Chronic Lung Function Decline in Cotton Textile Workers: Roles of Historical and Recent Exposures to Endotoxin

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BACKGROUND: Long-term occupational exposure to cotton dust that contains endotoxin is associated with chronic respiratory symptoms and excessive decline in forced expiratory volume in 1 sec (FEV₁), but the mechanisms of endotoxin-related chronic airflow obstruction remain unclear.

OBJECTIVE: In the current study, we examined temporal aspects of the exposure–response relationship between airborne endotoxin exposure, longitudinal change in FEV₁, and respiratory symptoms in a cohort of Chinese cotton textile workers.

METHODS: This prospective cohort study followed 447 cotton textile workers from 1981 to 2006, at approximately 5-year intervals. We used a generalized estimating equations approach to model FEV₁ level and respiratory symptoms as a function of past exposure (cumulative exposure up to the start of the most recent 5-year survey interval) and cumulative exposure (within the most recent interval) to endotoxins, after adjusting for other covariates. Models were stratified by active versus retired work status and by years employed before the baseline survey (< 5 and ≥ 5 years).

RESULTS AND CONCLUSIONS: Past exposure to endotoxin was associated with reduced FEV₁ level among retired cotton workers. Among all cotton workers, past exposure was more strongly associated with reduced FEV₁ for those hired < 5 years before baseline than for those who were hired ≥ 5 years after baseline. Recent endotoxin exposure was significantly associated with byssnosis, chronic bronchitis, and chronic cough.


Occupational exposure to cotton dust can cause acute respiratory responses such as chest tightness and bronchoconstriction (Merchant et al. 1973) and respiratory disease including byssnosis (Schilling et al. 1956). Longitudinal studies also indicate that long-term exposure to cotton dust may lead to chronic respiratory disease and excessive loss of pulmonary function (Beck et al. 1982; Christiani et al. 2001; Glindmeyer et al. 1991). Experimental and observational studies also suggest that bacterial endotoxin, present in cotton dust, may be a major causative agent contributing to airway inflammation and obstruction (Castellan et al. 1987; Christiani et al. 2001; Rylander et al. 1989). Generally released from bacterial lysis, endotoxins are ubiquitous in the airborne environment, but high airborne-endotoxin levels are observed in industrial environments, such as cotton mills, waste collection sites, swine barns, and grain handling equipment, where organic dusts are present (Liebers et al. 2006).

The acute respiratory response to occupational exposure to endotoxin has been described in longitudinal studies based in the cotton textile and agricultural industries (Mandryk et al. 1999; Wang et al. 2003a). However, the long-term exposure–response relationship between endotoxin and change in lung function and respiratory symptoms is not well understood. A 3-year longitudinal study of pig farmers observed a significant linear association between endotoxin exposure and annual decline in forced expiratory volume in 1 sec (FEV₁). In fact, a doubling of exposure was associated with a 19-mL increase in the average annual decline of FEV₁ (Vogelzang et al. 1998). Previous analyses of the present study population, a cohort of Chinese cotton textile workers, evaluated longitudinal change in FEV₁ and the occurrence of chronic respiratory symptoms in relation to cumulative endotoxin exposure. Significant associations with longitudinal change in FEV₁ and respiratory symptoms were identified for endotoxin exposures at 15 and 20 years of follow-up (Christiani et al. 2001; Wang et al. 2005). Whether the excessive decline in lung function and the occurrence of respiratory symptoms are influenced differently by more recent or more remote exposure to endotoxin is unknown.

The timing of exposure is not the only potential influence on the long-term effects of endotoxin on changes in lung function. Cohort eligibility requirements at baseline may also affect exposure–response relations because of variation in exposure histories before the baseline survey, a factor that has been observed in other long-term prospective studies of chronic disease (Applebaum et al. 2007; Chenard et al. 2007; Le Moulal et al. 2008). For example, participants who worked many years before the baseline survey may have experienced significant declines in lung function that had already plateaued prior to the baseline evaluation, whereas participants with fewer years of employment before baseline might be more likely to experience deterioration of lung function during follow-up.

In the present study, we evaluated the exposure–response relationship between cumulative endotoxin exposure and longitudinal change in FEV₁ and the occurrence of respiratory symptoms in an updated follow-up of a 25-year prospective cohort study of Chinese cotton textile workers. We also examined whether chronic respiratory health effects were attributable to past or more recent exposure to endotoxin and whether effects of exposure on change in FEV₁ varied by work histories prior to the baseline survey.

Subjects and Methods

Detailed information on subject selection, methods for testing pulmonary function, and exposure assessment has been described elsewhere (Christiani et al. 1986, 1993, 2001) and is summarized below.

Study population. The Shanghai Textile Worker Cohort Study was established in 1981. It included 447 cotton textile workers who were exposed to airborne cotton dust and endotoxin from two cotton textile mills and 472 unexposed silk workers who worked in a

The authors thank the members of the Shanghai field team: the workers and staff of the First and Second Textile Mills and the First Silk Mill; and J. Frelich, M. Chertok, and F. Chen for data management and research assistance. This study was supported by grants from the National Institute for Occupational Safety and Health (RO1-OH02421) and from the National Institute of Environmental Health Sciences, National Institutes of Health (ES-00002).

The authors declare they have no actual or potential competing financial interests. Received 8 July 2009; accepted 25 August 2010.
American Thoracic Society (ATS) criteria and were supervised and recorded by trained techni-
cians at the cotton mills (Christiani et al. 1986, 2001). Forced expiratory spiromograms were
performed before and after work shifts on the first
day back to work after a 2-day rest period. In
addition, all available retirees were tested in the
cohort follow-up surveys. An 8-L water-sealed
field spirometer (W. E. Collins Co., Braintree,
MA, USA) calibrated twice a day with a 3-L
syringe was used to record spirometric maneu-
vers throughout the surveys. Workers were
asked to refrain from smoking for at least 1 hr
before performing the test. Each worker per-
formed up to seven trials to produce three
acceptable curves. The study analyses focused on
indices of FEV\textsubscript{1}. Acceptable FEV\textsubscript{1} tracings varied by no more than 5% or 100 mL, which-
ever was greater, and all values were corrected
for body temperature and pressure saturated
with water vapor [body temperature, (ambient)
pressure saturated]. The highest FEV\textsubscript{1} values from technically acceptable tests were used in
the analyses. At the 2006 survey, 30 cotton
workers and 44 silk workers did not perform
the spirometry testing because of poor health.

Respiratory questionnaire. We used a modi-
fied ATS standardized respiratory symptom
questionnaire (Ferris 1978), translated into
Chinese and back-translated into English, to
collect information on work, medical, and
smoking history. In this study, we used the
definitions of respiratory symptoms, including
chronic bronchitis, chronic cough, and dyspnear,
and of respiratory syndromes, including bys-
sinosis, that were previously described by
Wang et al. (2003a). We defined byssinosis (all grades)
as chest tightness or shortness of breath at work
that occurred on the first day or other days of
the work week (see Schilling et al. 1963).

Statistical analysis. We used generalized
estimating equations (GEEs) (Zeger and Liang
1986) to account for repeated measures in
generalized linear models for lung function
and prevalence of respiratory symptoms at
each survey using PROC GENMOD (SAS
Institute Inc., Cary, NC, USA). We compared
Akaike Information Criterion (AIC) statistics
to evaluate the goodness of fit. An exchange-
able correlation structure, with constant cor-
relation between repeated measures of the
outcome within each subject over time, was
chosen based on AIC, from among biologically
plausible candidates. We used an identity link
function when the outcome was FEV\textsubscript{1} level (at
each survey over 25 years) and a logit link func-
tion when the outcome was SEV\textsubscript{1} or chronic bronchitis,
chronic cough, dyspnea, or byssinosis.

Cumulative exposure to endotoxins that
was estimated at each survey was divided into
two time windows: past endotoxin exposure,
from date of hire up to the start of each survey
interval, and recent endotoxin exposure within
each current interval (Figure 1). Cumulative
exposure to cotton dust was not included in
the model because cumulative dust and endo-
toxin exposure were strongly correlated (r = 0.92) among the cotton workers. All models
for FEV\textsubscript{1} level and symptoms were adjusted
for age (year), height (centimeters), sex (female
as reference), smoking status (current or for-
ermer smoker with never smoker as reference),
work status (active vs. retired) and years since
cessation of exposure. All covariates were
treated as time-dependent factors except sex
and height (defined as the average of the first
three surveys). Years since cessation of ex-
posure was defined as zero during active employ-
ment and as the time (years) between the date
last worked in an endotoxin-exposed job in
the cotton mill and the date of the current sur-
vey. Models for FEV\textsubscript{1} level were stratified on
employment status (active workers vs. retirees)
and by years hired prior to the baseline (1981)
survey (< 5 and ≥ 5 years). A p-value < 0.05
was selected to indicate statistical significance.

To evaluate assumptions of linearity in
the exposure–response models, FEV\textsubscript{1} was also
modeled as a smoothed function of past endo-
toxin exposure, recent exposure, and years since
cessation of exposure, using penalized splines
in generalized additive mixed models (Eilers
and Marx 1996). The degrees of freedom
were selected for the smoothed terms accord-
ing to the minimum AIC. R (version 2.8.1; R
was used to perform the GAMM analyses.

Results

Compared with cotton workers, nonpartici-
pants were more likely to be men, older, and
nonsmokers and to have had significantly
larger annualized declines in FEV\textsubscript{1} from
baseline to the 2001 survey (Table 1). The
average intensity of endotoxin exposure was
lower at the 1996 survey than at previous sur-
veys because the cotton mills began to blend
synthetic fiber with cotton between the third
(1992) and fourth (1996) surveys, and pure
cotton yarn production slowed.

![Figure 1. Cumulative exposure to endotoxin illustrated as time windows of exposure.](image-url)
We modeled both recent exposure and years since cessation of exposure as continuous terms because results from penalized spline models (data not shown) suggested that associations with FEV \(_1\) did not significantly deviate from linearity (p = 0.08 and 0.45, respectively). By contrast, evidence from penalized splines suggested associations with past exposure were nonlinear. Thus we treated past exposure as a discrete variable with high-, medium-, and low-level categories that were derived from tertile cutoffs of past cumulative endotoxin exposure at each survey.

When cotton workers were examined as a whole, high and medium levels of past endotoxin exposure were associated with higher FEV \(_1\) relative to low level of past exposure, but only the association with the medium level was statistically significant (Table 2). A positive association was also observed between recent endotoxin exposure and FEV \(_1\) level among all cotton workers. FEV \(_1\) level increased significantly with years since cessation of exposure, which suggests that active versus retired workers status might be an important confounder or effect modifier of endotoxin exposure. The association between past endotoxin exposure and FEV \(_1\) level was positive among active workers and negative (inverse) among retired cotton workers, whereas the association between recent endotoxin exposure and FEV \(_1\) level was inverse among active workers and positive among retired workers. Among all cotton workers, interactions between high and medium levels of past endotoxin exposure and retired status (p = 0.02, p = 0.52, respectively) and between recent endotoxin exposure and retired status (p = 0.55) were not statistically significant.

Cotton workers worked for 16.4 years, on average, before the baseline survey, and only 14.8% had worked < 5 years. We observed a stronger inverse association between FEV \(_1\) level and past endotoxin exposure for cotton workers who were employed < 5 years before the baseline evaluation than for workers who had worked for a longer period of time (Table 3). Significant interactions (p < 0.05 for high-past exposure; p < 0.0001 for medium-past exposure) were observed between < 5-year work tenure and high and medium levels of past endotoxin exposure.

Odds ratios for self-reported byssinosis and dyspnea were significantly increased for continuous recent endotoxin exposure (Table 4). Years since cessation was significantly associated with lower odds of byssinosis, chronic bronchitis, and chronic cough. The results were similar in a pooled model that included 472 unexposed silk workers who were also enrolled in the study (data not shown).

**Discussion**

In the most recent follow-up of a 25-year prospective cohort study of cotton textile workers, we observed decrements in FEV \(_1\) level for retired workers with higher past cumulative exposure to endotoxin. Among all exposed workers, the inverse effect of past cumulative exposure on FEV \(_1\) level was largest for those with shorter work histories before the baseline survey. In contrast, recent exposure to endotoxin, rather than past exposure, was associated with byssinosis and chronic bronchitis.

When cumulative exposure to endotoxin was partitioned into two time windows of exposure, past cumulative exposure ending approximately 5 years before the survey date, rather than recent exposure to endotoxin, was inversely associated with FEV \(_1\) level after retirement. A lag period between exposure and disease onset has been observed for occupational exposure-related diseases such as cancer and pneumoconiosis (Checkoway et al. 1990). Lagged effects of exposure are typically detected by censoring the exposure by a fixed time period of \(k\) years prior to time at risk (Salvan et al. 1995). In contrast with a lagged exposure, the time windows presented in this study allowed for evaluation of past and recent exposures in the same model. The results suggest that cumulative endotoxin exposure > 5 years may influence FEV \(_1\) more than recent exposures over the 25-year study period, but other exposure lag periods were not assessed.

Few studies have previously investigated the different effects of historical and recent exposure to endotoxins on respiratory symptoms among cotton workers. A previous cross-sectional analysis of this population showed that a high level of current endotoxin exposure was associated with increased prevalence of chronic bronchitis and byssinosis (Kennedy et al. 1987). The results of our current study suggest that dyspnea and byssinosis may be more strongly associated with endotoxin exposure in the recent survey interval than with past cumulative exposure. Why past cumulative exposure is more strongly associated with FEV \(_1\) level and recent exposure is more strongly associated with respiratory symptoms of dyspnea and byssinosis is not entirely clear.

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**Table 1. Demographic characteristics of participants and nonparticipants at the last survey in 2006.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants</th>
<th>Nonparticipants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (n)</td>
<td>317</td>
<td>130</td>
</tr>
<tr>
<td>Men [n(%)]</td>
<td>140 (44.2)</td>
<td>73 (56.2)</td>
</tr>
<tr>
<td>Baseline age [year]</td>
<td>36.5 ± 10.0*</td>
<td>41.1 ± 11.4</td>
</tr>
<tr>
<td>Baseline FEV (_1)</td>
<td>2959.6 ± 707.6</td>
<td>2816.2 ± 760.3</td>
</tr>
<tr>
<td>Baseline ever smoking status [n(%)]</td>
<td>121 (38.2)</td>
<td>37 (28.5)</td>
</tr>
<tr>
<td>Years since cessation of exposure (b)</td>
<td>12.7 ± 5.3**</td>
<td>17.7 ± 4.3</td>
</tr>
<tr>
<td>Cumulative endotoxin exposure (EU/m(^3)-years) (c)</td>
<td>52,820 ± 45,507</td>
<td>61,451 ± 58,626</td>
</tr>
<tr>
<td>Intensity of endotoxin (EU/m(^3)) (c)</td>
<td>2,086 (677–3,779)</td>
<td>3,003 (881–3,638)</td>
</tr>
<tr>
<td>1981</td>
<td>1,078 (698–5,072)</td>
<td>3,584 (849–5,883)</td>
</tr>
<tr>
<td>1992</td>
<td>1,289 (646–5,021)</td>
<td>1,082 (117–2,259)</td>
</tr>
<tr>
<td>1996</td>
<td>98 (0–878)</td>
<td>797 (0–1,594)</td>
</tr>
<tr>
<td>Annualized changes in FEV (_1) over the first 20 years [mL/year] (c)</td>
<td>-31.8 ± 16.5§</td>
<td>-41.3 ± 21.7</td>
</tr>
</tbody>
</table>

*Values are mean ± SD, unless otherwise stated. **Comparison made only among retired participants at the 2001 survey. *Comparison made only among participants at the 2001 survey. §Median (interquartile range) of work area concentration for cotton workers. *Significant difference between participants and nonparticipants, p < 0.0001. **Calculated among retired workers only, difference between participants and nonparticipants, p = 0.07. *Significant difference between participants and nonparticipants, p < 0.01.

**Table 2. Regression coefficients from GEE model for associations of FEV \(_1\) (milliliters) with endotoxin exposures among cotton workers evaluated at successive 5-year survey intervals over 25-year follow-up.**

<table>
<thead>
<tr>
<th></th>
<th>All cotton workers</th>
<th>Actively employed</th>
<th>Retired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years since cessation of exposure</td>
<td>6.02 (0.82 to 11.21)*</td>
<td>NA</td>
<td>14.53 (6.35 to 22.71)*</td>
</tr>
<tr>
<td>Past endotoxin exposure</td>
<td>16.72 (–42.04 to 75.49)</td>
<td>14.12 (–41.77 to 70.02)</td>
<td>–132.64 (–281.11 to 15.83)</td>
</tr>
<tr>
<td>(high)</td>
<td>53.82 (10.68 to 96.96)</td>
<td>39.40 (1.04 to 77.77)</td>
<td>–153.56 (–312.33 to 5.21)</td>
</tr>
<tr>
<td>Past endotoxin exposure</td>
<td>0.77 (–0.50 to 2.04)</td>
<td>–0.07 (–1.51 to 1.37)</td>
<td>3.32 (–0.91 to 7.54)</td>
</tr>
<tr>
<td>(medium)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(low)</td>
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<td></td>
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* p < 0.05.
We observed a stronger association with FEV₁ for medium than for high past cumulative exposure, and the association varied by work tenure at baseline, with the results suggesting a stronger adverse effect of past exposure among workers hired closer to the baseline evaluation. One possible explanation is that healthier workers continue to work longer than workers who are less healthy (Arighi and Hertz-Picciotto 1994; Meijers et al. 1989). Another possible explanation for the observation is left truncation, also referred to as survivor bias, which occurs in cohort studies when an entry criterion must be met prior to start of follow-up (Szkló 1987). In occupational studies this can occur if the study population includes subjects who were hired long before the start of follow-up and who are still at work when follow-up begins. For example, Applebaum et al. (2007) found that including subjects who were hired before the start of follow-up introduced survivor bias among participants in a cohort study of Vermont granite workers. The stronger association with endotoxin among the more recently hired is consistent with such a survivor effect. That is, participants hired many years before the baseline survey may be a survivor subset of their coworkers including those no longer working. The earlier hires may also have experienced significant declines in lung function prior to baseline, with a subsequent plateau in FEV₁ during follow-up, in contrast to those who had worked fewer years and whose deterioration in lung function was observed during follow-up. Studies of newly hired cotton textile workers have observed decrements in lung function, increased airway reactivity, and occurrence of respiratory symptoms within the first year of employment (Bakiri et al. 2007; Wang et al. 2003a, 2003b). Furthermore, workers who report symptoms tend to leave employment earlier, whereas for those who stay employed, a tolerance effect may develop (Bakiri et al. 2007).

Another explanation is that workers with longer work tenures who were available at the baseline survey may have been less susceptible to effects of endotoxin exposure compared with workers who left the industry before baseline. The findings from recent studies in cotton textile and agricultural workers suggest that the association between endotoxin exposure and reduction in lung function and occurrence of symptoms may also vary by genetic susceptibility to the inflammatory and oxidative response to the endotoxin (Hang et al. 2005; Zhang et al. 2007).

Evidence from both human exposure studies (Castellan et al. 1987; Rylander et al. 1989) and prospective epidemiologic studies (Christiani et al. 2001; Wang et al. 2005) suggest that the most likely agent in cotton dust responsible for acute and chronic pulmonary responses is gram-negative bacterial endotoxin. Previous analyses of this cohort of cotton workers also suggested that the observed associations with FEV₁ were stronger for cumulative endotoxin exposure than for cotton dust (Christiani et al. 2001; Wang et al. 2005). Endotoxin is a potent, nonspecific stimulant of the immune system that results in adverse effects. Human and animal inhalation exposure studies of endotoxin demonstrate acute effects including airway and alveolar inflammation and decrements in lung function (Burrell 1990; Reed and Milton 2001).

However, the biological mechanism for endotoxin-related development of chronic airway disease is still unclear. An in vitro study of rat cells, García-Verdugo et al. (2008) observed that LPS via toll-like receptor 4 induces a time-dependent increase in P2Y(2) receptors. This increase may lead to prolonged agonist-induced Ca(2+) responses that trigger higher activity in vesicle fusion and secretion. Further, these researchers suggested that long-term, but not short-term, exposure to endotoxin sensitizes alveolar type II cells, resulting in an increased extracellular surfactant pool, thus aiding pulmonary host defense mechanisms. If there is a wide range in human cellular defense responses to endotoxin, which result in acute and chronic airway inflammation, there may be variation in the time between exposure and response, as observed in our study.

The present study had several limitations. Because of the inherent limitation of the study design, surveys were conducted at approximately 5-year intervals over 25 years of follow-up. More frequent follow-up with exposure assessment and FEV₁ measurement would have been required to evaluate lag timing of endotoxin exposure on FEV₁ level more precisely. Selection bias may have possibly resulted from loss to follow-up, lack of participation, unacceptable pulmonary function testing, and healthy worker survivor effect. A total of 39 cotton workers and 31 silk workers died before the last survey. Participation in the questionnaire surveys was remarkably high during the 25-year follow-up. In the last survey, 36 workers participated in the survey, but they did not complete the spirometry testing, or their test results were unsatisfactory. These workers tended to be older, to have

<table>
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<tr>
<th>Table 3. Adjusted estimates for FEV₁ level (milliliters) over 25-year follow-up, stratified by work tenure at baseline survey. a</th>
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<tbody>
<tr>
<td>Hired &lt; 5 years before baseline (n = 68)</td>
</tr>
<tr>
<td>Hired ≥ 5 years before baseline (n = 381)</td>
</tr>
<tr>
<td>Hired ≥ 10 years before baseline (n = 285)</td>
</tr>
<tr>
<td>Years since cessation of exposure</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>−10.69 (−34.50 to 13.12)</td>
</tr>
<tr>
<td>−3.03 (−10.63 to 4.57)</td>
</tr>
<tr>
<td>−3.91 (−12.69 to 4.87)</td>
</tr>
<tr>
<td>Past endotoxin exposure</td>
</tr>
<tr>
<td>(high)</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>−93.13 (−204.99 to 18.72)</td>
</tr>
<tr>
<td>−30.30 (−103.63 to 43.03)</td>
</tr>
<tr>
<td>−39.19 (−128.69 to 50.32)</td>
</tr>
<tr>
<td>(medium)</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>−37.93 (−109.33 to 33.47)</td>
</tr>
<tr>
<td>27.54 (−23.15 to 78.23)</td>
</tr>
<tr>
<td>5.09 (−71.53 to 81.70)</td>
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<tr>
<td>Recent endotoxin exposure</td>
</tr>
<tr>
<td>(1,000 EU/m²-years)</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>−0.09 (−2.89 to 3.06)</td>
</tr>
<tr>
<td>1.16 (−0.32 to 2.63)</td>
</tr>
<tr>
<td>1.56 (−0.27 to 3.39)</td>
</tr>
</tbody>
</table>

a Estimated from GEE models using all available data from 447 cotton workers. All variables except sex and height were treated as time-dependent variables. Models were adjusted for age, mean height of the first three surveys, sex, and smoking status. Past endotoxin exposure was defined as cumulative exposure to endotoxin (EU/m²-years) before the start of the survey interval in which FEV₁ was measured, but was modeled with two binary variables comparing high with low and medium with low levels. Tertile percent cutoffs of past endotoxin exposure at each survey was used to defined low, medium, and high levels. For workers hired < 5 years before the baseline survey, past endotoxin exposure before 1981 was zero. Recent endotoxin exposure was defined as cumulative exposure within the 5 years prior to each FEV₁ measurement and was modeled continuously; estimates indicate the change in FEV₁ level associated with a 1,000 EU/m²-years increase in endotoxin exposure.

b p < 0.05.

<table>
<thead>
<tr>
<th>Table 4. Adjusted odds ratios (95% CIs) for self-reported respiratory symptoms among cotton workers over 25 years. a</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of workers who ever had symptoms</td>
</tr>
<tr>
<td>Bousiness</td>
</tr>
<tr>
<td>139/447</td>
</tr>
<tr>
<td>Years since cessation of exposure</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>0.89 (0.84–0.94)*</td>
</tr>
<tr>
<td>0.95 (0.90–1.00)</td>
</tr>
<tr>
<td>0.98 (0.95–1.02)</td>
</tr>
<tr>
<td>0.93 (0.89–0.99)*</td>
</tr>
<tr>
<td>Past endotoxin exposure</td>
</tr>
<tr>
<td>(high)</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>0.97 (0.55–1.38)</td>
</tr>
<tr>
<td>1.21 (0.81–1.80)</td>
</tr>
<tr>
<td>1.07 (0.79–1.48)</td>
</tr>
<tr>
<td>1.42 (0.94–2.14)</td>
</tr>
<tr>
<td>Recent endotoxin exposure</td>
</tr>
<tr>
<td>(1,000 EU/m²-years)</td>
</tr>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>1.02 (1.00–1.04)*</td>
</tr>
<tr>
<td>1.00 (0.99–1.02)</td>
</tr>
<tr>
<td>1.01 (1.00–1.03)*</td>
</tr>
<tr>
<td>1.00 (0.98–1.01)</td>
</tr>
</tbody>
</table>

a GEE analysis was performed using all available data from 447 cotton workers over 25 years of follow-up. All variables except height and sex were treated as time-dependent variables. Models were adjusted for age, mean height of the first three surveys, sex, and smoking status. Past endotoxin exposure was defined as cumulative exposure to endotoxin (EU/m²-years) prior to start of the survey interval but was modeled as a binary variable comparing high with low levels. The selected cut point for high level of exposure was the 75th percentile of the distribution of past endotoxin exposure at each survey. For workers hired < 5 years before the baseline survey, past endotoxin exposure before 1981 was zero. Recent endotoxin exposure was defined as cumulative exposure within the 5 years prior to each FEV₁ measurement and was modeled continuously; estimates indicate the change in FEV₁ level associated with a 1,000 EU/m²-years increase in endotoxin exposure.

b p < 0.05.
lower baseline FEV1, and to experience much higher cumulative endotoxin exposure. These individuals also had significantly greater FEV1 decline over the first 20 years of the study (57 mL/year) compared with participants who completed spirometry testing at the last survey (31 mL/year). This may represent another potential source for downward bias on the association between past cumulative endotoxin exposure and decline in FEV1 level.

Airborne endotoxin concentration was also estimated from sampling airborne cotton dust at fixed positions in work areas, rather than from sampling the air in the personal breathing zone of each participant. Although a reasonable correlation between personal and work area measures of airborne endotoxin has been observed in the Shanghai cotton textile industry (Meha et al. 2008), the lack of personal air sampling data may be a possible source of exposure misclassification for this study. Moreover, air sampling of dust and bacterial endotoxin was not performed throughout the entire period of follow-up but at 5-year intervals for a duration of 3–6 months. Thus, the estimated personal cumulative exposure might not accurately reflect the actual level of individual exposure. Additionally, the LAL assay is a common assay for quantifying airborne endotoxin concentration from cotton dust samples, but there is no universally accepted standard protocol (Dungan and Leytem 2009). However, Spana et al. (2008), in a study of sewage-derived endotoxin exposure, suggested that the LAL assay did not result in much exposure misclassification after comparison of sampling and analytical techniques. Meha et al. (2008) also observed a high correlation in estimated airborne endotoxin concentration (log EU/m3) between two laboratories performing an analysis of duplicate samples of airborne cotton dust. In general, background levels of endotoxin in the environment are < 10 EU/m3. However, endotoxin concentrations in several occupational settings with airborne exposure to organic dusts or decaying organic matter have ranged from several EU/m3 (Burger et al. 2007) to 7,500 EU/m3 (Schier et al. 2007). The range of mean endotoxin concentrations reported in work areas of our study (Christiani et al. 1994), approximately 40–5,800 EU/m3, is similar to the range (20–4,500 EU/m3) estimated in a meta-analysis of airborne endotoxin concentration in the cotton textile industry (Lane et al. 2004).

In summary, past rather than recent cumulative exposure to endotoxins before baseline FEV1 measurement was associated with an annual decline in FEV1 among retired Chinese cotton textile workers in a 25-year prospective study. Among all exposed workers, the largest annual decline in FEV1 was associated with past cumulative exposure to endotoxin.

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References


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