesticides, fertilizers, soil (silica), lubricating oil, metal fragments, and paint chips.[5,7,12] The specific composition of grain dust varies with location, altitude, season, humidity, amount of rain, age of the grain, and methods of storage, handling, and processing of the grain.[15,21] More than one of the possible constituents is likely to act as an etiological agent, although microorganisms have been implicated in many of the health effects.

Proposed mechanisms by which grain dust exerts its toxic action include simple physical irritation, allergic response to fungi, grain mites, and weevils; activation of the alternative complement pathway; and inflammatory reaction to glucans and endotoxins.[22] Several authors have proposed that a hypersensitivity reaction to foreign proteins may be involved.[23−24] While HP is thought to be an immune response to thermophilic actinomycetes, it is proposed that bacterial endotoxins in organic dust may also play a role.[25−26]

Endotoxin is now believed to be the responsible agent for the majority of acute grain dust-related respiratory effects. Recent animal and human exposure studies have shown that endotoxin increases proinflammatory cytokines when interacted with alveolar macrophages.[27−30] Cosma and Martinez have shown that endotoxin is responsible for 70 percent of the inflammatory response by rat alveolar macrophages exposed to wheat and corn dust in vitro.[31] Human inhalation studies have shown that endotoxin in cotton dust is associated with dose-dependent airflow obstruction.[32−33] Several epidemiological studies have demonstrated associations between endotoxin exposure among swine building, animal feed industry, and cotton workers and respiratory symptoms or pulmonary function declines.[34−36]

Farmers in northeastern Colorado have elevated dust exposures during wheat harvest.[12] Endotoxin levels in the dust are in the range at which mucous membrane irritation and acute pulmonary function changes have been documented.[37] Because of these exposures, and the fact that farmers have been seldom studied during harvest, a cross-shift study was carried out to correlate symptoms and lung function change with dust and endotoxin exposure during wheat harvest.

METHODS AND MATERIALS

Subject Selection and Recruitment

Subjects were selected via a purposive two-step process. First, farm owners in northeastern Colorado with over 1000 acres of winter wheat were recruited for the study. Second, upon arrival at the farm during harvest, all eligible workers were asked to participate in the study. Eligibility was defined as: over 18 years of age, not on medication for recent surgery, cold, or heart or lung disease, no collapsed lung in the previous six months, and not using a bronchodilator or corticosteroid medication during that workday. Both male and female harvest workers, including farm owners and operators, were included in the study. Workers performing all harvest tasks were included to ensure that a wide range of exposures was represented. The full questionnaire was administered to eligible subjects and pre-shift spirometry and dust sampling were performed immediately thereafter.

Because human subjects were involved, the study was approved by the Colorado State University Human Research Committee prior to implementation. The subjects were provided results of the spirometric screen and dust exposure monitoring, and a ball cap or $10 cash in appreciation of their time and to offset any lost wages. Study subjects with abnormal spirometric values were also offered a free follow-up diagnostic examination.

Data Collection Instruments

Data collection instruments developed for the study included the questionnaires (eligibility screener, smoking history, pre-shift and post-shift questionnaires); farm information, phone log, farm/subject link, and informed consent forms; HF5 spirometry log sheet; dust and endotoxin data collection forms; field observations form; and request for health and safety information form. The questionnaires were pre-tested on interviewers for the Colorado Farm Family Health and Hazard Surveillance (CFFHHS).[38] Questionnaires were modified based on the pre-test findings.

The Pre-Shift questionnaire addressed acute and chronic respiratory symptoms and work history. The acute symptoms questions included symptoms previously reported at a prevalence of 11–77 percent among grain workers—eye, nose, and throat irritation, cough, phlegm, wheezing, dyspnea, and chest discomfort.[1]

In addition, tingling fingers and blurred vision were included to serve as control symptoms, that is, symptoms not expected to be associated with dust exposure. Each subject was asked to rate the severity of each acute symptom based on how they felt at that moment. The rating was on a scale of 1 to 5, with 1 indicating no problem and 5 indicating a very severe problem.

Chronic respiratory symptoms questions were based on (1) the Third National Health and Nutrition Examination Surveys (NHANES III) Adult Respiratory and Allergy Section,[39] and (2) proposed questions for identifying ODTS.[40] Questions about family history of allergies, asthma, chronic bronchitis, and emphysema were also included as recommended in the Epidemiology Standardization Project.[41] The questionnaire limited recall about chronic respiratory conditions to the last 12 months, thus minimizing recall bias.

Work history questions addressed previous exposures to visible dusts, metal fumes, gases, vapors, herbicides, and insecticides, as well as how many years the subject had lived and worked on a farm and harvested wheat.

The Smoking History questionnaire, based on the CFFHHS questionnaire, included questions to determine smoking status and pack-years of smoking.

The Post-Shift questionnaire was administered at the end of the harvest workday. This questionnaire was designed to address cross-shift changes in acute symptoms. Thus, questions were identical to the pre-shift acute symptom questions except that they had been reordered to reduce the possibility of subjects attempting to match their pre-shift responses. Each subject was also asked to estimate the amount of dust exposure experienced during the day, whether they had used medications, and whether they had smoked during the day.

Measurement of Respiratory Function

National Institute of Occuptional Safety and Health-(NIOSH) trained field staff conducted spirometry tests on each subject before beginning harvest work for the day and at the end of the workday immediately upon conclusion of exposure monitoring, using NIOSH's HF5 system. This system features a rolling seal spirometer, an IBM-compatible notebook computer, automated calibration and operation, comparison of the subject's performance, and a real-time display of flow-volume curves. The pre- and post-shift testing temperature was maintained within 5°F to allow for accurate cross-shift comparisons.[42] All spirometry tests and calibrations were conducted in accordance with NIOSH's Spirometry Procedure Manual.[43] Date, time, spirometer identification, team leader, ambient temperature and barometric pressure, the age, weight, height, gender, and race of the subject, whether the subject had smoked or eaten a heavy meal in the past hour or had an upper respiratory infection in the past three weeks, and the total number of maneuvers and quality code were all recorded.

Subjects were in a sitting position, and wore a nose clip during the maneuver. The HF5 system presented FVC, FEV_1, and PEFR results immediately following each test. Up to eight maneuvers were obtained to achieve the desired reproducibility in three maneuvers, that is, the three best FVCs were within +/−5 percent of each other, the three best FEV_1s were within +/−5 percent of each other, and the two best PEFRs were within +/−10 percent of each other, in compliance with the existing 1987 American Thoracic Society standards.[44]

The computer software converted lung volumes and flow rates from ambient conditions to values corrected for body temperature, ambient pressure, water-vapor saturated (BTPS) values using standard conversion factors, and then calculated FVC, FEV_1, FEV_6, $FEF_{25-75\%}$, PEFR, and FVC/FEV_1 from the spirograms for each subject. The starting points for FEV_1 and FEV_6 were obtained by backward extrapolation. If the extrapolated volume exceeded 5 percent of the FVC, the test was not included. The largest of the three FVCs was recorded as the FVC for the test. The largest of the three FEV_1s was recorded as the FEV_1, even if the two values did not occur on the same maneuver.

The computer files were returned to NIOSH for data abstraction and review by a pulmonary physiologist. Percent of predicted spirometric values were calculated from Knudson for the age, gender, and height of each subject.[45] Reports were returned to the investigators for use in the study data analysis and for inclusion in reports to each study participant.

Exposure Monitoring

Each subject was monitored for total dust and endotoxin for the entire workshift, or at least six hours, depending on work schedules. NIOSH Method 0500 for personal sampling of total dust was used for sample collection.[46] Sampling was performed between 1.5 and 2.0 liters per minute with pre-weighed, 37-mm glass fiber filters housed in two-piece, closed-face cassettes. Temperature, pressure, and humidity were recorded at the beginning and end of the sampling period. The final air volumes were corrected for differences between calibration and sampling conditions.

After each sample collection, cassettes were sealed and placed in a cooler with ice. Cassettes were transferred to a standard freezer upon arrival back at the field office, approximately 2 to 12 hours after sample collection. Total dust analysis was then performed gravimetrically in accordance with NIOSH Method 0500 for nuisance dust.[46] After weighing, filters were placed in 50-ml sterile polypropylene conical centrifuge tubes with screw-on caps and shipped on dry ice to NIOSH's laboratory in Morgantown, West Virginia, for endotoxin analysis using the quantitative chromogenic modification of the *Limulus* amoebocyte lysate (LAL) assay.[47–48]

At intervals throughout the day, the tasks performed by each subject and their duration, and other important exposure variables, such as use of respiratory protection, observation of visible dust, wetting of dusty operations, enclosed tractors, or other dust sources, were recorded.

Factors such as humidity and rain create different regional grain dust composition at harvest and, thus, different exposure patterns. These potential confounders were controlled by performing the study in a limited geographical area during a single harvest season.

Data Analysis

All data from the study were entered into dBase V by subject identification number. A series of data logic checks were run to ensure the accuracy of data entry. The data were then transferred as an ASCII file for analyses using SAS, version 6.03 software. The logarithm of the eight-hour TWA total dust and endotoxin expsoure was used in all calculations involving expsoure as a variable.

RESULTS AND DISCUSSION

Study Participation Rates

Sixty-seven farm owners were recruited into the study before the 1994 winter wheat harvest. The 1994 growing season was extremely hot and dry so that the wheat crops were harvested sooner and in a shorter time period than typical. Thus, the field teams were able to visit only 25 of the recruited farms.

Of a total of 129 workers present at the 25 farms visited, 98 were recruited into the study (14 were ineligible, 8 started work before the field team arrived, 3 were not included due to insufficient sampling pumps). Only five percent (6 of the 129 available workers) refused to participate. Four refusals came from farm owners who claimed to be too busy. Two workers were just not interested in participating. All recruited subjects completed the study.

Study Population

Table I presents basic qualitative demographic characteristics of the subjects enrolled in the study by gender. There were 90 male and 8 female subjects. One male subject was black. Two male subjects considered themselves Hispanic. All other subjects were non-Hispanic and Caucasian. The most frequent education level was high school graduate (n = 29). However, a large number of subjects had at least some college (n = 50) and others had attended technical school beyond high school (n = 8). There was no statistically significant difference between male and female subjects in the frequency of these demographic characteristics.

Table II presents the quantitative characteristics of the study subjects. The mean ages of the men and women were 38 and 34 years, respectively. For the men, this age was comparable to the 38- to 40-year mean age of grain elevator worker populations previously studied.[1–2,8] The study population was somewhat younger than previously studied farmer populations whose mean ages were 42 and 45 for men and 41 for women.[4,34]

Not unexpectedly, the male subjects were significantly taller and heavier, and had higher body mass indices than the women. The men were slightly taller and heavier than other male grain elevator populations studied, whose mean height ranged from 172 to 177 cm, and mean weight ranged from 82 to 83 kg.[1–2,8]

Table III presents the smoking characteristics of the study subjects. At the time of the study, 19 (19%) of the subjects were current smokers, 30 (31%) were ex-smokers, and 49 (50%) had never smoked. Thirteen of the nonsmokers were considered passive smokers, that is, they reported that other people smoked in their homes. There were no significant differences between men and women in smoking status. The percentage of smokers

TABLE I
Demographic characteristics of the study population by gender

Characteristic	Number of individuals (percent)[A] Male-90	Female-8	p[B]
Race:			
White	89 (99%)	8 (100%)	1.00
Black	1 (1%)	0 (0%)	
Hispanic:			
Yes	2 (2%)	0 (0%)	1.00
No	88 (98%)	8 (100%)	
Education:			
≤8th grade	4 (4%)	0 (0%)	0.90
Some high school	6 (7%)	1 (12.5%)	
High school graduate	26 (29%)	3 (37.5%)	
Some technical school	2 (2%)	0 (0%)	
Technical school graduate	6 (7%)	0 (0%)	
Some college	22 (24%)	3 (37.5%)	
College graduate	22 (24%)	1 (12.5%)	
Postgraduate degree	2 (2%)	0 (0%)	

[A]Column percents.
[B]Fisher's exact X^2 (2-tailed) between males and females.

TABLE II
Physical characteristics of the study population by gender

Characteristic	Mean	Range	Std. dev.	p[A]
Age (years)				
All subjects	38	18–76	15	
Male	38	18–76	15	
Female	34	19–48	9	0.423
Height (cm)				
All subjects	176	157–192	8	
Male	178	160–192	7	
Female	166	157–170	5	<0.0001
Weight (lb)				
All subjects	187	115–350	38	
Male	191	130–350	36	
Female	141	115–200	26	0.0003

[A]T-test (2-tailed) between males and females.

TABLE III
Smoking characteristics of the study population

Smoking status	Number of individuals (percent)[A] Male	Female	p[B]
Smoking status I:			
Current smoker (n = 19)	17 (19%)	2 (25%)	0.18
Ex-smoker (n = 30)	30 (33%)	0 (0%)	
Passive smoker (n = 13)	11 (12%)	2 (25%)	
Never smoked (n = 36)	32 (36%)	4 (50%)	
Smoking status II:			
Smoker (n = 49) (current + ex)	47 (52%)	2 (25%)	0.27
Non-smoker (n = 49) (passive + never)	43 (48%)	6 (75%)	
Smoking history for smokers (current plus ex-smokers)	**Mean**	**Range**	**Standard deviation**
Packs of cigarettes smoked/day (n = 49)	1.08	0.05–3.50	0.91
Number years smoked (n = 49)	19.01	0.50–59.5	16.31
Smoking pack-years:			
All smokers	15.65	2–42	10.22
Males	15.13	2–42	10.04
Females	28.00	23–33	7.07

[A]Column percents.
[B]Fisher's exact X^2 (2-tailed) between males and females.

in the study population was much lower than in previously studied grain elevator populations, whose smoking rates have ranged from 35 to 60 percent,[(1–2,8)] and farming populations, whose smoking rates have ranged from 30 to 34 percent.[(4)] The 49 smokers (current plus ex-smokers) reported smoking between 1 cigarette per day and 3.5 packs of cigarettes per day (mean = 1.08 packs) for between 6 months and 59.5 years (mean = 19.0 years). The range of smoking pack-years was from 2 to 42 (mean = 15.65 pack-years). The smoking pack-years was comparable to the mean of 14 pack-years for farmers, but lower than the mean of 22 pack-years for grain elevator workers previously reported.[(2)]

As regards past work histories, 87 of the subjects had lived on a farm for a period during their lifetimes, ranging from 1 to 76 years (mean = 16 yrs). Thirty-seven currently lived on the study farm. The subjects had worked on farms for 1 to 65 years (mean = 14 yrs) and had harvested wheat for 1 to 55 years (mean = 14 yrs). These exposure years are slightly higher than the range of means of 8 to 14 years reported for grain elevator populations, and lower than the mean of 22 years for a farmer population.[(1–2,4,8)]

Forty-eight percent of the subjects were study farm family members, 26 percent were local hires, and 24 percent were custom cutters. The healthy worker effect is not expected to be as great among family farmers as among grain elevator workers.[(4,8,19)] However, custom cutters represent a population in which severely affected individuals may have been forced to change jobs. Thus, the study population may be "healthier" than the general population.

The average number of days the subjects spent harvesting wheat ranged from 4 to 180 days (mean = 35 days). In 1994, the subjects had spent between 0 and 50 days (mean = 14 days) harvesting wheat prior to the study date. Fifty-nine of the subjects reported previous work using herbicides or insecticides, primarily 2,4-D. However, only five subjects reported work with organophosphate pesticides, which has been associated with bronchial asthma.[(49)]

Non-farming jobs held in the past by the subjects included welding, painting, ammonia work, coal work, firefighting, gas station work, and other miscellaneous jobs. The subjects had worked at these jobs for 1 to 10 years.

Subject Exposures

The geometric mean, range and geometric standard deviation (GSD) for the 8-hr TWA subject exposures to total airborne dust and endotoxin, and for the ratio of endotoxin to dust concentration are presented in Table IV. The frequency of airborne dust and endotoxin concentrations followed approximately lognormal distributions. There was a detectable quantity of dust and endotoxin on all samples, and thus no data was censored.

The geometric mean total dust was 0.83 mg/m^3 and the arithmetic mean was 1.32 mg/m^3. Only one subject was exposed above OSHA's PEL of 10 mg/m^3 total dust, while eight (8%) subjects were exposed at or above ACGIH's TLV of 4 mg/m^3 total dust. The dust exposures and number of exceedances above the occupational exposure limits found during the study were comparable to exposures found during an earlier study of grain elevator workers in northeastern Colorado.[(50)] During the 1992 harvest, the mean personal total dust exposure of 8.4 mg/m^3 was significantly higher than the present study.[(12)] This is likely due to the drought and resultant poor harvest conditions of the present study. Nonetheless, the upper exposure limits were comparable between the two studies (1992 upper limit: 15.2 mg/m^3).

TABLE IV
8-hr TWA dust and endotoxin exposures for the study subjects

8-hr TWA exposure	Geometric mean	GSD	Arithmetic mean	Range
Total dust (mg/m^3)	0.83	2.44	1.32	0.09–15.33
Endotoxin (EU/m^3)	54.24	3.27	104.6	4.4–744.4
Endotoxin/dust ratio (EU/mg)	56.99	2.38	82.8	6.1–525.7

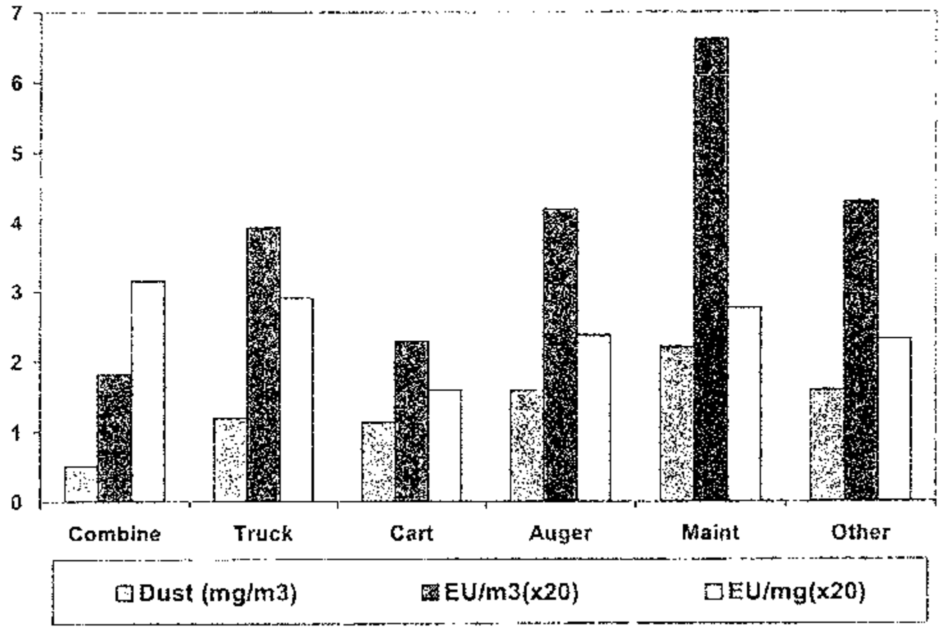

FIGURE 1
Mean exposures by job category.

The geometric mean endotoxin exposure was 54.24 EU/m^3 and the arithmetic mean was 104.6 EU/m^3. Thirty-two (33%) subjects were exposed to endotoxin levels greater than 90 EU/m^3, the level suggested as a threshold for acute mucous membrane irritation and pulmonary change among cotton workers.[37] The mean endotoxin exposure was comparable to the mean of 106 EU/m^3 (range 61.5 to 237 EU/m^3) found during the 1993 wheat harvest.[12]

Since there is currently no occupational standard for endotoxin, the relationship between total dust and endotoxin exposures was compared to determine how well total dust measurements predict endotoxin levels. The linear correlation coefficient, r, between the logarithms of these two exposures was 0.69 ($r^2 = 0.47$), indicating a moderately good relationship. Humidity did not have a significant effect on either airborne dust or endotoxin exposures.

The study included all the harvest workers at the study farms. Thus, a number of job categories were represented with different potential exposures (see Figure 1).There was a significant difference in both total dust and endotoxin exposure among the job categories (GLM-Tukey's test: $p = 0.005$ for dust, $p = 0.062$ for endotoxin). While the "maintenance" and "other" categories had the highest total dust and endotoxin exposures, there were only one and two persons in these categories, respectively. The high exposures for these jobs are likely due to tasks such as blowing the grain dust out of the engine and radiator.

The similarity of the mid-range exposures for auger operators and truck drivers is likely due to exposure to grain dust in a similar process state. In fact, many of the truck drivers actually operated the auger for part of the workday. While the combine operators had the lowest total dust and endotoxin exposure (as would be expected since almost all the cabs were enclosed and ventilated), their endotoxin to dust ratio was the highest of all job categories. This is probably due to the fact that the dust was not a mixture of grain dust and road dust, to which the truck drivers and other workers were likely exposed. It might also be due to the fact that only small particles enter the cab, and these may likely be the particles containing higher concentrations of endotoxin.

Four subjects wore a dust mask during the day of the study, but only for short periods during very dusty operations, such as when wheat was being dumped from the truck into the auger vessel. Of these, two wore disposable paper dust masks and two wore half-face air-purifying respirators with HEPA filters.

History of Respiratory Symptoms

Table V presents the prevalence of self-reported chronic respiratory symptoms by smoking status category among the study population. The prevalence of cough, phlegm, shortness of breath, wheezing, chest tightness with dusty work, and flu-like symptoms among the study population was comparable to the large farmer populations studied previously. The most frequently reported tasks associated with both chest tightness and flu-like symptoms involved working with wheat dusts. The other reported tasks involved working with corn, beans, seeds, livestock, hay, and pear dusts.

The 26 to 29 percent prevalence of family history of asthma was higher than the 12 percent reported in other farmer studies.[4] The 2 to 6 percent family history of chronic bronchitis was lower than the 7 percent found among a grain worker population.[2]

TABLE V
Prevalence rates of chronic respiratory symptoms by smoking status

Self-reported chronic respiratory symptom	Number of subjects (per 100) or extent of symptom[A] Current/ex smokers (n = 49)	Never smoked (n = 49)	p[A]
Cough (3 consecutive mos) (n = 9)	6 (12%)	3 (6%)	0.487[B]
Phlegm (3 consecutive mos) (n = 14)	9 (18%)	5 (10%)	0.387[B]
Shortness of breath on slight hill (n = 11)	6 (12%)	5 (10%)	1.00[B]
Wheezing (past 12 mos) (n = 24)	12 (24%)	12 (24%)	1.00[B]
- Mean number of wheezing episodes	5.6 Range: 1–14 SD: 5.6	2.2 Range: 1–5 SD: 1.6	0.057[C]
- Mean number of hospitalizations	0	0	NA
Chest tightness (with dusty work) (n = 30)	15 (31%)	15 (31%)	1.00[B]
Flu-like symptoms (past 12 mos) (n = 8)	4 (8%)	4 (8%)	1.00[B]
Flu-like symptoms (ever) (n = 23)	9 (18%)	14 (29%)	1.00[B]
- Mean number of flu-like episodes in life	7.8 Range: 1–30 SD: 9.6	3.0 Range: 1–12 SD: 3	0.123[C]
Family history:			
Allergies (n = 46)	22 (48%)	24 (49%)	1.00[B]
Asthma (n = 27)	14 (29%)	13 (26%)	1.00
Chronic bronchitis (n = 4)	3 (6%)	1 (2%)	0.617
Emphysema (n = 8)	5 (10%)	3 (6%)	0.715

[A]Column percents.
[B]Fisher's exact X^2 test (2-tailed) between smoking classes.
[C]T-test (2-tailed) between smoking classes. SD = standard deviation, NA = not applicable.

Although there was no statistically significant difference between study smokers and non-smokers in their self-report of any respiratory symptom, the prevalence rates were generally higher for smokers. In addition, smokers had significantly more episodes of wheezing in the last 12 months ($p = 0.057$) and somewhat more flu-like episodes in their lifetimes ($p = 0.123$) than non-smokers. While studies with larger populations have found significant differences between smokers and non-smokers with regard to respiratory symptoms, this study supports the conclusion that smokers have somewhat more respiratory symptoms.

Fisher's exact chi-square tests were used to determine the significance of the association between self-reported symptoms and past exposure to herbicides, and non-farming exposure to visible dust, metal fumes, and gases or vapors. The only significant associations were that self report of "sinus in the past 12 months" was associated with past exposure to visible metal fumes ($p = 0.010$) and the report of "any respiratory symptom" was slightly associated with past exposure to herbicides ($p = 0.10$).

Baseline (Pre-Shift) Lung Function

While the pre-shift spirometry results were primarily obtained for comparison to the post-shift spirometry results, the pre-shift results were also used to determine if any subject had evidence of existing disease at the start of the study. Moderate obstructive disease was indicated if (1) the FEV_1/FVC was less than 70 percent, or (2) the FEV_1 was less than 70 percent of predicted. A restrictive disease was indicated when the observed FVC/predicted FVC was less than 80 percent.

No subject exhibited restrictive disease via spirometric testing. Ten of the 98 (10 percent) subjects had a pre-shift FEV_1/FVC less than 70 percent indicating obstructive disease. All subjects with airways obstruction were male. Eight of the 10 were or had been smokers, that is, they had smoked at least 100 cigarettes in their lifetimes. The mean age ($p = <0.001$) and mean years of farm work ($p = 0.003$) were both significantly higher for the subjects with obstruction. Smoking status, but not pack-years, was marginally associated with obstruction ($p = 0.091$). There was no difference in obstruction based on gender or employee status (family member, local worker, or custom cutter). Interestingly, of the four subjects who wore a mask during the study, the only smoker who wore a mask also had obstruction.

Despite the use of conservative criteria for disease classification, the prevalence rate of 10 percent obstruction found during this study falls in the range of 4 to 42 percent abnormal pulmonary function reported for grain elevator workers.[1–2,8] It was also comparable to the prevalence of 13 percent found in

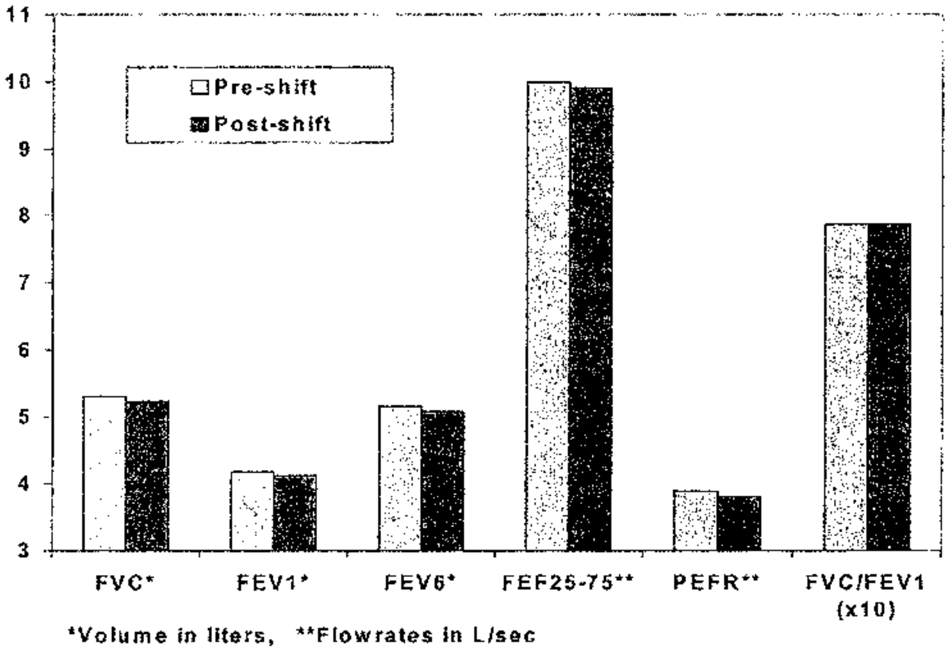

FIGURE 2
Pre- and post-shift lung function values.

a general population survey of males ages 20–69, all smoking categories, in Glenwood Springs, Colorado.[51]

Cross-Shift Lung Function Changes

Figure 2 shows the mean pre- and post-shift lung function values. While the changes do not appear large, the mean cross-shift decrease in FVC, FEV_1, and FEV_6 were all statistically significant. Cross-shift decreases in FVC and FEV_1 have been most often reported among grain workers, while controls experience smaller decreases or increases in these parameters. In a study of farmers, the cross-shift decrease in FVC and FEV_1 was −1 percent.[35] Slightly larger cross-shift decreases were found during this study. While the changes are statistically significant, it is important to note that biologically significant changes would have required cross-shift changes of 10 to 20 percent, depending on the lung function parameter.

The numerical values for the cross-shift lung function changes are summarized in Table VI for all subjects and for subjects with and without obstruction. The cross-shift changes in FEV_6 and $FEF_{25-75\%}$ were significantly different for subjects with obstruction as compared to those without obstruction. For subjects with obstruction, FEV_6 increased slightly (+1.2%) over the workshift, while FEV_6 decreased slightly (−1.8%) for subjects without obstruction. For subjects with obstruction, $FEF_{25-75\%}$ increased significantly (+11.4%) over the workshift, while $FEF_{25-75\%}$ decreased slightly (−1.9%) for subjects without obstruction. The cross-shift changes in FEV_1 and PEFR were marginally different for subjects with obstruction

TABLE VI
Cross-shift change in lung function values

Cross-shift change in lung function value	All Subjects (n = 98)	p^A	Subjects with obstruction (n = 10)	Subjects without obstruction (n = 88)	p^B
FVC, % Δ	−1.479	0.0001	0.042	−1.652	0.159
FEV_1, % Δ	−1.288	0.0089	1.340	−1.587	0.066
FEV_6, % Δ	−1.525	0.0001	1.225	−1.838	0.014
FEF_{25-75}, % Δ	−0.608	0.6724	11.377	−1.970	0.004
FEV_1/FVC, % Δ	0.159	0.5818	1.205	0.040	0.221
PEFR, % Δ	−0.376	0.5242	2.952	−0.754	0.056

[A]Matched pairs t-test between pre- and post-lung function value.
[B]T-test (2-tailed) between those with and without obstruction.

as compared to those without obstruction. For subjects with obstruction, FEV_1 and PEFR increased slightly (+1.3% and +2.9%, respectively) over the workshift, while FEV_1 and PEFR decreased slightly (−1.6% and −0.7%, respectively) for subjects without obstruction.

Because there is a normal diurnal variation in lung function parameters, it is important to assess whether the cross-shift changes experienced by the study subjects differ from unexposed populations. In a population of 944 unexposed blue-collar workers, the cross-shift change in FEV_1 was +0.8 percent.[52] While the study subjects experienced a cross-shift decrease in FEV_1, the difference between the two groups was not statistically significant.

Diurnal variation in flow rates is inherently more variable than lung volumes. For random samples of the general population, the mean percent diurnal (morning to evening) change in PEFR ranges from +4.9 percent to +8.9 percent, significantly different than the −0.4 percent decrease seen in the study population.[53–55] A study of asthmatics in the general population showed a mean diurnal increase in PEFR of as high as +51 percent.[53] Blue-collar workers have been shown to experience a cross-shift increase in PEFR of +2.1 to +11.6 percent, which is statistically different than the current study subjects' decrease of −0.4 percent ($p < 0.05$ by z-test).[52] In a group of cotton mill workers, linear declines in FEV_1, FVC, and PEFR were seen over the course of the workday and work week.[56] Declines in FEV_1 and FVC were not apparent by the end of the week, supporting the suggestion that PEFR may be the more sensitive indicator of exposure effects.[57] The declines observed among cotton workers are larger, but in the same direction as the subjects in the current study.

Cross-Shift Change in Respiratory Symptoms

Table VII presents the number of subjects by smoking status who reported an increase or decrease in each acute respiratory symptom over the course of the workshift. No significant difference was found between the two smoking classes for self-report of change in cross-shift symptoms, except for "mucous." Smokers generally reported decreased mucous accumulation, while non-smokers reported increased mucous accumulation at the end of the day as compared to the start of the day.

To determine whether any reported cross-shift change in respiratory symptom was associated with exposure, a linear regression was run for each acute respiratory symptom and the logarithm of total dust, endotoxin, and endotoxin to dust ratio with smoking status included in the model. There were no significant relationships found between exposure and change in any individual respiratory symptom.

Table VII shows that the majority of subjects reported no change in most of the respiratory symptoms. Thus, an additional measure, called the "respiratory index," was created. The respiratory index was the sum of the responses for changes in all the listed symptoms, thus providing a measure of whether any symptom changed as well as the extent of change. The calculated respiratory indices ranged from −3 to +7.

A positive and significant association was found between the respiratory index and both total dust and endotoxin exposure (Spearman correlation: $p = 0.036$ for total dust, $p = 0.036$ for

TABLE VII

Subjects reporting a cross-shift change in respiratory symptoms by smoking status

Respiratory symptom	Number of subjects reporting a change in respiratory symptom: Current/ex smokers (n = 49)			Never smoked (n = 49)			
	Increase	N/C[B]	Decrease	Increase	N/C[B]	Decrease	p[A]
Cough	2	39	8	6	31	12	0.669
Mucous	2	37	10	9	6	4	0.015
Eye irritation	12	33	4	14	30	5	1.00
Nose irritation	5	35	9	10	33	6	0.272
Throat irritation	6	8	5	9	38	2	0.361
Chest discomfort	3	5	1	6	41	2	1.00
Chest wheezing	0	46	3	0	47	2	NA
Shortness of breath	3	43	3	6	43	0	0.182
Fever or chills	0	49	0	0	49	0	NA
Tingling fingers	0	49	0	2	45	2	NA
Blurred vision	0	49	0	2	46	1	NA

[A]Fisher's exact X^2 test (2-tailed) between smoking classes.
[B]N/C = No change in cross-shift symptom.

TABLE VIII

Regression analysis: Variables significantly associated with change in lung function values and respiratory index

Cross-shift lung function change	Significant independent variable(s)	Parameter estimate	p-value	Intercept	R^2
FVC, % Δ	Smoking status	1.549	0.034	0.313	0.266
	Age	−0.062	0.006		
	Pre-smoke	−10.039	<0.001		
	Post-smoke	9.154	<0.001		
FEV_1, % Δ	Obstruction	3.329	0.0362	1.368	0.294
	Age	−0.085	0.0081		
	Pre-smoke	−10.890	<0.001		
	Post-smoke	13.170	<0.001		
FEV_6, % Δ	Obstruction	3.812	0.002	1.267	0.310
	Age	−0.083	0.001		
	Pre-smoke	−8.926	<0.001		
	Post-smoke	9.099	<0.001		
FEV_1/FVC, % Δ	Chronic respiratory symptoms	−1.309	0.0381	0.828	0.130
	Post-smoke	2.204	0.008		
FEF_{25-75}, % Δ	Obstruction	14.953	0.001	0.091	0.144
	Smoking status	−6.792	0.025		
	Post-smoke	8.831	0.044		
Δ Peak Flow, % Δ	Obstruction	3.706	0.056	−0.754	0.038
Index of respiratory symptom, Δ	Total dust exposure (log TWA)	1.081	0.017	1.192	0.120
	Age	−0.020	0.085		
	Post-smoke	−1.11	0.030		

Independent variables included in models: Total dust exposure (log TWA), endotoxin exposure log TWA), age, obstruction, smoking status, smoke before pre-test, smoke before post-test, mask, pre-test exposure, number days in 1994 harvest, chronic symptom, past herbicide exposure.

endotoxin). This means that the number and/or extent of respiratory symptoms increased over the work shift as exposure to both total dust and endotoxin increased.

Other variables suspected to affect cross-shift respiratory symptoms, such as number of days harvested before the study, years of farm and harvesting work, report of chronic respiratory symptoms, presence of lung obstruction, job category, and whether the subject took over-the-counter medication during the day, were not related to the respiratory index.

It was thought that cross-shift changes in lung function parameters might be related to the respiratory index. Some studies of grain workers have shown larger falls in FEV_1 and $FEF_{50\%}$ among symptomatic workers.[19] However, a relationship between cross-shift symptoms (respiratory index) and cross-shift lung function was not demonstrated among the current study subjects.

Importantly, the subject's self-rating of his or her exposure level during the day was not related to the respiratory index. This implies that the perception of exposure level did not affect the self-reporting of respiratory symptoms. Related to this issue is the subject's self-rating of exposure level as compared to their actual exposure. The Pearson correlation coefficients for subject's self-rating of exposure versus actual exposure were −0.065 ($p = 0.52$) for total dust, 0.070 ($p = 0.49$) for endotoxin, and 0.193 ($p = 0.056$) for endotoxin to dust ratio. This means that the subjects were not able to accurately estimate their dust or endotoxin exposure levels. However, as the endotoxin concentration in the dust increased, they reported higher dust levels. This may mean that higher endotoxin concentration, not exposure, causes the acute reaction, which is interpreted as higher dust exposure by the subjects.

Models of Cross-Shift Lung Function Change

A backward regression model was employed to determine the significance of independent variables thought to be associated with cross-shift change in each lung function parameter and the respiratory index. The results are listed in Table VIII. The independent variables included in the models are listed at the bottom of the table. The findings were:

- Four variables met a 0.05 level of significance for the cross-shift change in FVC: age, smoking status, whether the subject smoked before the pre-test, and whether the subject smoked before the post-test. Age and smoking before the pre-test were negatively associated with change in FVC.

- Four variables met a 0.05 level of significance for the cross-shift change in FEV_1 and FEV_6: age, obstruction, whether the subject smoked before the pre-test, and whether the subject smoked before the post-test. Age and smoking before the pre-test were negatively associated with change in both FEV_1 and FEV_6.
- Only two variables met a 0.05 level of significance for the cross-shift change in the ratio FEV_1/FVC: chronic respiratory symptoms and whether the subject smoked before the post-test.
- Three variables significantly explained the cross-shift change in $FEF_{25-75\%}$: obstruction, smoking status, and whether the subject smoked before the post-test. Only one variable, obstruction, significantly explained the cross-shift change in PEFR.
- Finally, three variables met a 0.05 level of significance for the respiratory index: total dust exposure, age, and whether the subject smoked before the post-test. The model for respiratory index was the only one where exposure was a significant explanatory variable. There was also a small measure of protection for respiratory index associated with age. This may be related to the healthy worker effect. Those individuals most severely affected by the respiratory hazards are likely to have changed jobs or avoid harvest activities.

Although the variables included in the models were significant at reasonable p-values, the R-square values for models were small, suggesting that the significant variables could not explain the majority of the variation in the dependent variable. Therefore, the models do not provide reliable models from which to make inferences. Ultimately this means that lung function changes by spirometry and respiratory index are not well explained by total dust or endotoxin exposure, or the other significant variables. However, given the poor harvest and lower than normal dust levels (most below the TLV), a strong relationship between dust and respiratory response would not be expected.

CONCLUSIONS AND RECOMMENDATIONS

This research adds new data about worker exposure to dust and endotoxin during harvest in northeastern Colorado, and the relationship between those exposures and cross-shift respiratory changes. It is the only known study that compares cross-shift lung function change and dust and endotoxin exposure during harvest activities, which may be applicable to workers in other agricultural situations. This research confirms that dust exposure can be high at farms during harvest, even during a poor harvest season. Further, it was shown that endotoxin exposure could also be high during harvest. The exposure data indicated that acute cross-shift respiratory effects would be mild, with slight mucous membrane and mild bronchoconstriction expected. In fact, 60 subjects reported a cross-shift change in at least one acute respiratory symptom.

Individual correlation analysis showed that the respiratory index was significantly related to total dust and endotoxin exposure. Multiple regression analysis showed that the respiratory index was related to total dust exposure, age, and smoking before the final spirometry test. Mild, but measurable cross-shift decreases in lung volumes (FVC, FEV_1, and FEV_6) were observed. Moreover, PEFR was found to decrease over the work day, similar to that experienced by cotton workers, as compared to the general unexposed working population whose PEFRs typically increase over the day. Multiple regression analysis showed that smoking, age, presence of obstruction, and history of chronic respiratory symptoms, but not dust or endotoxin exposure, were associated with cross-shift change in the spirometric variables. More specific studies would have to be undertaken to validate any causal links suggested.

A number of recommendations have been made in previous studies conducted in agricultural environments. While ventilation has been added to harvest equipment over the years (generally for comfort, not dust control), this study shows that endotoxin levels may still be elevated in ventilated cabs. While substitution or technology change is preferred over personal protective devices, it is recommended that NIOSH-approved air-purifying respirators be worn by workers during dusty operations, such as unloading wheat from trucks or operating augers. These respirators have been shown to reduce pulmonary and systemic effects associated with farmer's lung under experimental challenge and during farm activities.[58] While a reduction was observed, pulmonary and systemic symptoms were not completely prevented, the few workers in this study who wore respirators reported reduced symptoms when wearing them. Because two of the four subjects wore disposable, single-strapped dust masks, some education on respirator selection would be useful.

Another recommendation is that an exposure level based on endotoxin (rather than total dust) should be considered. Endotoxin was associated with respiratory symptoms in this and many other epidemiology studies, and has been shown to be responsible for at least 70 percent of the inflammatory response to grain dust in cell cultures.

Based on the scope and findings of this research, future research areas might include:

- Investigation of lung function changes and endotoxin exposure during higher dust activities, such as working in the grain bins.
- Evaluation of lung function changes hourly for four to six hours after exposure ends, in addition to the immediate post-shift testing conducted in this study.
- Focused (case-study) endotoxin testing during more productive crop years, in particular to examine the effect of cab design and maintenance.
- Study of lung lavage, blood, or sputum inflammatory mediators (T-cell subsets or monocyte reactivity) in exposed workers and correlated with lung function changes.

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