Rapid Decline in Forced Expiratory Volume in 1 Second (FEV_1) and the Development of Bronchitic Symptoms Among New Chinese Coal Miners

Mei-Lin Wang, MD
Zhi-En Wu, MD
Qin-Guo Du, MD
Kai-Liang Peng, MD
Ya-Dong Li
Shao-Kui Li
Gui-Hai Han
Edward L. Petsonk, MD

Objective: *To investigate the relationship between the development of bronchitic symptoms and the early rapid decline of forced expiratory volume in 1 second (FEV_1).* ***Methods:*** *A two-stage and a mixed model approach were used to analyze data from 260 newly hired Chinese coal miners who completed approximately 5 to 16 health surveys during 3 years.* ***Results:*** *The proportion of miners with onset of bronchitic symptoms was significantly elevated after 11 months of underground mining. Miners with incident symptoms had greater declines in FEV_1 compared with those who did not (−65 vs −23 mL/yr, P < 0.05). At 24 months follow-up, FEV_1 had declined an average 235 mL among the 26 miners who developed bronchitic symptoms and smoked, compared with a decline of 96 mL among the 132 nonsmoking miners without symptoms.* ***Conclusions:*** *Among new coal miners, a sharp early decline in FEV_1 is associated with the development of bronchitic symptoms.* (J Occup Environ Med. *2007;49:1143–1148*)

From the Division of Respiratory Disease Studies (Drs Wang and Petsonk), National Institute for Occupational Safety and Health, Morgantown, West Virginia; Tongji Medical College of Huazhong University of Science and Technology (Drs Wu and Peng), Wuhan, People's Republic of China; and Xuzhou Mining Group Company Ltd. (Drs Du, Y-D Li, S-K Li, and Han), Xuzhou, Jiangsu, People's Republic of China.

The findings and conclusions in this report are those of the authors, and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

Address correspondence to: Edward L. Petsonk, MD, FCCP, NIOSH, Mail Stop H-G900.2, 1095 Willowdale Rd., Morgantown, WV 26505; E-mail: elp2@cdc.gov.

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Prolonged inhalation of respirable particulates can result in the development of chronic obstructive pulmonary disease.[1] In a recent study of a group of newly hired Chinese coal miners, the miners experienced a rapid decline in forced expiratory volume in 1 second (FEV_1) during the first year of employment, a plateau during the second year, and partial recovery during the third year of dust exposure.[2] The mechanism for the rapid dust-related lung function declines observed in this and other studies[3,4] is not known. Nevertheless, symptoms of bronchitis are frequently reported by miners and have been associated with important deficits in lung function.[5–7] We hypothesized that the early sharp decline in lung function observed in studies of dust-exposed workers may be related to the development of inflammation in the walls of the larger conducting airways. The associated bronchial gland enlargement and increased mucous production may result in a reduction in the caliber of these airways, as observed in association with bronchitic symptoms by Hankinson and colleagues.[8] To test the hypothesis that development of bronchitis is a potential pathophysiologic mechanism for the observed early FEV_1 losses, we investigated the relationship between development of bronchitic symptoms and early decline of FEV_1 among a cohort of coal miners in Jiangsu province, China.

Materials and Methods

Participants, Health Surveys, and Environmental Monitoring

A 3-year prospective cohort study was completed among 317 newly hired underground coal miner volunteers between October 1995 and January 1999. Chinese health professionals performed an initial (pre-employment) and 15 follow-up health surveys at three mine sites. The first health survey consisted of an initial questionnaire, measurement of height and weight, a chest radiograph, and spirometry, including bronchodilator (BD) testing, to assess for airway reactivity.[2] Follow-up health surveys were performed on a monthly basis for the first 3 months, every 2 months for the next 6 surveys, then every 3 months for five surveys, and the last follow-up survey was performed at a 6-month interval. Each health survey included a standardized follow-up questionnaire on respiratory symptoms, and spirometry testing (BD testing was not repeated). To minimize the bias from missing results, this analysis includes only the 260 miners who completed at least 5, and up to 16 health surveys, resulting in the exclusion of 53 participants. In addition, four participants who reported symptoms of cough or phlegm at the initial survey were also excluded from this analysis. Spirometry testing was performed at the worksite using a National Institute for Occupational Safety and Health (NIOSH) dry rolling-seal spirometer (NIOSH HF6) by Chinese pulmonary function technicians instructed in spirometry standards.[9] Data were processed using NIOSH spirometry software. NIOSH investigators reviewed flow-volume curves, calibration, and leak checks from each test session. Percent predicted FEV_1 was calculated using Hankinson's reference equations for a male Mexican-American population, derived from the National Health and Nutrition Examination Survey III data.[10] These reference values were selected by comparing the spirometry values observed in these Chinese coal miners to values from reference equations based on the study of several racial groups (data not shown). The Mine Bureau authorities in Xuzou, China approved the study protocol. Because an existing data set without personal identifiers was used, the Institutional Review Board of the Centers for Disease Control and Prevention specified that board review was not required for this study.

The methods, results, and limitations of the dust sampling, and the relationship of individual dust exposure estimates to the health outcomes in this study have previously been reported.[2] Briefly, total and respirable dust area sampling was performed twice a month in the 3 underground mines at 24 representative work areas, by Chinese mine inspectors using a battery-operated two-stage dust sampler (Model AKFC-92A, Changzhou Analytical Instrument Company, Changzhou, Jiangsu Province, China). Each individual miner's exposures to total and respirable dust were estimated monthly, based on the sampling results from the miner's work area.

Grouping by Combinations of Bronchitic Symptoms and Smoking Status

Bronchitic symptoms were defined as cough or phlegm production or both for four or more days per week. Development of bronchitic symptoms refers to workers who denied these symptoms at the initial survey ($N = 260$) but reported them at two or more follow-up surveys. Miners who reported incident symptoms at two or more follow-up surveys were categorized in the group with new onset bronchitic symptoms (Br+); otherwise miners were categorized as having no new bronchitic symptoms (Br−). The reporting of bronchitic symptoms on multiple surveys was considered an indirect indicator of the development of airway inflammation. Workers who reported smoking cigarettes at the initial health survey were classified as current smokers (Sm+); workers who reported never smoking and the three former smokers were classified as not current smokers (Sm−), referred in the text as nonsmokers. Pack-years of smoking was defined as the average number of packs of cigarettes smoked per day multiplied by the number of years smoked up to the time of the survey. Miners were further categorized by combinations of new onset bronchitic symptoms and smoking status at the initial survey into four subgroups of Br−Sm−, Br−Sm+, Br+Sm−, and Br+Sm+.

Data Analysis

The statistical analysis was performed using the SAS version 8.0 software package (SAS Institute, Cary, NC). Group comparisons of participant characteristics and spirometry indices were made between miners who developed bronchitic symptoms versus those who did not develop, using *t* tests for continuous variables, and χ^2 tests for dichotomous variables. Using a two-stage approach, first, each miner's longitudinal FEV_1 change (slope in mL/yr) was calculated using simple linear regression across the repeated measures. Then, analysis of variance was used to test the significance of differences in the means of the individual FEV_1 slopes for the four groups of miners.

A mixed-effects model was also used to investigate the patterns of FEV_1 change over time in groups of Br+ versus Br−; and further among groupings of Br−Sm−, Br+Sm−, Br−Sm+, and Br+Sm+. The health outcome variable was the repeated measurement of FEV_1. The major interest centered on differences between the groups in FEV_1 change over the period of study, controlling for age at time of recruitment (both linear and quadratic), height, pack-years of smoking, room temperature during testing, and mean respirable dust concentration. Interaction terms for both group and linear time, and

TABLE 1

Group Comparisons of Demographic and Spirometric Parameters at the Initial Survey, and 3-Year FEV_1 Slopes and Estimated Respirable Dust Exposures, for Newly Hired Chinese Coal Miners

		Development of Bronchitic Symptoms	
Grouping	Study Subjects (N = 260)	Yes (Br+, n = 48)	No (Br−, n = 212)
Age, yr	22.3 (2.5)	22.8 (2.9)	22.2 (2.5)
Height, cm	169.7 (4.6)	169.9 (4.2)	169.7 (4.5)
Weight, kg	62.7 (5.6)	63.2 (5.4)	62.6 (5.6)
Current smokers, n (%)	106 (40.8)	26 (54.2)	80 (37.7)*
Pack-years	0.63 (1.7)	0.81 (1.6)	0.59 (1.7)
FEV_1, L	4.46 (0.51)	4.44 (0.53)	4.47 (0.50)
FVC, L	5.29 (0.58)	5.40 (0.60)	5.26 (0.57)
FEV_1/FVC, %	84.6 (7.2)	82.4 (7.2)	85.1 (7.1)*
PP FEV_1, %	103.4 (10.3)	103.3 (10.4)	103.5 (10.3)
ΔFEV_1BD, %[a]	3.1 (5.7)	4.5 (4.4)	2.8 (5.9)*
BD responders, n (%)[b]	9 (3.5)	3 (6.3)	6 (2.8)
FEV_1 slope (L/yr)[c]	−0.030 (0.116)	−0.065 (0.098)	−0.023 (0.119)*
Respirable dust (mg/m^3)[d]	8.24 (16.78)	5.50 (16.76)	8.85 (10.93)

Unless otherwise indicated, values are mean (standard deviation).

*$P < 0.05$.

[a]ΔFEV_1BD was calculated as 100 × (post-bronchodilator FEV_1 − pre-bronchodilator FEV_1)/(pre-bronchodilator FEV_1).

[b]Bronchodilator (BD) responders were miners with ΔFEV_1BD ≥12%.

[c]Individual rate of change in FEV_1, calculated by simple linear regression over 3 years.

[d]Group mean of individual estimated respirable dust exposures. Individual exposure was estimated as the 3-year average of the monthly measurements from the miner's work area.

PP FEV_1 indicates percent predicted FEV_1.

group and quadratic time were included in the model.

Results

Table 1 displays participant characteristics, spirometry indices, and BD test results at the initial survey, as well as the FEV_1 slope and mean dust concentrations over the 3 years of follow-up. A total of 3208 spirometry tests were performed by the 260 miners. We excluded 25 tests from data analysis because of quality issues, resulting in 3183 valid spirometry measurements. For each individual, an average of 12 test results (range, 5 to 16) were used for the FEV_1 slope calculation. FEV_1 slopes among miners who developed bronchitic symptoms (Br+) were greater than among those who did not develop these symptoms (−65 vs. −23 mL/yr, $P < 0.05$). Demographic parameters and spirometry indices at the initial survey were similar for the two groups except that the Br+ group had a higher percentage of current smokers, a slightly greater increase in FEV_1 post-BD, and a somewhat lower FEV_1/forced vital capacity ratio, compared with the Br− group. Mean respirable dust concentrations over the 3-year study (8.9 mg/m^3) greatly exceeded the 2 mg/m^3 US permissible exposure limit, but did not differ significantly between Br+ and Br−. Among the group of 57 participants who were excluded (see Methods), the proportion of current smokers was somewhat higher than in the 260 study subjects (54% vs. 41%, P = 0.06) but there were no other differences ($P > 0.10$) for any of the values displayed in Table 1.

The FEV_1 changes over 3 years among the groups of Br−Sm−, Br−Sm+, Br+Sm−, and Br+Sm+ (n = 132, 80, 22, and 26, respectively) averaged −8, −46, −57, and −73 mL/yr, respectively. The mean slope for the Br−Sm− group differed significantly from the Br+Sm+ group (analysis of variance, P = 0.0114). All the chest radiographs were within normal limits and they were not analyzed further.

The proportion of miners with new bronchitic symptoms since the initial survey was significantly increased after 11 months of underground mining and stayed elevated thereafter, averaging 10.7%, compared with 1.3% during the first 11 months ($P <$ 0.0001).

Table 2 lists the parameter estimates obtained from the mixed-effects model after adjustment for initial age and the time-dependent variables of height, pack-years of smoking, room temperature during testing, and mean respirable dust concentration. Linear and quadratic time trends for FEV_1, and the interaction terms of group and time were highly significant in both the Br+ and Br− groups; the Br+ group lost about 4 mL more FEV_1 per month. Figure 1 shows the difference in the patterns of FEV_1 change between the Br+ and Br− groups, using the coefficients listed in Table 2. Both groups lost FEV_1 over time; the Br+ group lost more FEV_1 than the Br− group. At the end of the study, both Br + and Br− groups showed some recovery in FEV_1, although there was no decrease in the reporting of bronchitic symptoms.

A mixed-effects model analysis was also performed after stratifying the miners by combinations of symptom development and smoking status. Using the coefficients derived from the model, the patterns of FEV_1 change for each group are illustrated in Fig. 2. The Br−Sm− group lost less FEV_1 over time than the other groups. Among these new coal miners, both the development of bronchitic symptoms (Br+) and tobacco smoking (Sm+) contributed to a sharp early decline in lung function. After 24 months, a partial recovery in FEV_1 was observed except for the nonsmoking miners who developed bronchitic symptoms (Br+Sm− group).

TABLE 2
Parameter Estimates, Standard Errors, and *P* Values Obtained From Mixed-Effects Model Analysis of Repeated Measures of FEV_1 Over 3 Years Among 260 Newly Hired Chinese Coal Miners

Effect	Parameter Estimate (L)	Standard Error	*P*
Initial age, yr	0.2571	0.1130	0.0229
Age × age, yr²	−0.0059	0.0024	0.0134
Height, cm	0.0214	0.0040	<0.0001
Pack-years	−0.0166	0.0130	0.2035
Respirable dust, mg/m³	−0.0002	0.0002	0.4520
Room temperature, °C	0.0102	0.0003	<0.0001
Group			
Br−	−2.0874	1.4976	0.1635
Br+	−2.1256	1.5005	0.1567
Time* × group			
Br−	−0.0121	0.0011	<0.0001
Br+	−0.0159	0.0023	<0.0001
Time × time × group			
Br−	0.0003	0.00003	<0.0001
Br+	0.0003	0.00006	<0.0001

*Time is measured in months after the initial survey.

Br− indicates no new bronchitic symptoms, and refers to the group of workers who denied both cough and phlegm at the initial survey and did not report these symptoms at two or more follow-up surveys; Br+ indicates development of bronchitic symptoms, and refers to the group of workers who denied both cough and phlegm at the initial survey but reported them at two or more follow-up surveys.

Discussion

Inhalation of respirable dust can cause an early rapid loss in lung function and over time may lead to chronic airflow limitation; although the underlying pathologic processes are not fully understood.[2–6] This study investigated whether the development of bronchitis is a potential pathophysiologic mechanism for the early FEV_1 losses that have been observed in dust-exposed workers. FEV_1 losses were nearly 3 times as large among miners who developed bronchitic symptoms than among those who did not. Smoking miners who developed symptoms (the Br+Sm+ group) lost significantly more FEV_1 than nonsmokers who did not develop bronchitic symptoms (the Br−Sm− group). In addition, a partial FEV_1 recovery in the third year was not seen for the nonsmoking miners who developed bronchitic symptoms (Br+Sm− group). These findings support the hypothesis that the early sharp declines in lung function that have been observed in studies of dust-exposed workers may be related to the development of airway inflammation and hypersecretion.[8] Bronchospasm is an additional plausible mechanism for the early losses in lung function among dust-exposed individuals, because it also may result in relatively rapid reductions in airway caliber. In this study, miners who responded to BD did not show significantly greater losses in FEV_1 than nonresponders. When the miners were grouped by quartiles of FEV_1 change from pre- to post-BD, no consistent association was noted between the initial BD response and the 3-year FEV_1 slopes (data not shown). Nevertheless, because BD testing was done only at the initial pre-employment survey, the results of this study can not provide direct evidence about the role of bronchospasm in early rapid FEV_1 declines. A previous study found a relationship between peak expiratory flow (PEF) and chronic bronchitis.[11] We evaluated PEF measurements using an approach similar to the analysis of FEV_1. Nevertheless, for PEF, neither the mean, nor the percent predicted, nor the changes in PEF over time showed a significant relationship to the onset of bronchitic symptoms (data not shown).

Lung function loss may also result from inflammatory processes in small airways among dust-exposed individuals. Prominent dust-related changes are often observed in the terminal bronchioles in the lungs of coal miners, and both pathologic and physiologic evidence of small airways disease in coal miners has been reported.[12–15] To investigate a role of small airway disease in the early declines, we also analyzed the changes in the spirometry index of $FEF_{25–75}$ (the mean forced expiratory flow between 25% and 75% of the forced vital capacity), using the same approach as the analysis for FEV_1. The $FEF_{25–75}$ is said to reflect small airway caliber but is fairly nonspecific, and reductions can be seen with a number of diseases.[16,17] The $FEF_{25–75}$ demonstrated a similar relationship to bronchitic symptoms as the FEV_1 (which is not surprising because these two parameters were highly correlated) but the findings were less significant.* Further studies will be needed to better define the role of small airways inflammation in the early lung function declines seen in dust-exposed individuals. Also, a longer-term follow-up among the miners in this study and other cohorts would be helpful in determining the duration and magnitude of the FEV_1 recovery phase and in more fully assessing the long-term functional consequences of the development of bronchitic symptoms and the associated early rapid FEV_1 declines.

Counter to expectations, estimated dust exposure among the Br− group was slightly greater than that for the Br+ group, although the difference was not significant. Using either measured exposures or job categories as a surrogate, no significant

*The $FEF_{25–75}$ mean, percent predicted, and slopes were 4.49 L/s, 94.2%, and −0.129 L/s/yr for miners who developed bronchitic symptoms; and 4.83 L/s, 100.3%, and −0.077 L/s/yr for those who did not.

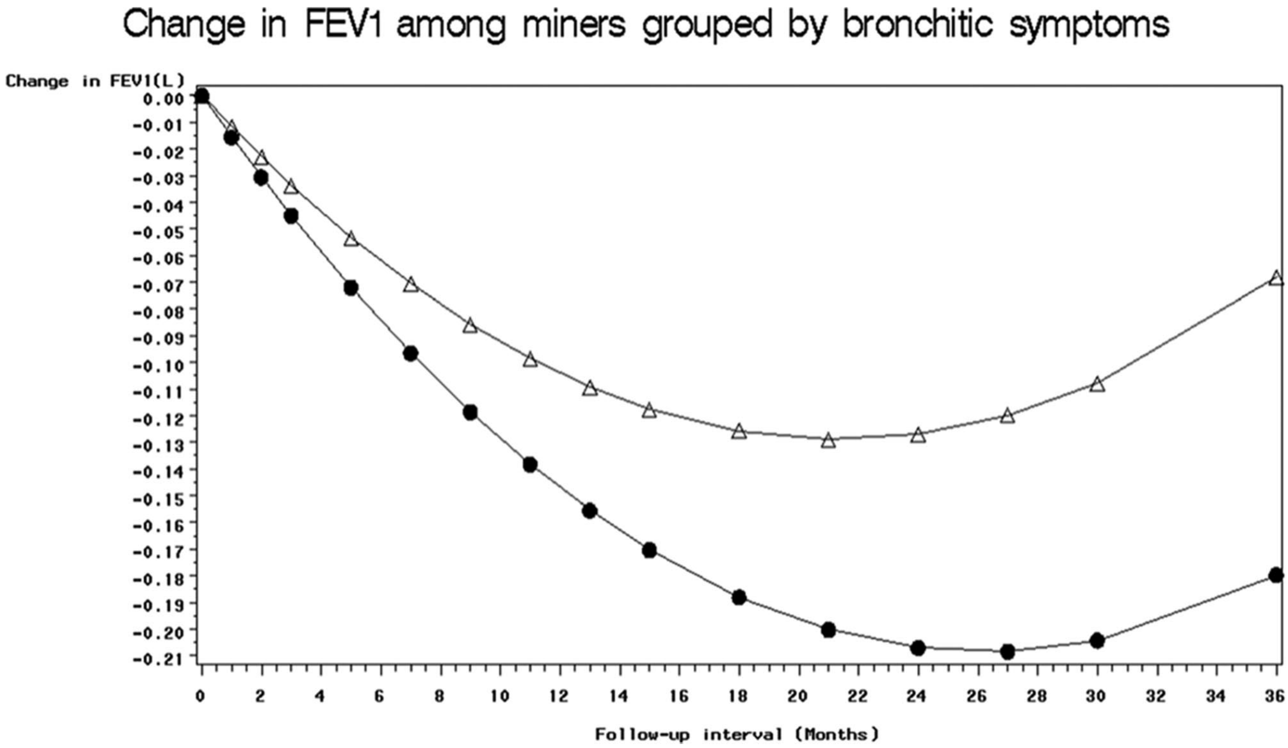

Fig. 1. Pattern of FEV_1 change over 3 years using coefficients from mixed model analysis, for 260 newly hired Chinese coal miners grouped by incident bronchitic symptoms [(△), Br−; (●), Br+]. The Br− group lost less FEV_1 over time than the Br+ group.

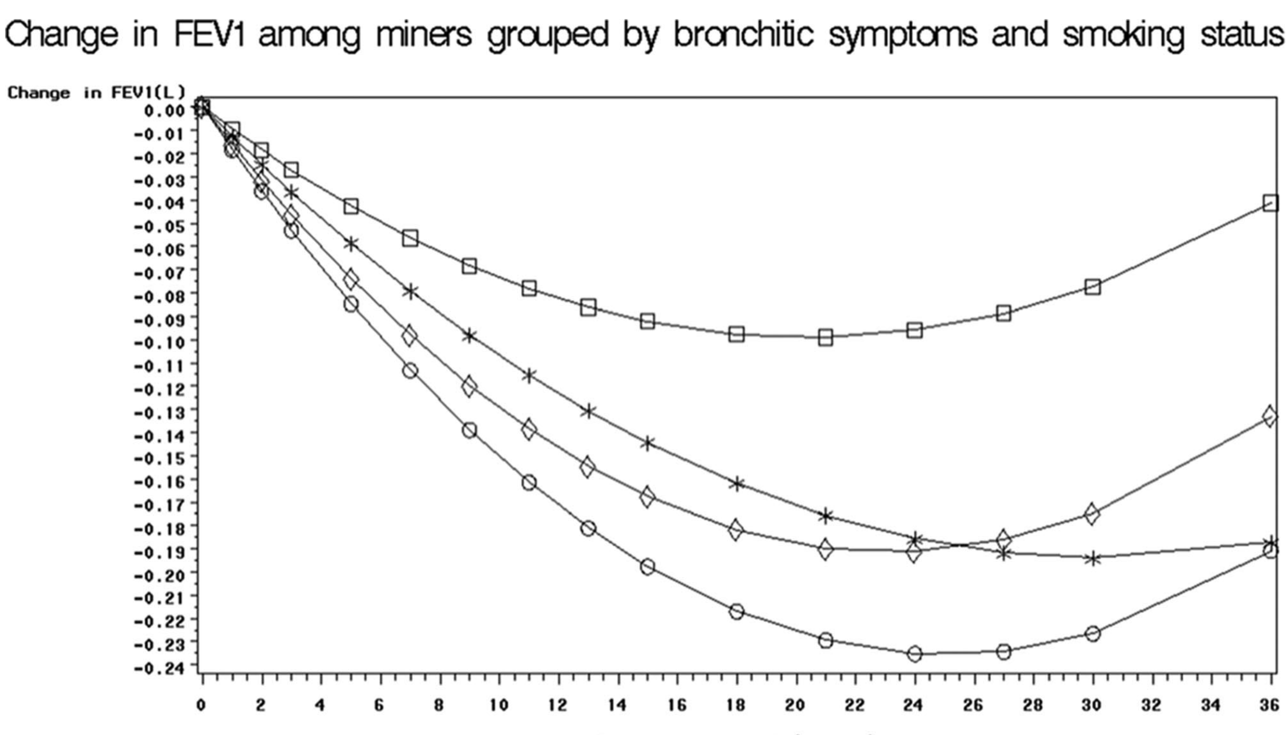

Fig. 2. Pattern of FEV_1 change over 3 years using coefficients from mixed model analysis, for 260 newly hired Chinese coal miners grouped by combinations of incident bronchitic symptoms and smoking status [(□), Br−Sm−; (*), Br+Sm−; (◇), Br−Sm+; and ○, Br+ Sm+]. The Br−Sm− group lost less FEV_1 over time than the other groups.

differences in exposures were detected between the Br+ and Br− groups. Nevertheless, as previously reported, all of the study miners experienced both total and respirable dust levels that were quite high compared with current coal mining conditions in Europe and North America.[2] None of the miners experienced a truly "low" dust exposure. Personal exposure estimates were based on area sampling, and this may have resulted in exposure misclassification of individual miners. In addition, study miners were all newly hired, and had a similar tenure (3 years) when they completed their last health survey. It is likely that the ability of the analysis to detect an exposure-response relationship was diminished by the limited range and relatively uniform duration of the miners' dust exposures, as well as some misclassification of personal exposures.

In this study, about 25% of the survey results were missing. Nevertheless, we did not detect any specific reasons for missing results or any relation to lung function or symptoms. Most absences were not due to health problems and it seemed that failure to attend a health survey was a random event. In addition, we only included those participating miners who had at least five survey results, with an average of 12 survey results per participant. The high number of tests requested for each participant in this study may partially compensate for the influence of missing data.

In summary, the results of this study suggest that among new coal miners, the development of bronchitic symptoms contributes to a sharp early decline in lung function, as does tobacco smoking. The findings support the hypothesis that the pathologic changes of bronchitis in the walls of large conducting airways, and the associated reduction in airway luminal diameter, represent a mechanism for early FEV_1 losses. The results also have implications for medical monitoring programs in coal mining and other dusty work—during the first several years of employment increased frequency of monitoring may be helpful to document the development of bronchitic symptoms and the associated declines in FEV_1. Because of the nonlinear patterns of lung function loss, caution is required in extrapolating early FEV_1 changes.

Acknowledgments

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