# OCCUPATIONALLY INDUCED AIRWAYS OBSTRUCTION

Eric Garshick, MD, MOH, Marc B. Schenker, MD, MPH,
and James A. Dosman, MD

Exposure to a variety of inorganic dusts, organic dusts, and gases and fumes may result in chronic airflow obstruction as well as chronic cough and phlegm (chronic bronchitis) independent of cigarette smoking. This article provides an overview of the occupations most at risk for the development of airflow obstruction and chronic bronchitis as a result of workplace exposure and the agents most likely responsible.

## IDENTIFYING OCCUPATIONALLY RELATED AIRWAY DISEASES

An occupational respiratory hazard may be identified as a result of a case report, such as in occupational asthma, or by epidemiologic methods. Epidemiologic studies allow the recognition of patterns of disease attributable to an exposure by comparing the occurrence of disease between exposed and unexposed individuals and by evaluating the importance of potential confounding factors such as cigarette smoking. Cross-sectional or prevalence studies of workers actively employed in an industry are a common study design but tend to underestimate the prevalence and extent of disease because workers particularly af-

fected by an exposure may have left the workplace before the completion of the survey (the "healthy worker effect").

Longitudinal studies are more difficult to conduct than are cross-sectional surveys but have the advantage that pulmonary function measurements are compared within individuals, thus reducing variability between individuals unaccounted for by age, stature, adjustment for cigarette smoking, and other potential confounding factors.[5] Exposed workers tested at the beginning of a longitudinal study have had better lung function than unexposed workers of the same age,[80, 101] with an effect of exposure found only after follow-up. A community-based or general population–based epidemiologic study has the advantage that individuals can be studied without the potential for exclusion based on disability or illness. Recent studies have demonstrated an association between broadly based exposure histories obtained in general population surveys (dusts, gases, fumes) with chronic bronchitis and airflow obstruction.[1, 2, 59, 67, 85, 88, 89, 121, 122, 129]

## CHRONIC AIRFLOW OBSTRUCTION IN INDUSTRY-BASED AND WORKPLACE-BASED STUDIES OF MINERAL DUST EXPOSURES

### Coal Mining

Pulmonary function and respiratory symptoms have been extensively studied among coal miners in relation to measurements of dust exposure. Exposure to coal dust may result in chronic bronchitis and chronic airflow obstruction unrelated to simple coal workers' pneumoconiosis or to progressive massive fibrosis.

### Chronic Bronchitis

In studies of American[84] and British[105] miners, chronic bronchitis was related to respirable particle exposure. Pathology studies have also demonstrated a relationship between lifetime respirable dust exposure and bronchial mucous gland thickness.[47]

Marine and coworkers,[96] reanalyzing a cohort of British miners initially studied by Rogan and colleagues,[105] found that the prevalence of bronchitis ranged from 16.1% to 56.2% among smokers and was 6.4% to 44.4% in nonsmokers depending on the extent of dust exposure and age (Fig. 1). The joint contribution of cigarette smoking and dust exposure on the occurrence of bronchitis was generally additive. Respirable dust exposure was high by current standards, with levels of 3.1 to 3.7 mg/m$^3$ considered intermediate and exposures of 6.1 to 7.2 mg/m$^3$ considered high. In contrast, the U.S. standard for respirable dust in a coal mine was set at 3.0 mg/m$^3$ in 1970 with a reduction to 2.0 mg/m$^3$ in 1973.[110] Lifetime dust exposure was expressed as gram-hours per cubic meter of sampled air (gh/m$^3$). Over 30 years of mine work,

workers with intermediate exposure would have a cumulative exposure of approximately 174 gh/m³, and highly exposed workers would have a cumulative exposure of 348 gh/m³ (see Fig. 1).

A cohort of 1185 U.S. miners who started working in 1970 or later was studied by Seixas and colleagues[110] in 1985 through 1988 to assess the health effects of dust exposure under the new standards introduced in 1970. Cumulative dust exposure was still a significant predictor of chronic cough, chronic phlegm, and chronic bronchitis. The prevalence of chronic bronchitis among current smokers was 29.2%, among ex-smokers was 15.3%, and among never-smokers was 16.1%. These results indicate that dust exposure in coal mines under the current standards still results in chronic bronchitis.

## Airflow Obstruction

Lifetime exposure to respirable dust in a coal mine is a significant predictor of a reduced forced expiratory volume in 1 second ($FEV_1$), adjusting for cigarette smoking.[105] The relationship between dust exposure and $FEV_1$ is not related to the radiographic category of simple coal workers' pneumoconiosis. The average dust exposure experienced by a cohort of British miners (174 gh/m³) resulted in a 100-mL decrement in $FEV_1$ (0.6 mL per gh/m³), equivalent to smoking 20 cigarettes per day or aging 2 years.[105] An interaction between age and dust exposure indicated that there was a greater effect of dust on $FEV_1$ loss in younger workers compared with older workers. There was no interaction between smoking and dust exposure.

Love and Miller[91] subsequently analyzed longitudinal change in $FEV_1$ in a subset of these miners. Dust exposure occurring over an 11-year follow-up period was not a predictor of $FEV_1$ decline but previous exposure was, further suggesting that exposure to dust in younger workers is an important determinant of subsequent lung function loss. A worker with an exposure of 174 gh/m³ would be predicted to have an average decline in $FEV_1$ of 63 mL attributable to exposure, slightly less than in the cross-sectional survey reported by Rogan and colleagues[105] for the same dust exposure. A worker with the average dust exposure in the group studied by Love and Miller[91] (117 gh/m³) would have an 11-year decrement in $FEV_1$ of 42 mL (3.8 mL/y) because of exposure, less than the average effect of smoking (122 mL or 11 mL/y). Workers with greater exposure, however, would be predicted to have a longitudinal decline in $FEV_1$ similar to smoking.

Marine and coworkers[96] calculated the prevalence of reduced values of $FEV_1$ in the cohort studied by Rogan and colleagues[105] (Fig. 2). The prevalence of workers with a reduction in $FEV_1$ depended on the extent of exposure, age, and smoking status. Among smokers age 55 to 64, the prevalence of an $FEV_1$ less than 80% of predicted ranged from 36.2% to 56.2%. Among nonsmokers the same age, the prevalence of an $FEV_1$ less than 80% of predicted ranged from 0 to 31.6% depending on the extent of dust exposure (see Fig. 2). The prevalence of a greater reduction in

Rights were not granted to include this figure in electronic media. Please refer to the printed journal.

Rights were not granted to include this figure in electronic media. Please refer to the printed journal.

**Figure 1.** Prevalence of bronchitis in British miners according to smoking status and cumulative respirable dust exposure expressed in gram-hours per cubic meter (see text). N = number of men in exposure groups. (*Adapted from* Marine WH, Gurr D, Jacobsen M: Clinically important respiratory effects of dust exposure and smoking in British coal miners. Am Rev Respir Dis 137:106–112, 1988; with permission.)

Rights were not granted to include this figure in electronic media. Please refer to the printed journal.

Rights were not granted to include this figure in electronic media. Please refer to the printed journal.

**Figure 2.** Prevalence of $FEV_1 < 80\%$ and $FEV_1 < 60\%$ of predicted in British miners according to smoking status and cumulative respirable dust exposure expressed in gram-hours per cubic meter (see text). Predicted values for FEV, were calculated based on nonsmoking workers without chronic bronchitis. N = number of men in exposure groups. (*From* Marine WH, Gurr D, Jacobsen M: Clinically important respiratory effects of dust exposure and smoking in British coal miners. Am Rev Respir Dis 137:106–112, 1988; with permission.)

$FEV_1$ (<65% of predicted) was 23% among smokers and 14% among nonsmokers age 55 to 64 with the greatest lifetime dust exposure.

Hurley and Soutar[68] identified a subgroup of 199 British coal miners with bronchitic symptoms who had left the industry before retirement age and determined that these workers had experienced a greater effect of dust exposure than workers previously studied.[91, 105] There was approximately a 2 mL per $gh/m^3$ decrement in $FEV_1$, leading to a decrement in $FEV_1$ of roughly 350 mL for an exposure of 174 $gh/m^3$.

Among Eastern U.S. surface coal miners,[51] the prevalence of significant airflow obstruction, defined as a decrease in the ratio of $FEV_1$ to forced vital capacity (FVC) more than 2 standard deviations below predicted for age, was 6.6% among nonsmokers and 18.9% among smokers. In another group of American miners, the prevalence of an $FEV_1$-to-FVC ratio more than 2 standard deviations below predicted was 6.3% among nonsmokers, 13.8% among ex-smokers, and 17.8% among smokers.[84]

Among U.S. miners hired since 1970, lifetime respirable dust exposure was still a significant predictor of lower levels of FVC, $FEV_1$, and $FEV_1/FVC$ measured in 1985 through 1988, despite more stringent dust standards and lower exposures.[110, 111] The greatest effect of exposure on lung function was during the initial period of study when a parallel decrement in FVC and $FEV_1$ was observed without a decrease in $FEV_1/$ FVC. Soutar and Hurley[117] also found a parallel decrement in FVC and $FEV_1$ because of dust exposure in nonsmoking coal miners, whereas smoking miners had an obstructive abnormality. The mechanisms responsible for the greater initial effects of exposure on lung function, also noted by Rogan and colleagues[105] and Love and Miller,[91] and the parallel effect of exposure on FVC and $FEV_1$ in some studies have not yet been determined. The studies reported by Fairman and associates,[51] Kibelstis and colleagues,[84] and Marine and coworkers[96] suggest that nonsmokers as well as smokers develop an obstructive abnormality because of coal dust exposure.

## Pathology Studies

Autopsy studies have demonstrated an excess of emphysema in coal miners compared with control groups.[35, 108] The presence of centriacinar emphysema is associated with increasing evidence of simple coal workers' pneumoconiosis, progressive massive fibrosis, greater amounts of dust retained in the lung,[107] and a reduction in $FEV_1$.[108] Lifetime respirable coal dust exposure was a predictor of centriacinar emphysema only in the setting of palpable fibrotic lung lesions, suggesting an association between fibrosis (coal workers' pneumoconiosis) and the presence of emphysema. Because decrement in $FEV_1$ in epidemiologic studies of coal miners occurs independently of radiographic grade of pneumoconiosis, it is likely that the pathologic correlate of a reduction in $FEV_1$ in coal miners is not exclusively attributable to emphysema.

## Gold Mining

### Chronic Bronchitis

South African gold miners are exposed to dust with a greater silica content (30% to 75%) than are coal miners. In 1967, Sluis-Cremer and coworkers[115] reported that the prevalence of bronchitis in currently smoking gold miners was 50.5% versus 28% in controls and in ex-smokers was 15.9% versus 6.6% in controls, but in nonsmokers there was little difference (8.2% in the miners and 6.7% in the comparison group). Wiles and Faure,[126] studying a larger cohort and using measurements of respirable dust, demonstrated that the prevalence of bronchitis increased in current smokers, ex-smokers, and nonsmokers with cumulative exposure, with evidence of a survivor or a healthy worker effect (Fig. 3). Additionally, Australian gold miners working underground for 20 years or more had a fivefold elevated risk of bronchitis compared with nonminers.[66]

### Airflow Obstruction

Analyses of the cohort of gold miners described by Wiles and Faure[126] demonstrated that greater amounts of lifetime respirable dust

Rights were not granted to include this figure in electronic media. Please refer to the printed journal.

Figure 3. Bronchitis prevalence and respirable dust level in 2209 South African gold miners aged 45 to 54 years. At greater cumulative exposure levels (equivalent to approximately 25 years at a moderate level of exposure), the prevalence of bronchitis did not increase further and decreased in some groups, suggestive of a survivor or healthy worker effect. (Adapted from Wiles FJ, Faure MH: Chronic obstructive lung disease in gold miners. In Walton WH, McGowan B (eds): Inhaled Particles IV, part 2. Oxford, Pergamon Press, 1977, pp 727–735; with permission.)

exposure were associated with a decrease in $FEV_1$, FVC, $FEV_1$/FVC, and mean forced expiratory flow over the middle half of the vital capacity ($FEF_{25\%-75\%}$) after adjustment for smoking and were not related to the presence of silicosis.[62, 63, 71] Based on a regression model, a 50-year-old gold miner exposed over 24 years to an average level of 0.3 mg/m³ (14.4 gh/m³) of respirable dust would have an excess $FEV_1$ loss of 236 mL (approximately 10 mL/y). For miners in the highest quartile of exposure (22 gh/m³), the $FEV_1$ loss because of dust would be 361 mL (15 mL/y). For a 30–pack-year smoker, the average effect of smoking would be a decrement in $FEV_1$ of 552 mL, an effect roughly double the average effect of dust exposure. The combined effect of smoking and dust exposure on $FEV_1$ was additive.

A study in 1197 black South African gold miners gave similar results.[37] Years of dust exposure, pack-years of cigarette smoking, and profusion of silicotic nodules on radiography were independent predictors of a reduced $FEV_1$, $FEV_1$/FVC, and $FEF_{25\%-75\%}$. The mean decrement in $FEV_1$ per year of dust exposure was 8 mL, or 200 mL over 25 years.

### Pathology Studies

Autopsy studies of South African gold miners have also demonstrated an excess of emphysema related to dust exposure.[7, 64] Years of work in high-dust areas of the mine and cumulative dust exposure were significant predictors for emphysema after adjusting for smoking and age. Silicosis grade was not a significant predictor of emphysema in one smaller study[7] (86 workers), whereas in other larger study[64] (1553 workers), a significant association was noted between silicosis and centriacinar emphysema.

Few nonsmoking gold miners, however, had significant emphysema.[64, 65] When these gold miners were analyzed separately from the smokers, the extent of emphysema was not associated with years of mining or cumulative dust exposure. These results suggest that the association between dust exposure and pathology evidence of emphysema in gold miners applies only in miners who smoke.

## Other Mineral Dust Exposed Workers

### Chronic Bronchitis and Airflow Obstruction

**Other Miners.** Among hard rock mining industry workers exposed to dust and fumes from zinc, copper, and nickel mining and processing,[95] with respirable dust exposure of underground workers ranging from 0.2 to 4.8 mg/m³ (median value of 0.5 mg/m³, 6% to 9% silica), the prevalence of cough and phlegm (symptoms of bronchitis) was more frequent among current smokers and never-smokers in underground miners than in controls. In an additional 7-year longitudinal study of 972 hard rock miners and smelter workers,[94] there was a decline in $FEV_1$ varying

between 33 and 69 mL per year for workers in various job categories. The decline in $FEV_1$ was of similar magnitude to that attributable to smoking.

Among hard rock miners (molybdenum miners in Colorado) studied 5 to 11 months after the closure of their mine and not currently employed,[86] there was an increase in total lung capacity (TLC) and residual volume (RV), a decrease in single-breath carbon monoxide diffusion capacity adjusted for alveolar volume ($DL_{CO}/V_A$), and a decrease in expiratory flow rates with cumulative dust exposure in smokers. In nonsmoking miners, there was a decrease in TLC and RV and an increase in $DL_{CO}/V_A$ with cumulative exposure. Maximal expiratory flows were increased when flow rates were compared at equivalent lung volumes, suggesting a restrictive rather than an obstructive abnormality attributable to dust exposure in nonsmoking miners.

**Asbestos Exposure.** Evidence of airflow obstruction attributable to asbestos exposure has been described by Becklake and coworkers.[6] Small airway abnormalities have been noted. In asbestos workers with normal values for $FEV_1$ and $FEV_1/FVC$ and normal chest radiographs, but with heavy dust exposure, maximal expiratory flows at any transpulmonary pressure were less over the range of lung volume than in workers with less exposure.[75] In nonsmoking asbestos workers with asbestosis compared with nonsmoking workers without asbestosis, there were reductions in flow at low lung volumes.[8, 9]

**Other Mineral Exposures.** Wollastonite is a fibrous monocalcium silicate used in the manufacture of wall tile, ceramics, grinding wheels, and refractory products. In a study of 108 workers in a wollastonite mine and mill, lifetime dust exposure was a significant predictor of a lower $FEV_1$, $FEV_1/FVC$, and peak flow rate adjusting for smoking and age.[57] Kauffmann and coworkers[79, 80] reported on a decline in $FEV_1$ of 51 to 65 mL per year (Table 1) among Paris-area factory workers attributable to occupational exposure to various mineral and plant dusts compared with 42 mL per year in unexposed workers.

**Mixed Dust, Gas, and Fume Exposures.** In a study among 861 foundry workers, the prevalence of phlegm production for at least 3 months out of the year was elevated among both current smokers and nonsmokers in high dust exposure areas relative to workers with less exposure.[77] An excess of bronchitis has also been reported among coke industry workers.[92, 123]

Welding produces a mixture of gases, particles, and metal oxide fumes. Much of the fume is of respirable size. Cross-sectional studies of pulmonary function have demonstrated a decrement primarily of mid-flow rates suggestive of an effect in the smaller airways.[112] Elevated rates of bronchitis and an increased yearly decline in $FEV_1$ also have been reported among smoking and nonsmoking welders.[32, 112]

*Pathologic Studies*

The earliest changes of asbestosis in animals are peribronchiolar inflammation with compression of the small airways.[10] Pathology evi-

**Table 1.** FEV₁ SLOPE ADJUSTED FOR AGE, SMOKING, AND FEV₁ LEVEL
ACCORDING TO OCCUPATIONAL EXPOSURE IN PARIS AREA WORKERS
WITH DUST EXPOSURE

Rights were not granted to include this data in electronic media. Please refer to the printed journal.

*From* Kauffmann F, Drouet D, Lellouch J, et al: Occupational exposure and 12-year spirometric changes among Paris area workers. Br J Ind Med 39:221–232, 1982; with permission.

dence of small airway abnormalities also has been noted in human studies, in which lung biopsy in three workers demonstrated macrophages and mononuclear cells in the alveoli as well as in the interstitium surrounding the small airways.[9] The small airways were distorted and narrowed, with thickened walls. Fibrosis of the walls of the respiratory bronchioles and alveolar ducts with pigment deposition was present.[127] At autopsy, long-term Canadian chrysotile miners had more fibrosis of the alveolar ducts and respiratory bronchioles than controls without occupational dust exposure matched on age and smoking history.[128]

Hard rock miners as well as workers in other dusty occupations (foundry worker, metal machinist, welder, construction worker) have pathologic changes in the airways similar to the changes in the airways of asbestos-exposed workers, with fibrosis in the walls of the alveolar ducts and respiratory bronchioles and pigment deposition.[33, 34] Among individuals who had a lobectomy or pneumonectomy because of lung cancer,[83] fibrosis and goblet cell metaplasia in the walls of the terminal bronchioles of workers with mineral dust exposure (>10 years) were present.

## CHRONIC AIRFLOW OBSTRUCTION IN INDUSTRY-BASED AND WORKPLACE-BASED STUDIES OF ORGANIC DUST EXPOSURES

### Grain Dust

Grain dust includes particles of grain as well as various insect and rodent parts and excreta, soil (including quartz), mites, and fungi.

Exposure to grain dust may cause acute reversible airflow obstruction (asthma) as well as shift-related and harvest season–related decrements in lung function.[74] Broder and coworkers[16] described a minimal restrictive defect rather than an obstructive defect in association with an increase in grain elevator work over 2.5 months. Respiratory symptoms such as cough and sputum production also occur soon after hire in grain workers, and symptoms improve after layoffs occur.[16, 18] Workers who do not develop respiratory symptoms such as cough and sputum production are more likely to stay on the job, consistent with a healthy worker effect.[15]

## Chronic Bronchitis

Surveys of various groups of grain industry workers have found an excess of bronchitic symptoms attributable to exposure.[17, 24, 43, 44] Dosman and coworkers[43, 44] demonstrated that among lifetime nonsmoking and currently smoking Saskatchewan grain workers, chronic bronchitis was present in 3.5% of nonsmoking community controls, 16.5% of nonsmoking grain workers, 25% of smoking controls, and 36.5% of smoking workers—a roughly additive effect of exposure and smoking on the prevalence of chronic bronchitis. DoPico and colleagues[41] studied 300 U.S. grain elevator workers and found that 30% of the nonsmokers had symptoms of chronic bronchitis. Average 8-hour total dust levels in these elevators were quite high and ranged from 10.3 to 253 mg/m$^3$, with 66% greater than 15 mg/m$^3$, the dust standard at the time.

Among grain workers studied by Chan-Yeung and coworkers[24] in five surveys of active workers between 1976 and 1988, the prevalence of respiratory symptoms was compared with a control group of civic workers at each survey. With the exception of wheeze in two of the surveys (Table 2), the smoking-adjusted and age-adjusted relative odds of the grain workers reporting cough, phlegm, wheeze, or dyspnea were consistently elevated. Average lifetime exposure was calculated for workers studied in the 1988 survey, and after adjustment for age and smoking, the prevalence of chronic cough and chronic wheeze increased with increasing exposure.[69]

## Airflow Obstruction

Multiple studies in grain dust–exposed workers have consistently related chronic exposure to lower levels of lung function. In a cross-sectional study, Dosman and coworkers[36, 42] reported that years of work as grain elevator operator was a predictor of a lower $FEF_{25\%-75\%}$, with an additive effect of smoking on $FEF_{25\%-75\%}$. A longitudinal study of workers in the Canadian grain industry (studied in three cycles—1978–1981, 1981–1984, and 1984–1987[100]) demonstrated that the decline in $FEV_1$ among nonsmoking grain workers was greater than reported for a sample of nonsmokers recruited from six U.S. cities (Table 3).[124] The grain workers exhibited a similar loss in FVC, suggestive of a restrictive

**Table 2.** ODDS RATIOS AND 95% CONFIDENCE INTERVALS (IN PARENTHESES) FOR RESPIRATORY SYMPTOMS IN BRITISH COLUMBIA GRAIN WORKERS COMPARED WITH CIVIC WORKERS, FIVE CROSS-SECTIONAL STUDIES, 1976–1988*

Rights were not granted to include this data in electronic media. Please refer to the printed journal.

*From* Chan-Yeung M, Dimich-Ward H, Enarson D, et al: Five cross-sectional studies in grain elevator workers. Am J Epidemiol 136:1269–1279, 1992; with permission.

rather than obstructive defect. Studies in British Columbia grain terminal workers also suggest the development of a restrictive rather than an obstructive defect because of chronic grain dust exposure.[24, 69] The average effect of each milligram per cubic meter of grain dust on FVC and $FEV_1$ was equivalent to smoking one sixth of a pack of cigarettes per day. Lung function loss was unrelated to atopy or respiratory symptoms.[118] Sufficient prospective data were not available to assess whether nonspecific bronchial responsiveness was a risk factor prospectively.

**Table 3.** $FEV_1$ DECLINE BY AGE GROUP IN NONSMOKING GRAIN ELEVATOR WORKERS COMPARED WITH POPULATION-BASED ESTIMATES FROM NONSMOKERS IN SIX U.S. CITIES*

Rights were not granted to include this data in electronic media. Please refer to the printed journal.

*From* Pahwa P, Senthilselvan A, McDuffie HH, Dosman J: Longitudinal estimates of pulmonary function decline in grain workers. Am Rev Respir Crit Care Med 150:656–662, 1994; with permission.

The pathologic correlate of the decrease in FVC and $FEV_1$ in grain workers is unknown, and the component of the grain dust responsible is unknown. In the studies by Chan-Yeung and coworkers,[24] radiographic films were obtained during the initial survey, and no evidence of pneumoconiosis was noted to account for this apparent restrictive ventilatory defect. During the studies previously noted, the Canadian standard for an 8-hour time-weighted average for exposure to grain dust was 10 mg/m$^3$. These results suggest that this standard may not be adequate because workers with average exposure below 10 mg/m$^3$ had an excess decline in lung function attributable to exposure. An alternative explanation is that an additional, unmeasured factor is also responsible. For example, in Dutch animal feed workers, airborne endotoxin levels were a stronger predictor of a reduced $FEV_1$ than were dust levels.[116]

## Cotton Dust

### Byssinosis and Chronic Bronchitis

Cotton dust is a mixture that is present in the air after handling or processing cotton and contains plant matter, bacteria, fungi, soil, and other contaminants. Inhalation of cotton, flax, or hemp dust is associated with byssinosis, a syndrome characterized by chest tightness and shortness of breath occurring on the Monday morning back at work. Cigarette smoking increases the prevalence of byssinosis,[12, 99] with one study demonstrating a more than additive effect of smoking in association with high dust levels.[97] Symptoms are generally associated with a reversible drop in $FEV_1$ across a work shift.[70, 132] Workers with byssinosis are likely to exhibit nonspecific bronchial hyperresponsiveness,[52] and atopy is a risk factor for developing an acute decrement in $FEV_1$ and bronchial responsiveness following cotton dust exposure.[73]

North Carolina textile workers studied in the early 1970s revealed a dose-response relationship between dust levels and the prevalence of byssinosis and between dust levels and drop in $FEV_1$ over 6 hours on a Monday following 2 days away from work.[97, 98] Exposure to cotton dust is associated with symptoms of chronic bronchitis that tend to coexist with byssinosis.[12, 70, 97, 99]

A dose-response relationship between airborne endotoxin concentrations and drop in $FEV_1$ independent of cotton dust concentrations has been noted.[22, 23] Kennedy and coworkers[81] studied Shanghai cotton mill workers and demonstrated a dose-response relationship between endotoxin levels and cross-shift change in $FEV_1$.

### Airflow Obstruction

In active and retired South Carolina textile workers, similar decrements in FVC and $FEV_1$ were found, suggestive of a restrictive rather

than an obstructive defect.[14] The effect of smoking and working as a textile worker was additive in the prediction of a reduced FVC and $FEV_1$.[3] Lung function loss was greater than in a control group in a 6-year follow-up study[4]; however, the study population may have been self selected on the basis of respiratory symptoms, and the use of this particular control group has been questioned.[38, 120]

The decline in $FEV_1$ in Lancashire cotton mill workers was not related to dust levels and was similar to that in a group of workers from a control mill.[11] In ex-Lancashire cotton workers, the effect of past work in the carding section of a mill was a decrement in $FEV_1$ of 150 to 180 mL compared with workers without dust exposure, and for all job categories, the $FEV_1$ was 2% to 8% less compared with unexposed workers.[50]

Cotton yarn manufacturing workers studied at least three times over 3 to 5 years had an annual decline in $FEV_1$ 1.5 times that of other cotton textile workers (cotton slashing or weaving) despite having lower cumulative dust exposures, suggesting differences in dust potency or the effect of an unmeasured factor.[55] Similar findings were noted for FVC, but the decline was less than the $FEV_1$, consistent with the development of an obstructive defect. There was an interaction between exposure and smoking, with current smokers exhibiting the greatest effects of exposure on lung function. Cross-shift change in $FEV_1$ was also a predictor of longitudinal decline in $FEV_1$.[56]

### Pathologic Studies

The available studies do not suggest that cotton dust exposure results in pathologic evidence of emphysema.[104] The changes described are those of chronic bronchitis.[48, 49]

## Agricultural and Farm Workers; Other Organic Dusts

Agricultural workers are potentially exposed to a variety of gases as well as various organic and inorganic dusts. Farmers and farm workers are exposed to silica and various nonfibrous silicates in soils and to minerals used as fillers in pesticides. Workers in animal confinement houses work in an enclosed environment that is often poorly ventilated with large numbers of animals in a relatively small space. In addition to the organic dust that is present (grain, animal, mites, insect, bacterial and fungal products) the animals produce large amounts of manure and urine that decompose. Gases given off include hydrogen sulfide, ammonia, and methane. Silo workers may also be exposed to nitrogen dioxide as well as to dust related to feed storage.

### Chronic Bronchitis

Pig farmers and swine containment workers have an increased risk of chronic bronchitis.[46, 72, 131] Chronic cough and chronic bronchitis in

swine producers have been related to endotoxin levels measured in swine containment buildings but were not related to measurements of respirable dust.[130] In a study of animal feed workers, the odds ratios for chronic cough and chronic phlegm were elevated in individuals with 2 to 10 years of work in the animal feed industry.[116] Dosman and colleagues[45] have demonstrated an increased prevalence of respiratory symptoms in grain farmers.[45] Manfreda and associates,[93] however, found no association between work as a grain farmer and cough, phlegm, or chronic bronchitis. Similarly, Gamsky and coworkers[53] studied 759 California Central Valley field workers and found a low prevalence of chronic cough (1.6%) and chronic phlegm (5.1%), but chronic cough was independently associated with agricultural work. Other organic dusts associated with bronchitis are wood dusts and dust from flour processing.[113, 114]

### Airflow Obstruction

Manfreda and coworkers[93] found little evidence of an effect of farming on pulmonary function in a study of grain farmers. In contrast, Dosman and colleagues[45] demonstrated a reduction in $FEV_1$ and FVC and an increased $FEV_1/FVC$ in farmers growing mainly wheat and other field crops. Similarly, in California grape workers, a reduction in FVC but not $FEV_1/FVC$ was noted, suggestive of a restrictive defect rather than an obstructive defect.[54] Pulmonary function abnormalities described in swine production workers have included a reduction in $FEV_1/FVC$, $FEV_1$, and $FEF_{25\%-75\%}$ relative to a control group[131] as well as reduced $FEV_1$ and FVC with a preserved $FEV_1/FVC$.[46] Endotoxin levels in swine containment buildings were significantly related to a reduced FVC but not $FEV_1$.[130] Dust exposure and exposure to ammonia were also predictors of changes in pulmonary function over a work week.[39]

In a study of 63 nonsmoking South African bakery workers and 63 nonsmoking controls who worked in a bottling plant, there were significantly lower values for $FEV_1$ and $FEV_1/FVC$ among the bakery workers.[114] Wood workers with respiratory symptoms had significantly lower values for $FEV_1$ and $FEV_1/FVC$ compared with other workers who were not symptomatic.[21] Shamssain[113] studied 145 nonsmoking workers exposed to wood dust in the furniture industry in South Africa and compared their pulmonary function with nonsmoking controls and had similar findings. The workers exposed to wood dust had lower values for $FEV_1$, $FEV_1/FVC$, and FVC.

## EXPOSURE TO GASES AND FUMES

Brooks and others[19, 119] have described reactive airways dysfunction syndrome (RADS), the asthmalike syndrome that may develop following exposure to high concentrations of an irritant gas, vapor, fume, or dust. Workers exposed to high concentrations of sulfur dioxide may develop this syndrome and exhibit persistent bronchial hyperresponsiveness. In

one study of six men followed after exposure, the greatest decrease in $FEV_1$, $FEV_1/FVC$, and FVC occurred at 1 week postexposure.[58] Four weeks postexposure, there was a slight improvement, but over the next 4 years a persistent obstructive pattern was noted with a mean $FEV_1$ of roughly 60% of predicted.

After acute gassing with sulfur dioxide in a paper mill, autopsies in two workers revealed denudation of airway mucosa and hemorrhagic alveolar edema. Among three survivors, pulmonary function tests 116 days after the event revealed that one subject had a severe obstructive defect with an $FEV_1$ of 61% of predicted 1 day after exposure falling to 38% of predicted, one person was asymptomatic with normal tests, and one person had mild airflow obstruction.[31]

Workers in a copper smelter more chronically exposed to sulfur dioxide did not have an accelerated loss of $FEV_1$.[106] In a cross-sectional survey in a pulp and paper mill, workers exposed to gases including sulfur dioxide also did not have decrements in pulmonary function compared with other workers.[29] In workers from a Berlin, New Hampshire paper mill who had experienced episodes in which they were overcome by gases or fumes (called *gassing* episodes, involving sulfur dioxide, hydrogen sulfide, or chlorine), however, the average effect of reporting a history of gassing was a decrement in $FEV_1$ of 292 mL, a decrement in FVC of 195 mL, and a decrease in $FEV_1/FVC$ of 5% relative to other workers.[61] Among workers who had been gassed in a pulp mill (mainly exposed to chlorine gas), there was a higher prevalence of wheezing and lower values of $FEV_1/FVC$.[85] In an additional study of pulp mill workers repeatedly exposed to chlorine, an 18- to 24-month follow-up identified a subset with persistent respiratory symptoms, airflow obstruction, and bronchial hyperresponsiveness.[13] Chan-Yeung and associates[27] further described three pulp mill workers with persistent asthma after multiple gassing episodes.

Acute chlorine exposure alone has resulted in persistent airflow obstruction and bronchial hyperreactivity or in airflow obstruction that can resolve.[30, 40, 103, 109] Weill and coworkers[125] studied 12 subjects for up to 7 years after exposure following a freight car derailment and found no appreciable abnormality. Similarly, Jones and coworkers[76] studied 60 workers over a 6-year period acutely exposed after a train derailment and found no new cases of asthma, no increase in respiratory symptoms, and no unexpected decline in $FEV_1$. Severe airflow obstruction persistent over 12 years and bronchiectasis have also been noted following acute ammonia inhalation.[78, 90] Thus, the long-term consequence of acute exposure to a gas or fume may result in persistent airflow obstruction and an asthmalike syndrome, or there may be resolution of initial abnormalities.

## CHRONIC PERSISTENT OCCUPATIONAL ASTHMA

Occupational asthma is discussed elsewhere in this issue. Despite removal of the worker from workplace, persistent asthma has been

described in asthma because of toluene diisocyanate, Western red cedar, and colophony as well as in crab processors.[26, 102] Chan-Yeung and coworkers[28] described Western red cedar workers with occupational asthma who remained symptomatic on average 3.5 years after leaving work, suggesting that the early diagnosis of occupational asthma may prevent subsequent airflow obstruction. Persistent asthma may result in irreversible airflow obstruction.[20]

## COMMUNITY SURVEYS

### Chronic Bronchitis

Korn and coworkers[85] reported on the association between respiratory symptoms and occupational exposures to dust or gases and fumes in a random sample of 8515 adults age 25 to 74 residing in six U.S. cities. Lifetime occupational histories were obtained by interviewer. The prevalence of any occupational dust exposure was 45% among the men and 19% among the women; 14% of the men and 10% of the women reported gas or fume exposure. A history of occupational dust exposure, history of exposure to gases or fumes, and the combined history of exposure were significant predictors of chronic cough, chronic phlegm, persistent wheeze, and breathlessness (Table 4). On repeat assessment 3 and 6 years later, workers with current exposure to dust or gases and fumes had a greater prevalence of respiratory symptoms compared with workers in whom exposure had ceased.

Studies have been done in general population samples from France,[89] the Netherlands,[59, 60] Poland,[87] Italy,[122] China,[129] Denmark,[121] and Norway.[2] Each study gave similar results with an increased odds of

**Table 4.** ODDS RATIOS AND 95% CONFIDENCE INTERVALS (IN PARENTHESES) FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE* AND RESPIRATORY SYMPTOMS IN SIX U.S. CITIES

Rights were not granted to include this data in electronic media. Please refer to the printed journal.

*From* Korn RJ, Dockery DW, Speizer FE, et al: Occupational exposure and chronic respiratory symptoms: A population based study. Am Rev Respir Dis 136:298–304, 1987; with permission.

reporting symptoms of chronic bronchitis, breathlessness, and wheeze after adjustment for age and potential confounding factors such as cigarette smoking (Table 5). Heederik and colleagues[59, 60] defined a syndrome called *chronic nonspecific lung disease* based on respiratory symptoms such as regular cough, phlegm, or wheezing and a clinical diagnosis of chronic obstructive pulmonary disease (COPD) by a physician. There was regular follow-up over 25 years (1960–1985). The rate ratio for the occurrence of chronic nonspecific lung disease over 25 years because of exposure to dust, gas, or fumes reported in 1960 was significantly elevated at 1.4 (95% confidence interval [CI] = 1.07, 1.85) adjusting for confounders.

Xu and coworkers[129] and Korn and colleagues[85] specifically addressed the interaction of smoking and occupational exposures and found that the joint effect was not more than additive. These authors also noted that with increasing years of exposure to dust, the greater the relative odds of reporting chronic cough, chronic phlegm, breathlessness, and persistent wheeze.

## Airflow Obstruction

Korn and coworkers[85] found that the relative odds of a decreased $FEV_1/FVC$ (<0.60) adjusting for smoking, age, and sex was significantly elevated in individuals from six U.S. cities reporting dust exposure and combined dust and gas exposure. The results of various studies of airflow obstruction and occupational exposure are summarized in Table 6. In 8692 men in France, Krzyzanowski and Kauffmann[89] found that dust exposure was a significant predictor of a decrease in $FEV_1/FVC$. In a study in a general population sample near Venice, Viegi and coworkers[122] found that men exposed to dusts, fumes, or chemicals had an increased odds of an $FEV_1/FVC$ less than 0.70 (odds ratio = 1.45; 95% CI = 1.03, 2.45). Krzyzanowski and coworkers[88] in a study in Poland found an excess average loss of function attributable to dust exposure of 6.9 mL per year in a 13-year longitudinal study. In Norway, there were increased odds of either asthma or COPD in those with dust, fume, or gas exposure.[1] Humerfelt and coworkers[67] reported that multiple occupational exposures to various dusts and gases resulted in an excess decline in $FEV_1$. Dust exposure and gas and fume exposure were independent predictors of reduced levels of FVC, $FEV_1$, $FEV_1/FVC$, and $FEF_{25\%-75\%}$ in a sample of the general population of Beijing.[129] Korn and associates[85] found no interaction between smoking and occupational exposure on the odds of a $FEV_1/FVC$ less than 0.60. Xu and coworkers,[129] however, found a multiplicative effect between smoking and dust exposure on a reduced $FEV_1/FVC$ suggesting that smokers were more susceptible to the effects of dust.

**Table 5.** RELATIONSHIP BETWEEN OCCUPATIONAL EXPOSURE TO DUST AND GAS/FUMES IN THE GENERAL POPULATION AND SELECTED RESPIRATORY SYMPTOMS ADJUSTED FOR AGE AND SMOKING

| Reference | Population | Exposure | Health Effect | Odds Ratio | 95% Confidence Interval |
|---|---|---|---|---|---|
| Krzyzanowski and Kauffmann[89] | 8692 men in France | 34% to dust, gas, or fumes | Chronic cough | 1.36 | 1.18, 1.57 |
| | | | Chronic bronchitis | 1.53 | 1.27, 1.85 |
| | | | Wheezing | 1.63 | 1.45, 1.83 |
| | 7772 women in France | 23% to dust, gas, or fumes | Chronic cough | 1.37 | 1.09, 1.73 |
| | | | Chronic bronchitis* | 2.09 | 1.41, 3.12 |
| | | | Wheezing | 1.70 | 1.45, 1.83 |
| Viegi et al[122] | 1027 men near Venice age 18–64 | 30.9% to dusts, chemicals, or fumes | Chronic cough | 1.69 | 1.17, 2.43 |
| | | | Chronic phlegm | 1.64 | 1.14, 2.36 |
| | | | Persistent wheeze | 1.41 | 0.94, 2.01 |
| Heederik et al[59] | 804 Dutch men 40–59 in 1960, followed to 1985 | 29.7% to dust, gas, or fume in 1960 | Episodes of respiratory symptoms or diagnosis of COPD | 1.40† | 1.07, 1.85 |
| Krzyzanowski and Jedrychowski[87] | 1132 men in Poland surveyed in 1968, 1973, 1981, age 19–60 in 1968 | 21.8% to dust both in 1968 and 1973 | Chronic phlegm reported in 1973 or 1981 | 2.10 | 1.50, 3.00 |
| Bakke et al[2] | 2220 men and 2249 women in Norway age 15–70 | 45.7% men, 11.9% women dust or gas | Chronic cough‡ | 1.80 | 1.40, 2.20 |
| | | | Phlegm with cough | 1.90 | 1.60, 2.20 |
| | | | Breathlessness | 1.70 | 1.40, 2.20 |
| Vestbo et al[121] | 698 men in Denmark surveyed in 1974 and 1985, mean age 56 in 1974 | 195 cement workers | Cough in 1974 and 1985 | 2.60 | 1.04, 6.51 |
| | | 360 other blue collar workers | Cough in 1974 and 1985 | 1.37 | 0.58, 3.24 |
| Xu et al[129] | 1762 men and 1844 women age 40–69 in Beijing, China | 37.7% dust in men; 27% dust in women | Chronic cough‡ | 1.32 | 1.09, 1.59 |
| | | | Chronic phlegm | 1.27 | 1.07, 1.50 |
| | | | Breathlessness | 1.39 | 1.16, 1.65 |
| | | | Persistent wheeze | 1.02 | 0.77, 1.36 |
| | | 24% gas/fume in men; 14.4% gas/fume in women | Chronic cough‡ | 1.17 | 0.94, 1.46 |
| | | | Chronic phlegm | 1.21 | 1.00, 1.48 |
| | | | Breathlessness | 1.31 | 1.06, 1.61 |
| | | | Persistent wheeze | 1.62 | 1.18, 2.21 |

*10 or more years' exposure.
†Rate ratio.
‡Adjusted for sex.
COPD = Chronic obstructive pulmonary disease.

Table 6. RELATIONSHIP BETWEEN OCCUPATIONAL EXPOSURE TO DUST AND GAS/FUMES IN THE GENERAL POPULATION AND PULMONARY FUNCTION ADJUSTED FOR AGE AND SMOKING

| Reference | Population | Exposure | Health Effect | Outcome |
|---|---|---|---|---|
| Krzyzanowski and Kauffmann[89] | 8692 men in France | 34% to dust, gas, or fumes | $FEV_1/FVC$ | Significant predictor of a decreased $FEV_1/FVC$ |
| Viegi et al[122] | 1027 men near Venice age 18–64 | 43% to dusts, chemicals, or fumes | Odds of $FEV_1/FVC <70\%$ or $FEV_1 <70\%$ | OR = 1.45 95% CI = 1.03, 2.05 |
| Krzyzanowski et al[88] | 759 men in Poland studied 1968–1981 | 30% exposed to dust in 1968 | $FEV_1$ slope between 1968–1981 | Slope = 6.9 mL/y related to dust exposure |
| Bakke et al[1] | 714 men and women in Norway age 18–73 | 3.5% with high exposure; 26.8% moderate exposure to dusts, fumes, or gases | Odds of asthma or COPD* (see text) | High exposure—OR = 3.60; 95% CI = 1.30, 9.90 Low exposure—OR = 1.40; 95% CI = 0.90, 3.00 |
| Xu et al[129] | 1094 men and women age 40–69 in Beijing, China | 27.8% dust only 8% fume or gas only 15.6% both | $FEV_1$; $FEF_{25\%-75\%}$ $FEV_1/FVC*$ $FVC$; $FEV_1$* | Dust exposure a predictor of reduced levels Decrease with greater categories of exposure |
| Humerfelt et al[67] | 911 men age 22–54 in Norway followed from 1965–1970 through 1988–1990 | Self-report of exposure at initial survey; 43% with dust, gas, or fume | $FEV_1$ slope | Increased slope for workers exposed to multiple agents; slope of 1.09 mL/y per agent |
| | | | $FEV_1/FVC <0.65$ | OR = 1.3; 95% CI = 0.80, 2.20 for any dust, gas, fume exposure |

*Adjusted for sex.
$FEV_1/FVC$ = Forced expiratory volume in 1 second/forced vital capacity; OR = odds ratio; CI = confidence interval; COPD = chronic obstructive pulmonary disease; $FEF_{25\%-75\%}$ = forced expiratory flow, midexpiratory phase.

## SUMMARY

The studies reviewed in this article indicate the association of occupational exposure to a variety of organic and inorganic dusts and various gases and fumes with chronic bronchitis and decrements in $FEV_1$. Usually an obstructive pattern was noted, although in some occupations a similar decrement in FVC was noted. The effect of smoking on chronic bronchitis, respiratory symptoms, and $FEV_1$ was usually additive, although workers exposed to cotton dust in one study[55] demonstrated an interaction between exposure and smoking, as did a study of a general population sample.[129] In coal workers, exposure to dust in younger workers resulted in a greater decline in lung function than if the exposure occurred in older workers. Studies in coal miners and grain workers further suggest that occupational standards in effect are not sufficient to protect the working population from adverse effects.

The magnitude of the effect of occupation on decrement in $FEV_1$ is usually less than cigarette smoking. Studies in coal miners[68] indicate, however, that a minority of workers could be more severely affected by exposure. When considered together with cigarette smoking, additional decrements in lung function because of occupational exposure could contribute to disability. Additional study is needed for better understanding of exposure-response relationships, host factors, potential interaction with cigarette smoking, and the pathophysiology of the development of occupationally induced airway disease.

## References

1. Bakke PS, Baste V, Hanoa R, et al: Prevalence of obstructive lung disease in a general population: Relation to occupational title and exposure to some airborne agents. Thorax 46:863–870, 1991
2. Bakke PS, Eide GE, Hanoa R, et al: Occupational dust or gas exposure and prevalences of respiratory symptoms and asthma in a general population. Eur Respir J 4:273–278, 1991
3. Beck GJ, Maunder LR, Schachter EM: Cotton dust and smoking effects on lung function in cotton textile workers. Am J Epidemiol 119:33–43, 1984
4. Beck GJ, Schachter EM, Maunder LR, et al: A prospective study of chronic lung disease in cotton textile workers. Ann Intern Med 97:645–651, 1982
5. Becklake MR: Chronic airflow obstruction: Its relationship to work in dusty occupations. Chest 88:608–617, 1985
6. Becklake MR, Fournier-Massey G, Rossiter CE, et al: Lung function in chrysotile asbestos mine and mill workers of Quebec. Arch Environ Health 24:401–409, 1972
7. Becklake MR, Irwig L, Kielowski D, et al: The predictors of emphysema in South African gold miners. Am Rev Respir Dis 135:1234–1241, 1987
8. Begin R, Boileau R, Peloquin S: Asbestos exposure, cigarette smoking, and airflow limitation in long-term Canadian chyrostile miners and millers. Am J Ind Med 11:55–66, 1987
9. Begin R, Cantin A, Berthiaume Y, et al: Airway function in lifetime-nonsmoking older asbestos workers. Am J Med 75:631–638, 1983
10. Begin R, Masse S, Bureau MA: Morphologic features and function of the airways in early asbestosis in the sheep model. Am Rev Respir Dis 120:870–876, 1982
11. Berry G, McKerrow CB, Molyneux MKB, et al: A study of the acute and chronic

changes in ventilatory capacity of workers in Lancashire cotton mills. Br J Ind Med 30:25–36, 1973

12. Berry G, Molyneux MKB, Tombleson JBL: Relationships between dust level and byssinosis and bronchitis in Lancashire cotton mills. Br J Ind Med 31:18–27, 1974

13. Bherer L, Cushman R, Courteau JP, et al: Survey of construction workers repeatedly exposed to chlorine gas over a three to six month period in a pulpmill: II. Follow-up of affected workers by questionnaire, spirometry, and assessment of bronchial responsiveness 18 to 24 months after exposure ended. Occup Environ Med 51:225–228, 1994

14. Bouhuys A, Schoenberg JB, Beck GJ, et al: Epidemiology of chronic lung disease in a cotton mill community. Lung 154:167–186, 1977

15. Broder I, Corey P, Davies G, et al: Longitudinal study of grain elevator and control workers with demonstration of healthy worker effect. J Occup Med 27:873–880, 1985

16. Broder I, Hutcheon M, Mintz S, et al: Changes in respiratory variables of grain handlers and civic workers during their initial months of employment. Br J Ind Med 41:94–99, 1984

17. Broder I, Mintz S, Hutcheon MA, et al: Comparison of respiratory variables in grain elevator workers and civic outside workers of Thunder Bay, Canada. Am Rev Respir Dis 119:193–203, 1979

18. Broder I, Mintz S, Hutcheon MA, et al: Effect of layoff and rehire on respiratory variables of grain elevator workers. Am Rev Respir Dis 122:601–608, 1980

19. Brooks SM, Weiss MA, Bernstein IL: Reactive airways dysfunction (Rads): Persistent asthma syndrome after high level irritant exposures. Chest 86:376–384, 1985

20. Brown PJ, Greville HW, Finucane KE: Asthma and irreversible airflow obstruction. Thorax 39:131–136, 1984

21. Carosso A, Ruffino C, Bugiani M: Respiratory diseases in wood workers. Br J Ind Med 44:53–56, 1987

22. Castellan RM, Olenchock SA, Kinsley KB, et al: Inhaled endotoxin and decreased spirometric values: An exposure-response relation for cotton dust. N Engl J Med 317:605–610, 1987

23. Cavagna G, Foa V, Vigliani EC: Effects in man and rabbits of inhalation of cotton dust or extracts and purified endotoxins. Br J Ind Med 26:314–321, 1969

24. Chan-Yeung M, Dimich-Ward H, Enarson D, et al: Five cross-sectional studies in grain elevator workers. Am J Epidemiol 136:1269–1279, 1992

25. Chan-Yeung M, Enarson DA, Kennedy SM: The impact of grain dust on respiratory health. Am Rev Respir Dis 145:476–487, 1992

26. Chan-Yeung M, Lam S: State of the art: Occupational asthma. Am Rev Respir Dis 133:686–703, 1986

27. Chan-Yeung M, Lam S, Kennedy SM: Persistent asthma after repeated exposure to high concentrations of gases in pulpmills. Am J Respir Crit Care Med 149:1676–1680, 1994

28. Chan-Yeung M, Lam S, Koener S: Clinical features and natural history of occupational asthma to Western Red Cedar (Thuja plicata). Am J Med 72:411–415, 1982

29. Chan-Yeung M, Wong R, MacLean L, et al: Respiratory survey of workers in a pulp and paper mill in Powell River, British Columbia. Am Rev Respir Dis 122:249–257, 1980

30. Charan NB, Lakshminarayan S, Myers GC, et al: Effects of accidental chlorine inhalation on pulmonary function. West J Med 143:333–336, 1985

31. Charan NB, Myers GC, Lakshminarayan S, et al: Pulmonary injuries associated with acute sulfur dioxide inhalation. Am Rev Respir Dis 119:555–560, 1979

32. Chinn DJ, Stevenson IC, Cotes JE: Longitudinal respiratory survey of shipyard workers: Effects of trade and atopic status. Br J Ind Med 47:83–90, 1990

33. Churg A, Wright JL: Small-airway lesions in patients exposed to nonasbestos mineral dusts. Hum Pathol 14:688–693, 1983

34. Churg A, Wright JL: Small-airway lesions induced by asbestos and nonasbestos mineral dusts. Chest 85:36S–38S, 1985

35. Cockcroft A, Wagner JC, Ryder R, et al: Post-mortem study of emphysema in coal-workers and non-coalworkers. Lancet 2:600–603, 1982

36. Cotton DJ, Graham BL, Li KYR, et al: Effects of grain dust and smoking on respiratory symptoms and lung function. J Occup Med 25:131–140, 1983
37. Cowie RL, Mabena SK: Silicosis, chronic airflow limitation, and chronic bronchitis in South African gold miners. Am Rev Respir Dis 143:80–84, 1991
38. Diem JE: A statistical assessment of the scientific evidence relating cotton dust exposure to chronic lung disease. Am Stat 37:395–403, 1983
39. Donham KJ, Reynolds SJ, Whitten PW, et al: Respiratory dysfunction in swine production facility workers: Dose-response relationships of environmental exposures and pulmonary function. Am J Ind Med 27:405–418, 1995
40. Donnelly SC, FitzGerald MX: Reactive airways dysfunction (RADS) due to chlorine gas exposure. Irish J Med Sci 159:275–277, 1990
41. DoPico GA, Reddan W, Flaherty D, et al: Respiratory abnormalities among grain handlers: A clinical, physiologic, and immunologic study. Am Rev Respir Dis 115:915–927, 1977
42. Dosman JA: Chronic obstructive pulmonary disease and smoking in grain workers. Ann Intern Med 87:784–786, 1977
43. Dosman JA, Cotton DJ, Graham BL, et al: Chronic bronchitis and decreased forced expiratory flow rates in lifetime nonsmoking grain workers. Am Rev Respir Dis 121:11–16, 1980
44. Dosman JA, Graham BL, Cotton DJ: Chronic bronchitis and exposure to cereal grain dust [edit]. Am Rev Respir Dis 120:477–480, 1979
45. Dosman JA, Graham BL, Hall D, et al: Respiratory symptoms and pulmonary function in farmers. J Occup Med 29:38–43, 1987
46. Dosman JA, Graham BL, Hall D, et al: Respiratory symptoms and alterations in pulmonary function in swine producers in Saskatchewan: Results of a survey of farmers. J Occup Med 30:715–720, 1988
47. Douglas AN, Lamb D, Ruckley VA: Bronchial gland dimensions in coalminers: Influence of smoking and dust exposure. Thorax 37:760–764, 1982
48. Edwards C, Carlile A, Rooke G: The larger bronchi in byssinosis: A morphometric study. Thorax 38:20–23, 1984
49. Edwards C, Macartney J, Rooke G, et al: The pathology of the lung in byssinotics. Thorax 30:612–623, 1975
50. Elwood PC, Sweetnam PM, Bevan C, et al: Respiratory disability in ex-cotton workers. Br J Ind Med 43:580–586, 1986
51. Fairman RP, O'Brien RJ, Swecker S, et al: Respiratory status of surface coal miners in the United States. Arch Environ Health 32:211–215, 1977
52. Fishwick D, Fletcher AM, Pickering A, et al: Lung function, bronchial reactivity, atopic status, and dust exposure in Lancashire cotton mill operations. Am Rev Respir Dis 145:1103–1108, 1992
53. Gamsky TE, McCurdy SA, Samuels SJ, et al: Smoking, respiratory symptoms, and pulmonary function among a population of Hispanic farmworkers. Chest 101:1361–1368, 1992
54. Gamsky TE, Schenker MB, Curdy SA, et al: Reduced FVC among California grape workers. Am Rev Respir Dis 145:257–262, 1992
55. Glindmeyer HW, Lefante JL, Jones RJ, et al: Exposure-related declines in the lung function of cotton textile workers. Am Rev Respir Dis 144:675–683, 1991
56. Glindmeyer HW, Lefante JL, Jones RJ, et al: Cotton dust and across-shift change in $FEV_1$ as predictors of annual change in $FEV_1$. Am J Respir Crit Care Med 149:584–590, 1994
57. Hanke W, Sepulveda M-J, Watson A, et al: Respiratory morbidity in wollastonite workers. Br J Ind Med 41:474–479, 1984
58. Harkonen H, Nordman H, Korhonen O, et al: Long-term effects of exposure to sulfur dioxide: Lung function four years after a pyrite dust explosion. Am Rev Respir Dis 128:890–893, 1983
59. Heederik D, Kromhout H, Burema J, et al: Occupational exposure and 25-year incidence rate of non-specific lung disease: The Zutphen study. Int J Epidemiol 19:945–952, 1990
60. Heederik D, Pouwels H, Kromhout H, et al: Chronic nonspecific lung disease and

occupational exposures estimated by means of a job exposure matrix: The Zutphen study. Int J Epidemiol 18:382–389, 1989

61. Henneberger PK, Ferris BG, Sheehe PR: Accidental gassing incidents and the pulmonary function of pulp mill workers. Am Rev Respir Dis 148:63–67, 1993

62. Hnizdo E: Health risks among white South African gold miners—dust, smoking, and chronic obstructive pulmonary disease. S Afr J Med 81:512–517, 1992

63. Hnizdo E, Baskind E, Sluis-Cremer GK: Combined effect of silica dust exposure and tobacco smoking on the prevalence of respiratory impairments among gold miners. Scand J Work Environ Health 16:411–422, 1990

64. Hnizdo E, Sluis-Cremer GK, Abramowitz JA: Emphysema type in relation to silica dust exposure in South African gold miners. Am Rev Respir Dis 143:1241–1247, 1991

65. Hnizdo E, Sluis-Cremer GK, Baskind E, et al: Emphysema and airway obstruction in non-smoking South African gold miners with long exposure to silica dust. Occup Environ Med 51:557–563, 1994

66. Holman CDJ, Psaila-Savona P, Roberts M, et al: Determinants of chronic bronchitis in Western Australian gold miners. Br J Ind Med 44:810–818, 1987

67. Humerfelt S, Gulsvik A, Skjaerven R: Decline in FEV$_1$ and airflow limitation related to occupational exposures in men of an urban community. Eur Respir J 6:1095–1103, 1993

68. Hurley JF, Soutar CA: Can exposure to coalmine dust cause a severe impairment of lung function? Br J Ind Med 43:150–157, 1986

69. Huy T, DeSchipper K, Chan-Yeung M, et al: Grain dust and lung function: Dose-response relationships. Am Rev Respir Dis 144:1314–1321, 1991

70. Imbus HR, Suh MW: Byssinosis: A study of 10,133 textile workers. Arch Environ Health 26:183–191, 1973

71. Irwig LM, Rocks P: Lung function and respiratory symptoms in silicotic and nonsilicotic gold miners. Am Rev Respir Dis 117:429–435, 1978

72. Iversen M, Dahl R, Korsgaard J, et al: Respiratory symptoms in Danish farmers: An epidemiological study of risk factors. Thorax 43:872–877, 1988

73. Jacobs RR, Boehlecke B, Vav Hage-Hamsten M, et al: Bronchial reactivity, atopy, and airway response. Am Rev Respir Dis 148:19–24, 1993

74. James AL, Cookson WOCM, Buters G, et al: Symptoms and longitudinal changes in lung function in young seasonal grain handlers. Br J Ind Med 43:587–591, 1986

75. Jodoin G, Gibbs GW, Macklem P, et al: Early effects of asbestos on lung function. Am Rev Respir Dis 104:525–535, 1971

76. Jones RN, Hughes LM, Glindmeyer H, et al: Lung function after acute chlorine exposure. Am Rev Respir Dis 134:1190–1195, 1986

77. Karava R, Hernberg S, Koskela RS, et al: Prevalence of pneumoconiosis and chronic bronchitis in foundry workers. Scand J Work Environ Health 2(suppl):64–72, 1976

78. Kass I, Zamel N, Dobry CA, et al: Bronchiectasis following ammonia burns of the respiratory tract. Chest 62:282–285, 1972

79. Kauffmann F, Drouet D, Lellouch J, et al: Twelve years spirometric changes among Paris area workers. Int J Epidemiol 8:201–211, 1979

80. Kauffmann F, Drouet D, Lellouch J, et al: Occupational exposure and 12-year spirometric changes among Paris area workers. Br J Ind Med 39:221–232, 1982

81. Kennedy SM, Christiani DC, Eisen EA, et al: Cotton dust and endotoxin exposure-response relationships in cotton textile workers. Am Rev Respir Dis 135:194–200, 1987

82. Kennedy SM, Enarson DA, Janssen RG, et al: Lung health consequences of repeated accidental chlorine gas exposures among pulpmill workers. Am Rev Respir Dis 143:74–79, 1991

83. Kennedy SM, Wright JL, Muller JB, et al: Pulmonary function and peripheral airway disease in patients with mineral dust or fume exposure. Am Rev Respir Dis 132:1294–1299, 1985

84. Kibelstis JA, Morgan EJ, Reger R, et al: Prevalence of bronchitis and airway obstruction in American bituminous coal miners. Am Rev Respir Dis 108:886–893, 1973

85. Korn RJ, Dockery DW, Speizer FE, et al: Occupational exposures and chronic respiratory symptoms: A population based study. Am Rev Respir Dis 136:298–304, 1987

86. Kreiss K, Greenberg LM, Kogut SJH, et al: Hard-rock mining exposures affect smokers and nonsmokers differently. Am Rev Respir Dis 139:1487–1493, 1989

87. Krzyzanowski M, Jedrychowski W: Occupational exposure and incidence of chronic respiratory symptoms among residents of Cracow followed for 13 years. Int Arch Occup Environ Health 62:311–317, 1990
88. Krzyzanowski M, Jedrychowski W, Wysocki M: Factors associated with the change in ventilatory function and the development of chronic obstructive pulmonary disease in a 13-year follow-up of the Cracow study. Am Rev Respir Dis 134:1011–1019, 1986
89. Krzyzanowski M, Kauffmann F: The relation of respiratory symptoms and ventilatory function to moderate occupational exposure in a general population. Int J Epidemiol 17:397–406, 1988
90. Leduc D, Gris P, Lheureux P, et al: Acute and long term damage following inhalation of ammonia. Thorax 47:755–757, 1992
91. Love RG, Miller BG: Longitudinal study of lung function in coal miners. Thorax 37:193–197, 1982
92. Madison R, Afifi AA, Mittman C: Respiratory impairment in coke oven workers: Relationship to work exposure and bronchial inflammation detected by sputum cytology. J Chron Dis 37:167–176, 1984
93. Manfreda J, Cheang M, Warren CPW: Chronic respiratory disorders related to farming and exposure to grain dust in a rural adult community. Am J Ind Med 15:7–17, 1989
94. Manfreda J, Johnston B: Occupational factors in the etiology of airflow obstruction. Am Rev Respir Dis 126:A341, 1987
95. Manfreda J, Sidwall G, Maini K, et al: Respiratory abnormalities in employees of the hard rock mining industry. Am Rev Respir Dis 126:629–634, 1982
96. Marine WH, Gurr D, Jacobsen M: Clinically important respiratory effects of dust exposure and smoking in British coal miners. Am Rev Respir Dis 137:106–112, 1988
97. Merchant JA, Lumsden JC, Kilburn KH, et al: An industrial study of the biological effects of cotton dust and cigarette smoke exposure. J Occup Med 15:212–221, 1973
98. Merchant JA, Lumsden JC, Kilburn KH, et al: An industrial study of the biological effects of cotton dust and cigarette smoke exposure. J Occup Med 15:222–230, 1973
99. Molyneux MKB, Tombleson JBL: An epidemiological study of respiratory symptoms in Lancashire mills, 1963–66. Br J Ind Med 27:225–234, 1970
100. Pahwa P, Senthilselvan A, McDuffie HH, et al: Longitudinal estimates of pulmonary function decline in grain workers. Am Rev Respir Crit Care Med 150:656–662, 1994
101. Pham QT, Mastrangelo G, Chau N, et al: Five year longitudinal comparison of respiratory symptoms and function in steelworkers and unexposed workers. Bull Eur Physiopathol Respir 15:469–480, 1979
102. Piggier PL, Vagaggini B, Bacci E, et al: Prognosis of occupational asthma. Eur Respir J 7:761–767, 1994
103. Ploysongsang Y, Beach BC, DiLisio RE: Pulmonary function changes after acute inhalation of chlorine gas. South Med J 75:23–26, 1982
104. Pratt PC, Vollmer RT, Miller JA: Epidemiology of pulmonary lesions in nontextile and cotton textile workers: A retrospective analysis. Arch Environ Health 35:133–138, 1980
105. Rogan JM, Attfield MD, Jacobsen M, et al: Role of dust in the working environment in the development of chronic bronchitis in British coal miners. Br J Ind Med 30:217–226, 1973
106. Rom WN, Wood SD, White GL, et al: Longitudinal evaluation of pulmonary function in copper smelter workers exposed to sulfur dioxide. Am Rev Respir Dis 133:830–833, 1986
107. Ruckley VA, Gauld SJ, Chapman JS, et al: Emphysema and dust exposure in a group of coal workers. Am Rev Respir Dis 129:528–532, 1984
108. Ryder R, Lyons JP, Campbell H, et al: Emphysema in coal workers' pneumoconiosis. BMJ 3:481–487, 1970
109. Schwartz DA, Smith DD, Lakshminarayan S: The pulmonary sequelae associated with accidental inhalation of chlorine gas. Chest 97:820–825, 1990
110. Seixas NS, Robins TG, Attfield MD, et al: Exposure-response relationships for coal mine dust and obstructive lung disease following enactment of the Federal Coal Mine and Safety Act of 1969. Am J Ind Med 21:715–734, 1992
111. Seixas NS, Robins TG, Attfield MD, et al: Longitudinal and cross sectional analyses

of exposure to coal mine dust and pulmonary function in new miners. Br J Ind Med 50:929–937, 1993

112. Sferlazza SJ, Beckett WS: The respiratory health of welders. Am Rev Respir Dis 143:1134–1148, 1991

113. Shamssain MH: Pulmonary function and symptoms in workers exposed to wood dust. Thorax 47:84–87, 1992

114. Shamssain MH: Respiratory symptoms and pulmonary function in flour processing workers in the baking industry. Am J Ind Med 27:359–365, 1995

115. Sluis-Cremer GK, Walters LG, Sichel HS: Chronic bronchitis in miners and non-miners: An epidemiological survey of a community in the gold-mining area in the Transvaal. Br J Ind Med 21:1–12, 1967

116. Smid T, Heederik D, Houba R, et al: Dust- and endotoxin-related respiratory effects in the animal feed industry. Am Rev Respir Dis 146:1474–1479, 1992

117. Soutar CA, Hurley JF: Relation between dust exposure and lung function in miners and ex-miners. Br J Ind Med 43:307–320, 1986

118. Tabona M, Chan-Yeung M, Enarson D, et al: Host factors affecting longitudinal decline in lung spirometry among grain elevator workers. Chest 85:782–786, 1984

119. Tarlo SM, Broder I: Irritant-induced occupational asthma. Chest 96:297–300, 1989

120. Tockman MS, Baser M: Is cotton dust exposure associated with chronic effects? Am Rev Respir Dis 130:1–3, 1984

121. Vestbo J, Knudsen KM, Rasmussen FV: The effect of smoking and occupation on changes in respiratory symptoms in middle-aged Danish men. Eur Respir J 3:880–885, 1990

122. Viegi G, Prediletto R, Paoletti P, et al: Respiratory effects of occupational exposure in a general population sample in North Italy. Am Rev Respir Dis 143:510–515, 1991

123. Walker DD, Archibald RM, Attfield MD: Bronchitis in men employed in the coke industry. Br J Ind Med 28:358–363, 1971

124. Ware JH, Dockery WD, Louis TA, et al: Longitudinal and cross-sectional estimates of pulmonary function decline in never-smoking adults. Am J Epidemiol 132:685–700, 1990

125. Weill H, George R, Schwarz M: Late evaluation of pulmonary function after acute exposure to chlorine gas. Am Rev Respir Dis 99:374–379, 1969

126. Wiles FJ, Faure MH: Chronic obstructive lung disease in gold miners. In Walton WH, McGowan B (eds): Inhaled Particles IV, part 2. Oxford, Pergamon Press, 1977, pp 727–735

127. Wright JL, Churg A: Morphology of small-airway lesions in patients with asbestos exposure. Hum Pathol 15:68–74, 1984

128. Wright JL, Churg A: Severe diffuse small-airways abnormalities in long term chrysotile asbestos miners. Br J Ind Med 42:556–559, 1985

129. Xu X, Christiani DC, Dockery DC, et al: Exposure-response relationships between occupational exposures and chronic respiratory illness: A community-based study. Am Rev Respir Dis 146:413–418, 1992

130. Zejda JE, Barber E, Dosman JA, et al: Respiratory health status in swine producers relates to endotoxin exposure in the presence of low dust levels. J Occup Med 36:49–56, 1994

131. Zejda JE, Hurst TS, Rhodes CS, et al: Respiratory health of swine producers. Chest 103:702–709, 1993

132. Zuskin E, Wolfson RL, Harpel G, et al: Byssinosis in carding and spinning workers. Arch Environ Health 19:666–673, 1969

*Address reprint requests to*

Eric Garshick, MD, MOH
Pulmonary and Critical Care Section
Brockton/West Roxbury Veterans Affairs Medical Center
1400 VFW Parkway
West Roxbury, MA 02132