Is Chronic Airway Obstruction From Cotton Dust Exposure Reversible?

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Background: Exposure to cotton dust is known to cause chronic airway obstruction, but there is little information on whether the obstructive impairment is reversible after the exposure stops.

Methods: Longitudinal changes in lung function were evaluated among 429 cotton textile workers and 449 silk workers in Shanghai, China, beginning in 1981. Both active and retired workers were tested every 4 to 6 years for 15 years.

Results: Overall, cotton workers had greater annual declines in forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC). Compared with active workers, retired cotton workers had lower annual loss of FEV_1, although the retired workers had a greater loss during their active employment than the currently active workers. No such trends were detected in silk workers. Annual declines in FEV_1 in retired cotton workers were smaller with increasing time since retirement. Multivariate analysis showed that retirement was a substantial contributing factor for improved FEV_1 and FVC in the cotton workers, especially among those who did not smoke. Correspondingly, remission of airflow obstruction, defined as a ratio of FEV_1 and FVC of less than 70%, was more common in retirees than in the active workers, and more common in nonsmokers than in smokers.

Conclusion: Chronic airway obstruction related to long-term exposure to cotton dust may be partially reversible after the exposure ceases, although lung function does not return to the level found in unexposed workers.

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Occupational exposure to cotton dust is associated with the development of obstructive lung disease. A number of previous studies investigated acute airway responses, which are typically expressed as cross-shift drops in forced expiratory volume in 1 second (FEV_1).[1–5] These acute changes in ventilatory function are usually reversible and are most notable during the first work shift of the week after a weekend away from cotton dust.[6]

Longitudinal studies provide growing evidence that long-term exposure to cotton dust may result in persistent respiratory disease and accelerated loss of pulmonary function.[7–11] Furthermore, some studies have observed that chronic losses of pulmonary function are associated not only with level of endotoxin exposure,[3,11,12] but also with acute drops in FEV_1.[9,10] These findings imply that chronic reductions in lung function may be a consequence of either repeated (or cumulative) exposure or repeated (or cumulative) acute airway responses to cotton dust, or both. However, it is not known whether the chronic airway response, (ie, excessive longitudinal decline in lung function) is reversible, because previous studies focused largely on active workers.

The present analysis concentrated on longitudinal spirometric changes in a group of workers after their long-term occupational exposure to cotton dust ended with their retirement. These workers were followed prospectively for 15 years; excessive loss of annual FEV_1 and increased byssinotic symptoms were observed.[11] Half of the cotton workers and the control group of silk workers had retired from the industry during the study period, providing an opportunity to assess whether chronic lung function change is reversible.

METHODS

The details of subject selection were described previously.[11,13] Briefly, the original cohort established in 1981 consisted of 447 active cotton textile workers from 2 cotton mills in Shanghai, China. In addition, 472 active silk workers were studied as a control group. The subsequent surveys were undertaken in 1986, 1992, and 1996 and included retirees. The follow-up rates were 86%, 88%, and 77%, respectively, for the cotton group, and 85%, 83%, and 72%, respectively,

for the silk group. The current analysis included 429 cotton workers and 449 silk workers after excluding 18 cotton and 23 silk workers who did not return to any of the subsequent surveys. We defined the times between baseline and 1986 survey, between 1986 and 1992 survey, and between 1992 and 1996 survey as periods I, II, and III, respectively. Figure 1 describes the retirement status of the cohort at each period. There was a small number of retirees (12% in the cotton group and 9% in the silk group) during period I, whereas approximately 50% in both groups had retired by the last survey. Because we were interested in observing longitudinal lung function changes, we defined a worker as a retiree if he or she had been retired from the industry for 1 year or longer by the last survey.

Personal exposures to dust and endotoxin were calculated using geometric mean levels of environmental samples from each time period multiplied by time spent in specific work areas, as described previously.[11] Information on complete personal work history, smoking history, and respiratory symptoms was collected at each survey[11,14] using a standardized questionnaire.[15] Workers were initially classified as either smokers or nonsmokers at the baseline survey, and changes in smoking habit were recorded in all follow-up surveys.

Forced expiratory spirograms were performed using an identical 8-L water-sealed field spirometer (W.E. Collins Co., Brainbtree, MA) throughout the study. Workers performed up to 7 trials to produce 3 acceptable curves before and after work shifts (cross-shift) on the first day back to work after a 2-day rest (for active workers). Acceptable FEV_1 values were allowed to vary by no more than 10% or 200 mL, whichever was greater, and the best FEV_1 and FVC values were used regardless of whether they were on the same tracing. The changes in pulmonary function were expressed as either annual changes or longitudinal changes over 15 years.

The Student *t* test was used to compare annual declines in FEV_1 and forced vital capacity (FVC) between retirees and active workers, and between cotton and silk workers. We applied generalized estimating equation (GEE) models with identity link function and constant variance function to examine the effects of retirement from the cotton industry. An exchangeable correlation structure was used.[16,17] Preshift FEV_1 and FVC measured repeatedly up to 4 times for each subject over a 15-year period were fitted as outcome variables (indicating periodic changes in lung function). We assessed cotton and silk workers in separate models. First, the models were fitted to determine possible interaction terms, including explanatory variables such as age, height, smoking status, pack-year, retirement status (as time-dependent variables), sex, years worked, and years since last worked (as fixed variables). Significant interaction terms (if any) were retained. Then, to the model fit for cotton workers, we added time-dependent covariates, including endotoxin and dust exposure levels, cross-shift drops in FEV_1 (ΔFEV_1, indicating differences in FEV_1 before and after a work shift), and presence or absence of byssinotic symptoms.

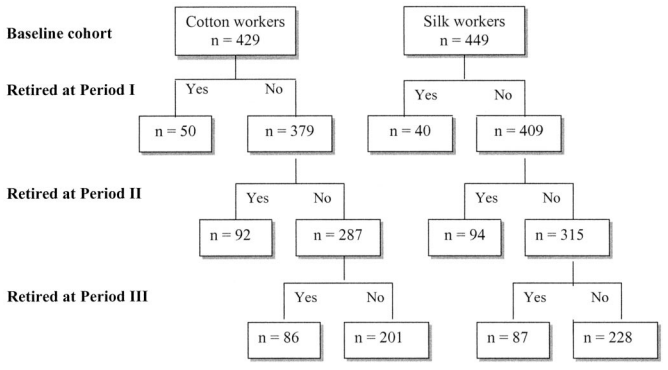

FIGURE 1. Flow chart of retirement status at each period of follow-up surveys in cotton and silk workers.

RESULTS

By the last survey, 228 (53%) cotton workers and 221 (49%) silk workers had retired. Table 1 displays demographic and spirometric data by retirement status. Smoking was more common in male cotton workers than in silk workers. All but 10 of the women were nonsmokers in the initial cohort. Years worked was longer in silk retirees than in cotton retirees. A total of 32% (n = 73) retired and 27% (n = 55) active cotton workers had byssinosis symptoms at some time over the 15-year period. Retired cotton workers had longer exposure years and higher cumulative levels of exposure to dust and endotoxin than active ones.

In this study, we were most interested in the potential changes in lung function during period III, because nearly half in both groups had retired by that time. Furthermore, there was a longer time since their leaving the industry at period III, thus making it more likely that we could detect a potential effect of exposure cessation on lung function. By contrast, the majority of workers were working during period I, which served as the reference period. A comparison of annual declines in FEV_1 and FVC is shown in Table 2. The retired workers, on average, were nearly 12 years older than the active workers with no difference in average age of cotton and silk workers of similar retirement status. Compared with active workers, retired cotton workers consistently had a greater annual decline in FEV_1 at period I but had a smaller decline at period III. A similar trend was seen in FVC. For silk workers, however, retirees had greater annual declines than active workers during both periods. Compared with silk workers, cotton workers had greater annual declines in FEV_1 and FVC, regardless of retirement status, particularly in active workers. Retirees in both cotton and silk groups had a

TABLE 1. Demographic and Spirometric Data at Baseline and Last Survey in Cotton and Silk Workers by Retirement Status at Last Survey

	Retired		Active	
	Cotton (n = 228)	**Silk (n = 221)**	**Cotton (n = 201)**	**Silk (n = 228)**
At baseline				
Male; no.(%)	105 (46)	98 (44)	98 (49)	94 (41)
Smoker; no.(%)	78 (34)	55 (25)	78 (39)	64 (28)
Age (years)	42.8 ± 9.8	43.1 ± 9.0	30.8 ± 7.2	29.6 ± 7.4
Height (cm)	162.1 ± 7.1	161.4 ± 6.8	165.8 ± 7.4	163.7 ± 7.5
Pack-years of smoking*	10.7 ± 11.0	14.1 ± 10.3	5.2 ± 6.3	4.6 ± 7.1
Years worked	21.2 ± 9.6	24.6 ± 9.9	10.5 ± 7.8	9.9 ± 8.5
Dust exposure (mg/m^3-years)	17.1 ± 12.8	—	8.9 ± 9.3	—
Endotoxin exposure (Eu/m^3-years)	30,867 ± 29,304	—	15,424 ± 13,947	—
FEV_1 (l)	2.67 ± 0.63	2.63 ± 0.52	3.21 ± 0.71	3.14 ± 0.69
FVC (l)	3.33 ± 0.70	3.28 ± 0.66	3.75 ± 0.80	3.60 ± 0.81
ΔFEV_1† (ml)	−43.3 ± 141.1	3.4 ± 12.1	−75.6 ± 168.2	−14.5 ± 142.4
At last survey‡				
Smoker; no.(%)	76 (40)	61 (31)	60 (39)	46 (32)
Pack-years of smoking*	19.1 ± 14.9	17.6 ± 14.8	11.7 ± 8.6	10.1 ± 6.2
Years worked	27.3 ± 9.9	32.8 ± 8.9	23.6 ± 6.3	22.5 ± 6.8
Years since last worked	6.7 ± 3.8	6.1 ± 3.7	—	—
Dust exposure (mg/m^3-years)	19.3 ± 12.9	—	16.0 ± 9.4	—
Endotoxin exposure (Eu/m^3-years)	56,524 ± 52,325	—	54,808 ± 52,824	—
FEV_1 (l)	2.21 ± 0.58	2.19 ± 0.49	2.76 ± 0.64	2.79 ± 0.57
FVC (l)	2.97 ± 0.65	2.92 ± 0.60	3.52 ± 0.80	3.53 ± 0.79
ΔFEV_1 (ml)	—	—	−67.6 ± 141.0	—

Mean and SD (in parentheses) unless otherwise stated.
*Calculated among smokers only.
†Cross shift drops in FEV_1. The cross-shift tests were not performed in retirees and silk workers at last survey.
‡Calculated based on 346 cotton workers and 338 silk workers who participated in the last survey.

TABLE 2. Annual Changes* (ml) in Lung Function by Retirement Status and Sex in Cotton and Silk Workers

	Men				Women			
	Cotton		Silk		Cotton		Silk	
	Retired	**Active**	**Retired**	**Active**	**Retired**	**Active**	**Retired**	**Active**
FEV_1								
Period I	−53.7 (4.3)	−45.8 (5.6)	−42.0 (4.4)	−44.3 (4.6)	−32.4 (3.1)	−23.8 (3.7)	−25.4 (3.3)	−13.1 (3.5)
Period III	−48.2 (5.6)	−52.7 (5.8)	−44.3 (5.2)	−38.3 (5.7)	−32.4 (3.3)	−44.1 (4.2)	−31.6 (3.7)	−18.2 (4.7)
Over 15 years	−43.8 (2.3)	−41.4 (2.5)	−39.9 (2.3)	−39.1 (2.1)	−24.8 (1.4)	−23.9 (2.0)	−24.1 (1.4)	−17.3 (2.1)
FVC								
Period I	−50.5 (6.2)	−30.7 (5.9)	−41.1 (5.6)	−16.8 (5.7)	−29.6 (4.6)	−8.5 (4.5)	−22.3 (4.1)	−2.7 (3.9)
Period III	−39.2 (7.7)	−32.3 (8.6)	−23.6 (7.0)	−5.6 (7.3)	−19.1 (4.9)	−25.5 (5.8)	−14.1 (4.4)	−3.0 (5.1)
Over 15 years	−34.3 (2.8)	−18.6 (3.0)	−34.5 (3.1)	−9.5 (2.9)	−19.1 (1.9)	−9.2 (2.8)	−15.6 (1.8)	−0.4 (2.4)

*Mean and SE (in parentheses). The calculations were based on 344 cotton workers and 341 silk workers at Period I; 315 cotton workers and 282 silk workers at Period III; and 312 cotton workers and 288 silk workers over 15 years.

greater loss of FVC over a 15-year period compared with the respective active workers.

The annual declines in FEV_1 during period III were compared further between cotton and silk workers. Both groups were divided into 4 subgroups according to years since last worked (0, 1–3, 4–7, and 8+ years). Cotton and silk workers had similar ages for the corresponding subgroups. As shown in Figure 2, annual declines in FEV_1 in cotton workers were smaller with increasing years since last worked, with a clearer trend in women. In silk workers, however, the values tended to be lower with increasing years. Correspondingly, the biggest gap between cotton and silk workers was seen in the active workers (subgroup 0), and then the gap narrowed with increasing years since retirement. The magnitude of declines in FEV_1 shown in female cotton workers was close to that shown in female silk workers after 4 years since last worked, whereas this similarity was found in males after 8 years.

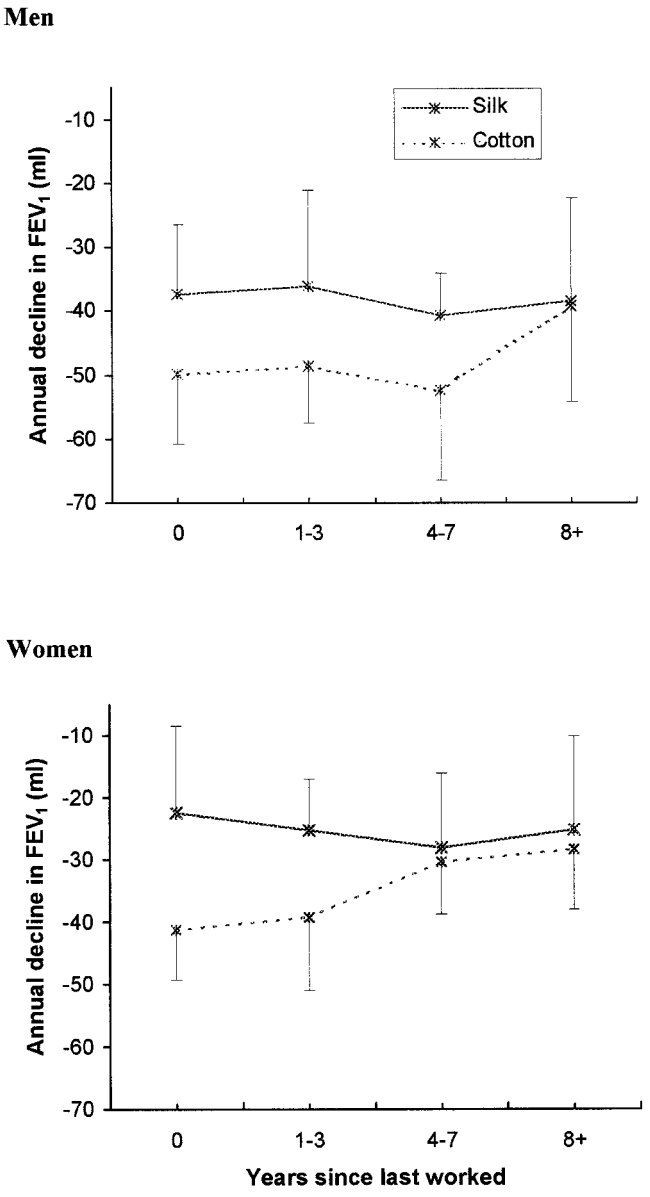

FIGURE 2. Annual declines in forced expiratory volume in 1 second during the period III in relation to years since last worked among cotton and silk workers, by sex. Bars indicate 95% confidence interval for each mean value.

We then used GEE models to estimate the effects of exposure cessation on the changes in lung function, which allowed fitting all available data repeatedly measured over the 15-year period. No significant interaction was found among age, years worked, years since last worked, retirement status, sex, and smoking status. As shown in Table 3, retirement from the mill was a substantial contributing factor for increased FEV_1 and FVC in cotton workers. Years since last worked was also related to improved lung function. In contrast, similar results were not observed in silk workers in whom retirement did not contribute to increasing FEV_1. Cross-shift drops in FEV_1 and exposure to endotoxin in cotton workers were negatively related to FEV_1, whereas

TABLE 3. Estimate (SE) from Multivariate Analysis for Lung Function Changes Over 15 Years

	FEV_1 (ml)	FVC (ml)
Cotton workers (n = 429)		
Retirement from mill	294.8 (121.8)	276.1 (140.8)
Years since last worked	16.9 (28.4)	24.5 (31.1)
Age (years)	−41.9 (9.4)	−20.0 (10.9)
Height (cm)	29.4 (7.3)	33.9 (8.5)
Gender (men)	740.2 (142.1)	896.1 (194.0)
ΔFEV_1 (ml)	−601.7 (244.2)	−576.7 (284.8)
Years worked	−5.8 (7.7)	−19.5 (10.0)
Endotoxin exposure (Eu/m^3)	−0.01 (0.0)	0.0 (0.0)
Dust exposure (mg/m^3)	3.7 (3.6)	1.3 (4.8)
Byssinosis	−63.3 (155.1)	−174.1 (171.8)
Smoker	−50.9 (99.9)	−27.3 (135.1)
Silk workers (n = 449)		
Retirement from mill	−71.5 (60.5)	8.7 (65.5)
Years since last worked	−10.1 (6.1)	0.5 (6.6)
Age (years)	−33.9 (2.0)	−24.1 (2.2)
Height (cm)	36.9 (4.9)	48.4 (5.3)
Gender (men)	412.2 (84.9)	555.8 (80.8)
Years worked	4.9 (3.7)	3.1 (3.6)
Smoker	−29.6 (65.2)	−55.5 (69.6)

Retirement from mill, sex, byssinosis symptom and smoker are category variables, whereas years since last worked, age, height, ΔFEV_1 (cross shift drops in FEV_1), years worked, endotoxin and dust exposure are continuous variables.

exposure to dust was not. In addition, age, height, and sex contributed to the declines in FEV_1 and FVC for both groups, whereas smoking or pack-years did not (the later was removed from the final model for a better fit).

We compared the age between smoking and nonsmoking male workers, and found that smokers were considerably younger than nonsmokers (52 vs. 59 years in the cotton group and 54 vs. 60 years in the silk group) according to last survey data. This result implies that the cumulative smoking effect on lung function might have been masked by the age difference. Further GEE models by smoking status were fitted among male workers (Table 4). Both smoking and nonsmoking cotton workers displayed improved FEV_1 and FVC associated with retirement. However, retirement from the cotton mill was a contributing factor to increased lung function in nonsmokers but not in smokers. The coefficients of FEV_1 and FVC in nonsmokers were nearly 3 times that in smokers, despite the older age in the former. This suggests that improved lung function related to cessation of cotton dust exposure is more evident in nonsmokers. In silk workers, no clear relationship was observed, whereas nonsmoking retirees had better lung function than smoking retirees.

To verify whether the exposure cessation was associated with improvement of airway obstruction among the cotton workers, we estimated individual occurrence of chronic obstructive pulmonary disease (COPD), defined as FEV_1/FVC lower than 70%, and then compared the prevalence between periods I and III (Table 5). Remission was also calculated, indicating those with COPD during period I and without during period III. Overall, the prevalence of COPD during period III was lower than during period I for both retired and active cotton workers, but the proportion of remission in retirees was higher than in the actives. When stratified by sex, COPD remission in female retirees was double as that in the actives. Male retirees appeared to have a higher prevalence of COPD during period III than during period I, but this was largely attributable to smoking effects, in which smokers had an increasing prevalence and the lowest remission of COPD. Silk workers had a lower prevalence of COPD at either period, with 27% during period I and 21% during period III for retirees. Their COPD remission was surprisingly close to that of their cotton counterparts. We also used 60% and 50% as cutpoints to define COPD and observed a similar result.

TABLE 4. Estimates (SE) for Lung Function Changes over a 15-Year Period in Relation to Retirement from Mill, by Smoking Status*

	FEV_1 (ml)	FVC (ml)
Cotton workers		
Smokers (n = 155)	174.4 (158.7)	230.3 (214.7)
Nonsmokers (n = 48)	636.2 (289.4)	619.8 (65.1)
Silk workers		
Smokers (n = 150)	−153.5 (209.0)	46.9 (18.6)
Nonsmokers (n = 42)	126.8 (154.2)	182.0 (215.2)

*Restricted to male workers, and adjusted by the covariates stated in Table 3, other than smoking status and sex.

TABLE 5. Prevalence of COPD* by Retirement, Sex and Smoking Status† in Cotton Workers

	Period I	Period III	Remission‡
Total			
Active	34/201 (17)	12/154 (8)	18/201 (9)
Retired	76/228 (33)	51/184 (28)	32/228 (14)
Women			
Active	14/103 (14)	2/87 (2)	8/103 (8)
Retired	37/123 (30)	15/97 (16)	19/123 (16)
Men			
Active	20/98 (20)	10/67 (15)	10/98 (10)
Retired	39/105 (37)	36/87 (41)	13/105 (12)
Smokers	17/64 (27)	26/55 (47)	3/64 (5)
Nonsmokers	11/30 (37)	8/24 (33)	4/30 (13)

*COPD was defined as the ratio of FEV1/FVC being lower than 70%. Actual numbers and percentages (in parentheses) are presented.
†Calculation by smoking status was restricted to retired workers only.
‡Remission indicates those with COPD at Period I, and without anymore at Period III.

DISCUSSION

Reversible airway obstruction has been shown to be characteristic of the early byssinosis syndrome, but it has been unknown whether the chronic airway changes related to long-term cotton dust exposure are reversible. To our knowledge, there are 2 studies that have addressed the issue directly. One is a cross-sectional study from China[18] that investigated 173 retired cotton textile workers who had worked for over 25 years in the preparatory and spinning departments. The results showed that respiratory symptoms improved significantly after these workers had left their textile job for from 1 to 10 years. In comparison with a group of retired silk workers who had the same age and smoking status, no substantial differences were observed in any of 8 spirometric parameters in the cotton workers, although they had lower values. The authors concluded no evidence of "chronic irreversible effects" from cotton dust exposure. Another study that followed both active and retied cotton textile workers for 6 years reported lung function recovery in retired women.[19] Further analysis using the same database showed that workers who had retired from the cotton mill had greater losses of FVC and FEV_1 than those who remained working.[20] However, no detailed smoking information was

given, and analysis was not stratified by smoking. In addition, both of these studies lacked information on workplace dust concentrations and individual exposure.

In the present study, we examined chronic changes in lung function among retired cotton textile workers by comparing them with both active cotton workers and retired silk workers. Chronic airway obstruction related to cotton dust exposure appeared to be improved or partially reversible if exposure ceases. Both male and female retirees in the cotton group had smaller annual loss of FEV_1 than the active workers, although they had a greater decline when most of them worked. The annual loss of FEV_1 tended to be smaller with increasing years since retirement. Also, the term of retirement from the cotton mill was found to be a significant contributing factor to increased FEV_1 and FVC over a 15-year period in the multivariate models in which other covariates and confounders were adjusted, a relationship that was not observed in the silk group. Furthermore, the cotton retirees had a higher proportion of COPD remission than the actives, which was similar to the silk workers, suggesting a favorable effect of exposure cessation on those with COPD. These results imply that chronic airway obstruction associated with cotton dust exposure, possibly as well as other vegetable dust exposure, may be reversible to some extent if exposure ceases. This situation contrasts with chronic disease induced by exposure to mineral dust such as silica, asbestos, and coal dust, in which pulmonary fibrosis and respiratory impairment develop progressively even after exposures cease.[21]

On the other hand, it is noteworthy that the annual losses of lung function in the retired cotton workers were not reduced to the level found in the retired silk workers. Although age, years since retirement, and smoking status were similar in the 2 subgroups, the cotton retirees had greater functional losses than the silk retirees. The absolute levels of lung function remained lower and the prevalence of COPD remained higher in the cotton retirees. These results suggest that the cumulative airway effects of cotton dust exposure may, more or less, persist even after the exposure stopped.

The extent of lung function recovery from the adverse effects of cotton dust was related to individual smoking status. The multivariate analysis revealed that improved lung function related to exposure cessation was more prominent in nonsmokers than in smokers. The COPD remission was also higher in the nonsmokers. This finding is not surprising because smoking is known to cause COPD. In addition, it has been reported that an interaction between smoking and cotton dust exposure may lead to worse lung function and higher incidence of byssinosis in smoking workers.[11,22] Consequently, it is expected that a substantial improvement of lung function is less likely to be observed in retirees who smoke.

There was an indication that the changes in FEV_1 were more closely related to level of exposure to endotoxin than to cotton dust itself. This finding is in agreement with some previous reports,[3,12] which suggest an exposure-response relationship between endotoxin exposure and chronic airway obstruction. In addition, the results of our study confirm that acute (cross-shift) changes in FEV_1 is a significant predictor for excessive annual declines in FEV_1 and FVC, whereas the presence of byssinotic symptoms was not significantly correlated with declines in lung function. It is still unknown whether acute and chronic airway responses that occur after a particular exposure are related independently to the exposure, whether the first leads to the second, or whether chronic airways obstruction may arise by either route.[23] In either case, it is evident that a worker is more likely to have chronic airway obstruction if he or she is exposed long-term to higher endotoxin or has substantial cross-shift drops in FEV_1 during the period of cotton dust exposure. These relationships are independent of exposure cessation. Therefore, the maximum reduction of adverse effects is ultimately achieved only through prevention of exposure rather than simply its cessation on retirement. Effective exposure control should be the top priority in the cotton textile industry, as well as in other workplaces that involve vegetable dust exposure.

The present findings were obtained from a long-term prospective follow-up observation in cotton textile workers. Despite the high follow-up rates in this study, there remained a small fraction of subjects who were lost at each follow-up survey. Bias may result from differential losses to follow up in a longitudinal study. To ascertain the possibility, we assessed participation status of both active and retired workers at all 3 follow-up surveys. The dropout rates were 6% to 23% in the cotton active workers, 7% to 37% in the silk actives, 7% to 16% in the cotton retirees, and 8% to 13% in the silk retirees. The rates were similar for the cotton and silk groups at a given survey. Furthermore, we compared preshift FEV_1 and FVC measured at the last survey between participants and nonparticipants, stratified by retirement status. As expected, the nonparticipants generally tended to have lower values of FEV_1 and FVC than the participants, regardless of exposure group and retirement status. This finding indicated that subjects with poorer health might have been more likely to drop out from follow-up surveys. We conclude that the results of the study were not substantially biased as a result of losses to follow up, which took place homogeneously in both the cotton and silk groups.

In summary, this study suggests that cessation of cotton dust exposure may slow annual loss of lung function and reduce airway obstruction in the long-term exposed workers. However, these data did not provide convincing evidence that the adverse effects of chronic cotton dust exposure would decrease to the level seen in an unexposed population. Given the independent relationships of chronic declines in lung function to the level of endotoxin exposure and acute drops in FEV_1, effective exposure control is the optimal way to reduce risk for cotton dust-related disease in exposed working populations.

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