Routledge
Taylor & Francis Group

Archives of Environmental Health: An International Journal

ISSN: 0003-9896 (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/vzeh20

Lung Function, Airway Reactivity, and Atopy in Newly Hired Female Cotton Textile Workers

Xiao-Rong Wang , Lei-Da Pan , Hong-Xi Zhang , Bi-Xiong Sun , He-Lian Dai & David C. Christiani

To cite this article: Xiao-Rong Wang , Lei-Da Pan , Hong-Xi Zhang , Bi-Xiong Sun , He-Lian Dai & David C. Christiani (2003) Lung Function, Airway Reactivity, and Atopy in Newly Hired Female Cotton Textile Workers, Archives of Environmental Health: An International Journal, 58:1, 6-13, DOI: 10.3200/AEOH.58.1.6-13

To link to this article: https://doi.org/10.3200/AEOH.58.1.6-13

Lung Function, Airway Reactivity, and Atopy in Newly Hired Female Cotton Textile Workers

XIAO-RONG WANG
Occupational Health Program
Department of Environmental Health
Harvard School of Public Health
Boston, Massachusetts
LEI-DA PAN
HONG-XI ZHANG
BI-XIONG SUN
HE-LIAN DAI
First Hospital of the Shanghai Textile Bureau
Shanghai, China

DAVID C. CHRISTIANI
Occupational Health Program
Department of Environmental Health
Harvard School of Public Health
Boston, Massachusetts
and
Pulmonary and Critical Care Unit
Massachusetts General Hospital
Department of Medicine
Harvard Medical School
Boston, Massachusetts

ABSTRACT. To assess changes in lung function and airway reactivity resulting from exposure to cotton dust, and the role of atopic status in these changes, the authors observed a group of 225 newly hired Chinese textile workers for 1 yr. All workers were female, lifelong nonsmokers, and none of them had been exposed previously to cotton or other occupational dust. Atopic status was determined at baseline. Spirometry, response to methacholine challenge, and total serum immunoglobulin E level were examined at baseline and again after subjects began work in the cotton mills. Obvious cross-shift drops in forced expiratory volume in 1 sec ($FEV_{1.0}$), and declines in forced vital capacity and $FEV_{1.0}$ over 1 yr, were observed. Atopic workers had a significantly greater acute drop in $FEV_{1.0}$ than did nonatopic workers. Both atopic and nonatopic workers had slightly increased airway reactivity at 1 yr, compared with baseline values. The results suggest that exposure to cotton dust is responsible for acute and longitudinal declines in lung function, as well as for slightly increased airway reactivity. Atopy may interact with cotton dust to accentuate the acute lung function response.

<Key words: atopy, cotton dust, endotoxin, occupational lung disease, pulmonary function, respiratory symptoms, textile workers>

OCCUPATIONAL EXPOSURE TO COTTON DUST is related to an increased prevalence of respiratory symptoms and decreased lung function. An acute drop in forced expiratory volume in 1 sec ($FEV_{1.0}$) over the work shift is one of the most important characteristic responses to cotton dust exposure. This drop—sometimes accompanied by symptoms of byssinosis—is greatest on Monday (or the 1st day back to work after a break), and may disappear later in the work week. Longitudinal cohort studies have shown that continuous and/or long-term exposure to cotton dust may lead to chronic and irreversible declines in $FEV_{1.0}$ and forced vital capacity (FVC).[1–3]

The mechanism or causative agent(s) by which airway obstruction is induced in cotton workers remains incompletely understood. Several risk factors for cotton-dust–induced disease have been described in previous epidemiologic studies, including the concentration of total or respirable cotton dust, length of exposure, cigarette smoking, and chronic obstructive lung disease or other cardiopulmonary diseases.[4–6] There is growing evidence that the concentration of inhaled endotoxin-contaminated dust may explain both acute chest tightness and airflow obstruction among cotton workers[7,8] and agricultural workers.[9] Bacterial endotoxin is likely a major causative agent. In addition, research has sug-

gested that an allergic diathesis (atopy) is involved in acute changes in lung function and disease development. Several studies report a differing response to cotton dust exposure between atopic and nonatopic subjects.[10–12] Previous studies investigating the importance of bronchial reactivity in cotton workers as a potential marker have shown a less-consistent relationship between preexposure bronchial reactivity and response to cotton dust.[13–15] Many previous observations of bronchial reactivity, lung function, and atopic status have been limited by cross-sectional design—ranging from several hours to several days—and by subject selection (e.g., inclusion of nonexposed volunteers, and both smokers and nonsmokers). Data from follow-up studies, and from nonsmoking cotton workers, are scarce, making it difficult to clarify the natural history of cotton-dust–induced airway disease.

The current 1-yr follow-up study was designed to evaluate changes in lung function and nonspecific airway reactivity in response to cotton dust exposure. The study subjects consisted of a group of lifelong nonsmoking female workers who were newly hired at cotton textile mills and naive to cotton dust exposure. In particular, we examined whether pulmonary function and nonspecific airway reactivity differed depending on atopic status. The study was approved by the institutional review boards of the Harvard School of Public Health and the First Hospital of Shanghai Textile Bureau.

Subjects and Method

Subjects. In March 1997, newly hired workers at 3 cotton mills in Shanghai, China, were invited to take part in a medical examination before starting work (baseline survey). Of 267 eligible new-hires in the yarn preparation areas, 240 agreed to participate. Enrollment in the cohort was restricted to (a) female workers (because of the small number of males who were newly hired), (b) lifelong nonsmokers (few females smoked), and (c) those who had no cardiopulmonary disease or symptoms at baseline. As a result, 225 workers meeting the criteria made up the original cohort; 15 workers (9 males, 5 females with respiratory disease, and 1 female lacking a completed questionnaire) were excluded. The average age of the cohort was 18 yr (range = 16–29 yr) at the outset, and none had been occupationally exposed to organic or inorganic dusts previously. Subjects' health status was reexamined at 3 mo and 1 yr after starting work in the cotton mills, and 194 (86%) and 136 (60%) subjects returned on each of these dates, respectively.

Environmental assessment. Environmental airborne cotton dust and Gram-negative bacterial endotoxins were measured at 3 mo in the various yarn preparation areas. Details of the exposure assessment methods have been described previously.[16] Vertical elutriators (General Metal Works, Inc. [Cleveland, Ohio]) were used to take environmental samples. Endotoxin assays were performed on the dust samples using the Limulus amoebocyte lysate assay, chromogenic method.[17] At least 8 measurements were taken in the various work areas, including the carding, drawing, roving, spinning, twisting, and bobbing areas. Irrespective of the mill, the concentrations of both cotton dust and endotoxin were highest in the carding and drawing areas, and lowest in the spinning area. The concentrations of cotton dust were similar within the corresponding work areas of the 3 mills, whereas the concentrations of endotoxin varied considerably. The geometric median concentrations were 0.35 mg/m^3 for cotton dust and 37 ng/m^3 for endotoxin. Correlation between dust and endotoxin was relatively high ($r = 0.73$, $p < 0.0001$). The production and working conditions were stable, and the workers remained at the same job title and in the same work area throughout the observation.

Questionnaire. Modified questionnaires, which were based on the 1978 American Thoracic Society standardized questionnaire,[16,18] were administered to obtain information on occupational and medical history. Given that none of the workers smoked, we inquired about regular passive smoking, either at home or at work. We separately reported respiratory symptoms and/or diseases that occurred during the observation period.

Skin test. Skin-prick testing was performed at baseline, using standard methods.[19] Briefly, the volar surface skin was cleaned with alcohol and allowed to dry. Twelve pricks were made in the skin approximately 2 cm apart with the Greer Scarifier (Greer Laboratories, Inc. [Lenoir, North Carolina]). Subjects were tested with 6 common local antigens and 6 standard antigens, including ragweed, mold, standardized mite DF (*Dermatophagoides farinae*), mulberry silk, summer pollen, and house dust, along with a glycerine (negative) control. Erythema and induration were measured at 20 min by reading 2 perpendicular lines across the test site. Positive reactions were defined as induration at least 5 × 5 mm after subtracting diameters of negative control reactions. Because the results of response to local antigens and to standard ones were nearly identical, we reported the results for local antigens only. Atopy was defined as a positive reaction to 2 or more allergen extracts.

Lung function tests. Spirometric measurements were conducted prior to beginning work in the mill, to obtain baseline values, and again at 3-mo and 1-yr follow-up surveys. An 8-l water-sealed field spirometer (W. E. Collins Co. [Braintree, Massachusetts]), calibrated twice a day with a 3-l syringe, was used throughout the study. At follow-up surveys, forced expiratory spirograms were conducted before and after work shifts (cross-shift) on the 1st day back to work after a 2-day rest. Each work-

er performed up to 7 trials to produce 3 acceptable curves. Acceptable $FEV_{1.0}$ tracings were allowed to vary by no more than 5% or 100 ml, whichever was greater, and the best $FEV_{1.0}$ and FVC were used, regardless of whether they were on the same tracing. The values were corrected to conditions of body temperature and pressure saturated with water vapor.

Measurement of airway reactivity. A test of airway reactivity was performed at baseline, and at the 1-yr follow-up survey, using graded doses of inhaled methacholine, according to the protocol described by Hendrick et al.[20] Solutions were inhaled through a Pari-Boy nebulizer (airflow = 8 l/min, output = 0.3 ml/min) (DeNilbiss Co. [Somerset, Pennsylvania]). Subjects inhaled the aerosol in a sitting position, while breathing quietly, for 2 min through the nebulizer. They first inhaled a diluent solution of 0.5% sodium chloride USP (United States Pharmacopeia), 0.275 sodium bicarbonate, and 0.4% phenol with a solution pH of 0.7, to provide a control baseline spirometric value. They then inhaled a methacholine solution, beginning at 0.5 mg/ml and gradually increasing in concentration to 1, 2, 5, 10, and 25 mg/ml. Spirometry was measured 60–120 sec after each inhalation. The test was terminated when $FEV_{1.0}$ had declined 15% from the post-diluent value, or when the methacholine concentration of 25 mg/ml was reached. Responders were expressed as PC_{10} and PC_{15}, defined as $FEV_{1.0}$ decreases of 10% and 15%, respectively, at the selected threshold value of 10 mg/ml of methacholine. At the 1-yr survey, the methacholine challenge test was performed before the work shift on the 1st day after a break.

Total serum immunoglobulin E (IgE) measurement. Total IgE concentration was examined at baseline, and at the 3-mo and 1-yr surveys. A modified classical radioimmunosorbent test was used.[21]

Statistical analysis. We assessed lung function responses referable to cotton dust exposure by determining acute and "longitudinal" (i.e., 3-mo and 1-yr) changes. Acute change was expressed as a cross-shift drop in $FEV_{1.0}$ ($\Delta FEV_{1.0}$ = $FEV_{1.0}$ after shift – $FEV_{1.0}$ before shift), whereas the differences in FVC and $FEV_{1.0}$ over 3 mo or 1 yr were regarded as longitudinal changes. Serum IgE concentrations were logarithmically transformed (log10) for the analysis because of their highly skewed distribution.

The differences between atopic and nonatopic workers were compared by 2-tailed *t* test for continuous variables, and by Fisher's exact test for categorical variables. Multivariate regression analysis was fitted to assess independent determinants for lung function responses. In addition to atopic status, the factors of age, height, spirometric values at baseline, passive smoking, log(IgE), and levels of exposure to cotton dust and endotoxin were considered as candidate predictor variables. A backward selection procedure was performed to select significant variables with a level of $p < 0.12$. The environmental measurements from work areas were used as a surrogate of personal exposure. Individual exposures to dust and endotoxin were expressed as high- or low-level, in terms of the median values of environmental measurements. Because no worker was permitted to smoke at the work site, passive smoking was considered only if a worker had 1 or more family members who smoked regularly at home. The analyses were performed with SAS personal computer software (ver. 8) (SAS Institute [Cary, North Carolina]).

Results

The demographic features, serum IgE concentrations, baseline spirometry, and atopic status of the original cohort are shown in Table 1. Sixty-eight workers (30%) showed cutaneous hypersensitivity to allergens by skin-prick test. Although age and height in atopic workers were similar to those in nonatopic workers, the latter had somewhat higher baseline spirometric values and lower log(IgE) levels. The proportion of passive smoking at home was slightly higher among nonatopic workers.

To estimate potential selection bias due to dropout from the follow-up surveys, baseline data and 3-mo data were compared between participants and dropouts after the 1-yr follow-up survey (Table 2). Baseline data showed no difference in demographic features, atopic status, log(IgE), or spirometric values between participants and dropouts at either 3 mo or 1 yr. However, workers who participated at 3 mo, but not at 1 yr, had

Table 1.—Characteristics of the Study Subjects Prior to Working at Cotton Mills

Variable	Overall (*n* = 225)	Atopic (*n* = 68)	Nonatopic (*n* = 157)
Age (yr)			
$\bar{x}$	18.3	18.0	18.4
SE	0.1	0.2	0.2
Height (cm)			
$\bar{x}$	160.1	159.7	160.2
SE	0.3	0.5	0.3
Smokers at home			
n	140	36	104
%	62	53	66
Log(IgE) log(mg/dl)			
$\bar{x}$	5.50	5.63	5.45
SE	0.07	0.12	0.08
$FEV_{1.0}$ (ml)			
$\bar{x}$	2,705.2	2,658.5	2,725.8
SE	21.0	35.1	25.9
FVC (ml)			
$\bar{x}$	3,030.9	2,944.0	3,050.8
SE	24.3	42.7	28.9

Notes: $\bar{x}$ = mean, *SE* = standard error, IgE = immunoglobulin E, $FEV_{1.0}$ = forced expiratory volume in 1 sec, and FVC = forced vital capacity.

Table 2.—Comparison of Basic Data for Followed Subjects vs. Dropouts

Variable	3 mo vs. baseline		1 yr vs. baseline		1 yr vs. 3 mo	
	Followed	Dropouts	Followed	Dropouts	Followed	Dropouts
n	194	31	136	89	136	58
Atopic						
n	59	9	40	26	40	19
%	30	29	29	29	29.4	32.8
Smokers at home						
n	124	19	84	56	84	40
%	64	61	62	63	61.8	69.0
Age (yr)						
$\bar{x}$	18.3	18.2	18.3	18.2	18.6	18.6
SD	1.6	1.5	1.6	1.5	1.6	1.5
Height (cm)						
$\bar{x}$	160.1	160.6	160.4	159.8	160.4	159.3
SD	3.8	3.5	3.6	3.6	3.6	3.9
Log(IgE), log(mg/dl)						
$\bar{x}$	5.49	5.55	5.79	5.76	5.79	5.76
SD	1.36	1.28	1.35	1.30	1.30	1.29
$FEV_{1.0}$ (ml)						
$\bar{x}$	2,705.2	2,707.1	2,699.3	2,710.6	2,647.1	2,510.6*
SD	292.1	293.4	285.7	297.2	263.0	300.0
FVC (ml)						
$\bar{x}$	3,030.9	3,053.1	3,046.7	3,036.1	2,984.1	2,799.4*
SD	309.2	353.7	298.9	349.1	301.7	332.8
$\Delta FEV_{1.0}$						
$\bar{x}$					–32.4	–7.6
SD					94.8	87.7

Notes: $\bar{x}$ = mean, *SD* = standard deviation, IgE = immunoglobulin E, $FEV_{1.0}$ = forced expiratory volume in 1 sec, and FVC = forced vital capacity.
*$p < 0.01$.

significantly lower preshift $FEV_{1.0}$ and FVC measured at 3 mo than those who participated at 1 yr, suggesting a "healthy worker" effect on spirometric outcomes at the 1-yr survey.

Dose-response characteristics for methacholine challenge testing in atopic and nonatopic workers are presented in Figures 1 and 2, respectively. Airway response to methacholine was increased at 1 yr for both atopic and nonatopic workers, compared with their own baseline values. The atopics did not show more airway responsiveness than the nonatopics at either baseline or the 1-yr survey. Nevertheless, the atopics appeared to have a slightly greater drop in $FEV_{1.0}$ at the highest dose at 1 yr, compared with their baseline values. More responders at either time were observed in nonatopic workers, but the number, though small, tended to increase in atopic workers from baseline to 1 yr, again indicating a slightly greater change in airway responsiveness in the atopics (Table 3).

Log(IgE) at 3 mo was elevated for all workers; atopics had a higher level than nonatopics (Table 4). At 1 yr, however, the values returned to near baseline levels in both subgroups.

At 3 mo, we observed a cross-shift drop in $FEV_{1.0}$ in both atopic and nonatopic workers (slightly greater in the atopics). No decrease in preshift FVC or $FEV_{1.0}$ was detected (Table 4). At 1 yr, not only did the acute drop in $FEV_{1.0}$ remain but declines in FVC and $FEV_{1.0}$ over the year were also evident. In the group as a whole, the reduction in FVC was 124 ml, and in $FEV_{1.0}$ it was 70 ml. Atopic workers did not show greater longitudinal de-

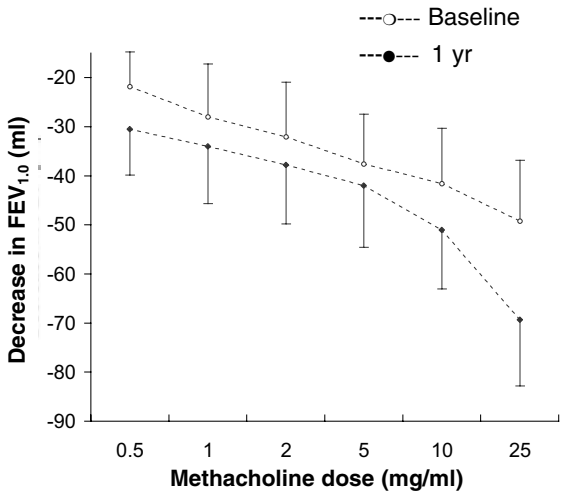

Fig. 1. Methacholine dose-response characteristics of the atopic group (*n* = 40). Data expressed as means and standard error of the means.

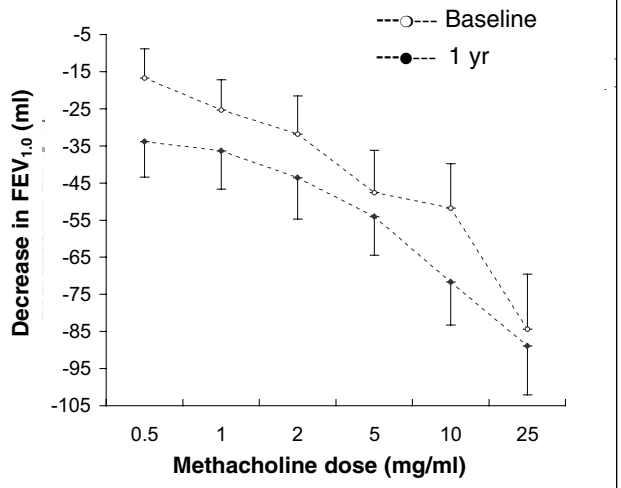

Fig. 2. Methacholine dose-response characteristics of the nonatopic group (*n* = 96). Data expressed as means and standard error of the means.

clines in $FEV_{1.0}$ and FVC than nonatopic workers, but an acute drop in $FEV_{1.0}$ was greater in the atopics, whose $\Delta FEV_{1.0}$ was almost 3 times lower than that of the nonatopics ($p = 0.07$). The proportion of an acute drop by 5% or more was significantly different between the 2 subgroups ($p < 0.05$).

Multivariate regression analyses focusing on lung function changes at 1 yr were performed using a backward selection procedure. The considered variables that reached a level of $p < 0.12$ are presented in Table 5. Our results revealed that atopic status was a significant predictor for excess cross-shift drop in $FEV_{1.0}$ at 1 yr ($p < 0.01$). Higher endotoxin exposure was marginally significantly associated with the acute drop in $FEV_{1.0}$ ($p = 0.06$). Atopy, or exposure to endotoxin, on the other hand, could not explain the declines in $FEV_{1.0}$ and FVC over a year; however, the level of exposure to dust was marginally significant in the model for estimating FVC. The terms for passive smoking and log(IgE) did not enter into any of the models.

Discussion

We observed natural changes in lung function and nonspecific airway reactivities among a group of newly hired nonsmoking textile workers. Of the 225 workers who were enrolled in the original cohort, 31 and 89 did not return for testing at 3 mo and 1 yr, respectively. A comparison of baseline data showed no differences in demographic features and health status between followed workers and those lost to follow-up. However, 58 workers who participated at 3 mo, but not at 1 yr, had significantly lower preshift $FEV_{1.0}$ and FVC than did the 136 remaining participants. This result indicated

Table 3.—Number of Responders to Methacholine Challenge Tests, by Atopic Status*

Status	Preexposure *n*	Preexposure %	After 1 yr *n*	After 1 yr %
Atopic (*n* = 40)				
PC_{10}	2	5	4	10†
PC_{15}	0	0	2	5
Nonatopic (*n* = 96)				
PC_{10}	15	16	13	14
PC_{15}	3	3	4	4

Notes: PC_{10} = forced expiratory volume in 1 sec ($FEV_{1.0}$) decrease of 10% at threshold value of 10 mg/ml methacholine, and PC_{15} = $FEV_{1.0}$ decrease of 15% at threshold value of 10 mg/ml methacholine.
*The analysis was restricted to those who participated in the 1-yr follow-up survey.
†$p = 0.05$ compared with preexposure (Fisher's exact test).

Table 4.—Changes (Relative to Baseline) in Spirometric Values and Total Serum IgE Levels after Working in Cotton Mills

Variable	Overall	Atopic	Nonatopic
At 3 mo			
n	194	59	135
Log(IgE), log(mg/dl)			
$\bar{x}$	0.26	0.34	0.23
SE	0.04	0.06	0.06
FVC (ml)			
$\bar{x}$	39.0	71.6	24.2
SE	15.9	27.7	19.3
$FEV_{1.0}$ (ml)			
$\bar{x}$	43.0	61.0	34.9
SE	11.8	18.4	14.9
$\Delta FEV_{1.0}$ (ml)			
$\bar{x}$	–18.4	–21.4	–15.5
SE	6.5	8.1	7.8
% $\Delta FEV_{1.0} \geq 5\%$			
n	25	8	17
%	12.9	13.6	12.6
At 1 yr			
n	136	40	96
Log(IgE), log(mg/dl)			
$\bar{x}$	–0.06	–0.05	–0.06
SE	0.05	0.07	0.06
FVC (ml)			
$\bar{x}$	–124.1	–108.6	–130.9
SE	16.7	19.3	16.3
$FEV_{1.0}$ (ml)			
$\bar{x}$	–70.1	–52.8	–77.4
SE	12.8	32.0	19.5
$\Delta FEV_{1.0}$ (ml)			
$\bar{x}$	–23.6	–43.0	–15.5
SE	7.0	10.3	5.1*
% $\Delta FEV_{1.0} \geq 5\%$			
n	10	6	4
%	7.4	15.0	4.2†

Notes: $\bar{x}$ = mean, *SE* = standard error, IgE = immunoglobulin E, FVC = forced vital capacity, and $FEV_{1.0}$ = forced expiratory volume in 1 sec.
*$p = 0.07$.
†$p < 0.05$, compared with atopic.

Table 5.—Regression Coefficients and Standard Errors for Independent Variables Included in a Multiple Linear Regression Model Predicting Changes in Lung Function at 1-Yr Follow-Up Survey

Variable	Coefficient or estimate	*SE*	*p*
$\Delta FEV_{1.0}$ (ml)			
Atopy	–35.6	15.2	0.02
High endotoxin	–28.9	15.5	0.06
Age (yr)	14.2	5.8	0.02
Baseline $FEV_{1.0}$ (ml)	–0.07	0.02	0.002
Intercept	–61.7	118.7	0.60
R^2 = .18			
FVC (ml)			
High dust	–103.8	58.8	0.08
Age (yr)	- 23.2	9.9	0.02
Baseline FVC (ml)	- 0.2	0.05	0.001
Intercept	416.5	167.1	0.01
R^2 = .15			
$FEV_{1.0}$ (ml)			
Height (cm)	8.6	3.6	0.02
Baseline $FEV_{1.0}$ (ml)	–0.3	0.04	< 0.0001
Intercept	–741.7	543.0	0.17
R^2 = .20			

Notes: SE = standard error, IgE = immunoglobulin E, $FEV_{1.0}$ = forced expiratory volume in 1 sec, and FVC = forced vital capacity. All considered variables in each model—including atopic status (0, 1), level of exposure to endotoxin (high, low) and dust (high, low), age, height, and baseline $FEV_{1.0}$ or FVC—were selected using a backward procedure at a level of $p < 0.12$.

that workers who were predisposed to being affected by exposure were more likely to be lost at the survey that followed. This probable "healthy worker" effect might have led to an underestimation of respiratory effects at 1 yr. On the other hand, the distinctive characteristics of the cohort—same gender, young, all lifelong nonsmokers, previously unexposed to industrial dust, and healthy status (i.e., no cardiopulmonary disease or symptoms)—enabled us to evaluate relatively pure effects of cotton dust exposure.

These newly hired workers experienced remarkable changes in lung function after their initial year of exposure, in comparison with their baseline data. The changes were likely attributable to the effects of cotton dust exposure, yet we found that the atopic and nonatopic workers expressed different patterns in acute lung function response to cotton dust. Atopic workers had a significantly greater cross-shift drop in $FEV_{1.0}$ than nonatopic workers, and this drop was independent of age, height, or dust or endotoxin level in the work site.

The earliest evidence that atopy was important in the acute response to cotton dust was reported by Jones et al.,[10] who examined workers in several cotton seed-crushing mills by using cross-shift spirometry and skin prick tests for 10 common inhalant allergens. They reported significantly greater $FEV_{1.0}$ declines over the work shift in atopic workers than in their nonatopic counterparts; the $FEV_{1.0}$ difference was unrelated to differences in demographic profiles, smoking habits, or dust levels. In a later study, a significant relationship was reported between atopic status and the decrease in $FEV_{1.0}$ among previously nonexposed volunteers who were exposed to 1 mg/m^3 cotton dust in a model cardroom for 5 or 6 hr.[12,22] All of these studies were based on a cross-sectional design, with 1 or 2 days of observation. A recent study by Li et al. was conducted for an extended observation time (1 yr) among cotton textile workers.[23] Similar to the current study, subjects were selected from newly employed workers in a Chinese cotton mill. However, that study recruited both smokers and nonsmokers, as well as both males and females. Moreover, those who had respiratory symptoms or diseases prior to work were not excluded. Li et al. also observed a difference between atopic and nonatopic workers in acute $FEV_{1.0}$ drops and airway response to methacholine challenge testing, although health outcomes from exposure to cotton dust might have been overestimated as a result of to the recruitment of preexisting "unhealthy" factors.

Our results derived from the 1-yr follow-up are consistent with previous findings, and they support the hypothesis that atopy and cotton dust exposure interact to accentuate a cross-shift drop in $FEV_{1.0}$. Alternatively, atopics as a group have an increased susceptibility to the effects of airway inflammation induced by cotton dust. Furthermore, our results suggest that the expression of this increased susceptibility in atopic subjects may last for at least 1 yr (and probably longer) following the onset of exposure, rather than being expressed only in the initial stage of exposure. As stated by other authors,[24] we did not detect a direct effect of atopy on longitudinal lung function change. Nevertheless, we cannot exclude the possibility that atopic status affects chronic functional change in an indirect way for workers exposed long-term to cotton dust, because an acute drop in $FEV_{1.0}$ has been related to chronic declines in both $FEV_{1.0}$ and FVC.[3,25,26] Additional research, with a longer observation time, is needed to clarify the potential role of atopy in the chronic changes in lung function associated with cotton dust exposure.

Challenge testing with methacholine or histamine has been used in epidemiological studies of occupational populations. Most studies investigating the relationship between preexposure bronchial reactivity and the response to cotton dust inhalation have shown consistent results. In an experimental study,[27] a group of volunteers was tested for bronchial reactivity prior to exposure, and the following week they were exposed to airborne cotton dust (at 1 mg/m^3 for 6 hr). Their $FEV_{1.0}$ was measured before and after exposure. No significant association was found between preexposure bronchial re-

activity and the drop in $FEV_{1.0}$ that occurred during cotton dust exposure. Unfortunately, no postexposure measurement of bronchial reactivity was performed. Another study reported that baseline methacholine responsiveness was significantly greater in subjects designated as responsive to cotton bract extracts.[14] A similar result was observed in a model card-room study, in which a significant increase in airway reactivity was seen in previously unexposed volunteers after cotton dust exposure.[12] The discrepancy in these results may be due partly to differences in the methods used for assessing airway responsiveness and subject selection. Additionally, multiple pathophysiologic disturbances are involved in the nonspecific challenge test, including the immune system, the autonomic nervous system, the bronchial epithelium, and other structural elements of the airway.[28] Any change in these factors in study subjects can influence the test result, and could account for the inconsistency.

We observed a small difference in nonspecific airway reactivity between pre- and postexposure among the newly hired workers in our study. Although airway reactivity data at 3 mo were unavailable, the data at 1 yr showed a tendency for increased airway reactivity when compared with the baseline data. Overall, atopic workers did not have higher bronchial responsiveness than nonatopic workers. Jacobs et al.[12] evaluated bronchial responsiveness in 57 nonsmoking and nonasthmatic volunteers, all of whom were defined as atopic or nonatopic by questionnaire. Both atopic and nonatopic subjects developed significantly higher bronchial reactivity after exposure to cotton dust, with atopics exhibiting higher reactivity than nonatopics. Another cross-sectional study showed increased bronchial hyperreactivity in byssinotic workers, compared with asymptomatic workers, but no difference between atopic and nonatopic workers.[15] All of these data suggest that even nonatopic workers may experience an increase in airway reactivity produced by cotton dust exposure, that is, airway hyperreactivity may be a consequence of cotton dust exposure.

Early studies suggested that humoral antibody production (e.g., IgE) might mediate hypersensitivity to cotton dust components in the pathogenesis of cotton-dust–induced disease.[29] In a later study of serology among 24 cotton textile workers,[30] IgE was increased in a majority of cotton workers (62.5%) who had positive skin tests to cotton allergens. However, the elevated IgE level was not related to lung function abnormalities. A more recent study[31] showed a negative association between specific IgE levels and acute $FEV_{1.0}$ changes induced by cotton dust within an atopic group, and, in turn, a positive relationship between the presence of high numbers of a specific subtype of T cells and $FEV_{1.0}$ changes. The aforementioned study[31] suggests that, in atopics, cell reactivity and cell function affect cellular inflammatory mechanisms other than those associated with IgE production. We found that the change in IgE level was not consistent with changes in lung function. On average, IgE was elevated in both atopic and nonatopic workers at 3 mo, although a higher level was seen in the atopics. At 1 yr, however, the values of IgE returned nearly to preexposure levels for both subgroups. In contrast, lung function changes were conspicuously detected at 1 yr. This result supports the evidence that IgE level may not be the basis for the airway obstruction seen in cotton workers.[30]

Our study had 2 major limitations. First, the sample of studied subjects was not sufficiently large to reliably evaluate longitudinal change in lung function and airway reactivity attributable to cotton dust exposure. Given an overall dropout rate of 40% from the original cohort, follow-up observations were made on a reduced data set. Although no differences were seen in baseline data between the dropouts and participants at the 2 follow-up surveys, preshift $FEV_{1.0}$ and FVC measured at 3 mo were significantly different between the groups at 1 yr. Hence, a "healthy worker" effect might have led to underestimation of the changes in lung function and airway reactivity at 1 yr. Second, this study could not provide a basis for evaluation of exposure-response relationships because there was a lack of personal-exposure data. We used environmental measurements at each work area as surrogates for personal exposure, and it was assumed that working conditions were relatively stable during the observation period. Our results showed that high endotoxin exposure was related to an acute drop in $FEV_{1.0}$, but not to longitudinal $FEV_{1.0}$ changes. However, high dust exposure was associated with a decline in FVC over 1 yr. Our findings were consistent with those observed in workers in a swine confinement setting, whose cross-shift decrements in lung function were associated significantly with higher concentrations of endotoxin present in the bioaerosol.[9] Nevertheless, our results should be interpreted with caution because of the potential for exposure misclassification.

In summary, our study reconfirms that exposure to cotton dust is associated with both acute and longitudinal changes in lung function, even in young, nonsmoking, previously healthy workers. Preexisting atopic status may be an important risk factor for a cross-shift drop in $FEV_{1.0}$; however, no explanation was found for the change in methacholine-induced airway reactivity.

* * * * * * * * * * *

The authors thank the members of the Shanghai field team; Professors Gu Xue-qi, Lu Pei-lian, and Ye Ting-ting from Shanghai Medical University; the Shanghai Textile Bureau; workers and staff of the First and Second Textile Mills and the First Silk Mill; Professors Ellen Eisen and David Wegman of the University of Massachusetts at Lowell; Ms. Marcia Chertok, Ms. Janna Frelich, and Ms. Lucille Pothier for research assistance and computer programming; and Dr. Stephen Olenchock of NIOSH and Mr. Michael Whitmer for endotoxin analysis.

Support for this study was provided by NIOSH grant R01OH02421 and NIH grant ES00002.

Submitted for publication June 12, 2001; revised; accepted for publication December 28, 2001.

Requests for reprints should be sent to Dr. David Christiani, Occupational Health Program, Harvard School of Public Health, 665 Huntington Avenue, Boston MA 02115.

E-mail: dchris@hohp.harvard.edu

* * * * * * * * * * *

References

1. Beck GK, Schachter EN, Maunder LR, et al. A prospective study of chronic lung disease in cotton textile workers. Ann Intern Med 1982; 97:645–51.
2. Zuskin E, Valic F. Change in the respiratory response to coarse cotton dust over a ten-year period. Am Rev Respir Dis 1995; 112:417–21.
3. Christiani DC, Wang XR, Pan LD, et al. Longitudinal changes in pulmonary function and respiratory symptoms in cotton textile workers. A fifteen-year follow-up study. Am J Respir Crit Care Med 2001; 163:847–53.
4. NIOSH. Criteria for a Recommended Standard: Occupational Exposure to Cotton Dust. U.S. Department of Health and Human Services (DHHS), Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH), 1974. Washington, DC: Government Printing Office, DHHS (NIOSH) Pub. No. 75-118. Available at http://www.cdc.gov/niosh/75-118.html
5. 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 1973; 30:25–36.
6. Niven RM, Fletcher AM, Picjering CAC, et al. Chronic bronchitis in textile workers. Thorax 1997; 52:22–27.
7. Kennedy SM, Christiani DC, Eisen EA, et al. Cotton dust and endotoxin exposure-response relationships in cotton textile workers. Am Rev Respir Dis 1987; 135:194–200.
8. 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 1987; 317:605–10.
9. Schwartz DA, Donham KJ, Olenchock SA, et al. Determinants of longitudinal changes in spirometric function among swine confinement operators and farmers. Am J Respir Crit Care Med 1995; 151:47–53.
10. Jones RN, Butcher BT, Hammad YY, et al. Interaction of atopy and exposure to cotton dust in the bronchoconstrictor response. Br J Ind Med 1980; 37:141–46.
11. Jones RN, Hughes JM, Hammad YY, et al. Respiratory health in cottonseed crushing mills. Chest 1981; 79:30–33S.
12. Jacobs RR, Boehlecke B, Hage-Hamsten MV, et al. Bronchial reactivity, atopy and airway response to cotton dust. Am Rev Respir Dis 1993; 148:19–24.
13. Schachter EN, Brown S, Zuskin E, et al. Airway reactivity in cotton-bract–induced bronchial obstruction. Am Rev Respir Dis 1981; 123:273–76.
14. Schachter EN, Zuskin E, Buck M, et al. Airway reactivity and cotton bract–induced bronchial obstruction. Chest 1985; 87:51–55.
15. Fishwick D, Fletcher AM, Pickering AC, et al. Lung function, bronchial reactivity, atopic status, and dust exposure in Lancashire cotton mill operatives. Am Rev Respir Dis 1992; 145:1103–08.
16. Christiani DC, Ye TT, Wegman DH, et al. Pulmonary function among cotton textile workers. A study of variability in symptom reporting, across-shift drop in FEV_1, and longitudinal change. Chest 1994; 105:1713–21.
17. Olenchock SA, Christiani DC, Mull JC, et al. Airborne endotoxin concentrations in various work areas within two cotton mills in the People's Republic of China. Biomed Environ Sci 1990; 3: 443–51.
18. Ferris BG. Epidemiology standardization project. Am Rev Respir Dis 1978; 118(Suppl):55–88.
19. Pepys J. Skin testing. Br J Hosp Med 1975; 14:412–17.
20. Hendrick DJ, Fabbri LM, Hughes JM. Modification of the methacholine inhalation test and its epidemiologic use in polyurethane workers. Am Rev Respir Dis 1986; 133:600–04.
21. Voller A, Bidwell D. Enzyme-linked immunosorbent assay. In: Rose NR, Friedman H, Fahey JL (Eds). Manual of Clinical and Laboratory Immunology. 3rd ed. Washington, DC: American Society for Microbiology, 1986; pp 99–109.
22. Sepulveda MJ, Castellan RM, Hankinson JL, et al. Acute lung function response to cotton dust in atopic and non-atopic individuals. Br J Ind Med 1984; 41:487–91.
23. Li D, Zhong YN, Rylander R, et al. Longitudinal study of the health of cotton workers. Occup Environ Med 1995; 52:328–31.
24. Jennison E, Jacobs RR. Evaluation of the association of acute over-shift change in pulmonary function and atopy using OSHA cotton dust surveillance data. Am J Ind Med 1994; 25:737–47.
25. Glindmeyer GW, Lefante JJ, Jones RN, et al. Cotton dust and across-shift change in FEV1 as predictors of annual change in FEV1. Am J Respir Crit Care Med 1994; 149:584–90.
26. Christiani DC, Ye TT, Wegman DH, et al. Cotton dust exposure, across-shift drop in FEV_1, and five-year change in lung function. Am J Respir Crit Care Med 1994; 150:1250–55.
27. Boehlecke B. Report to National Institute for Occupational Safety and Health on Cooperative Agreement #81-OH-158, 1982.
28. O'Connor GT, Sparrow D, Degal MR, et al. Smoking, atopy, and methacholine airway responsiveness among middle-aged and elderly men. Am Rev Respir Dis 1989; 140:1520–26.
29. Salvaggio JE, O'Neil CE, Butcher BT. Immunologic response to inhaled cotton dust. Environ Health Perspect 1986; 66:17–23.
30. Zuskin E, Kancelijak B, Schachter EN, et al. Immunological findings and respiratory function in cotton textile workers. Int Arch Occup Environ Health 1992; 64:31–37.
31. Beijer L, Jacobs RR, Boehlecke B, et al. Monocyte responsiveness and T-cell subtype predict the effects induced by cotton dust exposure. Am J Respir Crit Care Med 1995; 152:1215–20.