Natural History and Risk Factors of Early Respiratory Responses to Exposure to Cotton Dust in Newly Exposed Workers

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Objective: *A prospective study of newly exposed cotton workers was performed to investigate the natural history of respiratory symptoms and lung function changes.* ***Methods:*** *A total of 157 workers naive to cotton dust exposure were investigated by questionnaire, spirometry, and skin tests. They were examined before employment (baseline) and at the end of the first week, and the first, third, sixth, and 12th month after starting work. Acute airway response was defined as either a cross–first-shift or a cross-week fall in forced expiratory volume in one second (FEV_1). The longitudinal change of lung function over the year was also calculated. Five hundred seventy-two personal dust sampling and 191 endotoxin measurements were performed to assess the exposure.* ***Results:*** *Forty percent of workers reported work-related symptoms in the first week of the study. Smoking, endotoxin, and dust concentrations were risk factors for all work-related symptoms. Acute airway responses were witnessed after immediate exposure. Female status was the only factor found to be predictive of acute airway response. The mean longitudinal fall in FEV_1 at 1 year was 65.5 mL (standard error = 37.2). Age, early respiratory symptoms, and early fall in cross-week FEV_1 were found to predict the 12-month fall in FEV_1. Cross–first-shift and cross-week falls in FEV_1 reduced in magnitude during the course of the study.* ***Conclusions:*** *This study of workers naive to cotton dust exposure has demonstrated that respiratory symptoms and acute airway responses develop early following first exposure, and a tolerance effect develops in those workers with the continued exposure. Current smoking and increasing exposure predicts the development of work-related lower respiratory tract symptoms, while early symptoms and acute airway changes across the working week predict the longitudinal loss of lung function at 1 year.* (J Occup Environ Med. *2007;49:853–861*)

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The effects of cotton exposure are many and varied. There is convincing epidemiological evidence of chronic effects in terms of symptoms, an asthma-like syndrome featuring bronchial reactivity but with an unusual symptomatic periodicity now known as chronic byssinosis, longstanding upper respiratory tract irritation, and possibly even chronic obstructive pulmonary disease. The acute effects while described have been less convincingly studied. Early reports are of quite dramatic responses including asthma patterns, poor toleration of the conditions, and even reports of profound immunological responses including "mill fever."[1] One question that has not been well answered is whether the recognized high labor turnover seen in workers first attempting to take employment in cotton mills was caused by certain high-risk individuals (atopic subjects, those demonstrating an immediate airway response) leaving early because of health effects.

Many of the reports of newly exposed workers are descriptive and few have been performed with a methodical, longitudinal approach. Two studies from China have recently reported on both symptoms and lung function changes occurring in populations of newly exposed naive cotton workers.[2,3]

We proposed to study the acute effects of first exposure to cotton dust in a Turkish population. The cotton mills selected for this study had a history of a high labor turnover and were situated in an area of rela-

TABLE 1
General Characteristics and the Demographic Data of the Study Population

Study Population	All N = 157	Leavers n = 73	Active Workers n = 84	P
Age (yr), *n* (%)				
15–16	45 (28.7)	17 (23.3)	28 (33.3)	
17–18	73 (46.5)	35 (47.9)	38 (45.2)	0.32
>18	39 (24.8)	21 (28.8)	18 (21.4)	
Male, n (%)	83 (52.9)	41 (56.2)	42 (50.0)	0.44
Mill, n (%)				
1	76 (48.4)	39 (53.4)	37 (44.0)	
2	23 (14.6)	9 (12.3)	14 (16.7)	0.48
3	58 (36.9)	25 (34.2)	33 (39.3)	
Smoking, n (%)				
Never smokers	103 (65.6)	43 (58.9)	60 (71.4)	
Ex smokers	5 (3.2)	1 (1.4)	4 (4.8)	0.06
Current smokers	49 (31.2)	29 (39.7)	20 (23.8)	
Atopic workers, *n** (%)	26 (20.8)	7 (17.1)	19 (22.6)	0.47
Dust concentration (mg/m^3), mean (SD)	2.39 (1.83)	2.39 (1.83)	2.39 (1.85)	0.99
Endotoxin concentration, *n* (%)				
Low (<140 EU/m^3)	55 (35.0)	24 (32.9)	31 (36.9)	
Medium (140–260 EU/m^3)	48 (30.6)	23 (31.5)	25 (29.8)	0.87
High (>260 EU/m^3)	54 (34.4)	26 (35.6)	28 (33.3)	
Irritation symptoms at start, *n* (%)	20 (12.7)	11 (15.1)	9 (10.7)	0.41

*n = 125.

tive deprivation. However, three mills had taken efforts to develop a healthy and safe conscious working environment.

We specifically aimed to answer the following questions in newly exposed workers:

- When do work-related respiratory (upper and lower) symptoms first occur?
- What proportion of newly exposed workers experience no symptoms or airway response?
- What factors predict either the development of respiratory symptoms or acute airway response?
- In workers who develop acute airway responses, do these ameliorate over time or do they necessarily lead to the worker leaving the industry? We have already reported on the factors that predict leaving the mill environment.[4]
- Do acute changes in airway physiology effect lung function decline at 1 year?

Materials and Methods

Study Population

Three cotton mills were selected because of the reasonable travel distance to the host university, their situation in a relatively deprived region close to Istanbul, and their known interest in providing a healthy and safe working environment (more likely to participate). Two of the mills had been producing cotton for several years and had relatively old machinery, but the third mill had modern spinning processes, and this feature allowed a range of cotton dust exposures and the single site made them highly desirable for the study.

One hundred ninety-eight consecutive newly hired workers identified to the research team by management were approached and invited to participate. Of these, 41 were excluded from the study: 23 workers left within the first week and data available were insufficient for analysis; 15 workers had previously worked in cotton mills and therefore were not cotton "naive"; and 3 workers had significant preemployment respiratory impairment (defined as preemployment forced expiratory volume in one second [FEV_1] less than 80% of predicted). The remaining 157 workers (79% of the target population) agreed to participate. The demographic features of this population are presented in Table 1.

Timing of Assessments

All assessments were performed before exposure (baseline − preemployment), during the first week of exposure, and then at months 1, 3, 6, and 12 after first employment. Seventy-three workers (46%) left employment before 12 months of employment had been completed.

Environmental Exposure Assessment

A total of 572 personal dust samples were collected using techniques previously reported.[5] In brief, this involved an Institute of Occupational Medicine sampling head, attached to a pump (Casella) running at 2 L/min. Preweighed Whatman GF/A microglass fiber filters were reweighed after exposure for a minimum of 4 hours of a normal working shift. After sampling and after allowing for conditioning, samples were reweighed and time-weighted exposure to gravimetric dust was calculated. Each worker and each occupational group was targeted on multiple occasions.

Endotoxin assays were performed on the sampling filters after transferring them into pyrogen-free glass tubes. The assay was performed after extraction in pyrogen-free water as previously described using a quantitative kinetic turbidometric method (LAL 5000e series).[6] Between collection and assay, samples were stored at room temperature.

Ascribing Individual Environmental Exposure

For each worker, personal cotton dust and endotoxin was ascribed as the geometric mean of two or more samples if they were available for that individual. For workers who did not have at least two samples available for personal ascribing, the median values of all workers within the same mill with the same occupational classification were used. For this exercise, median values were used, as it would minimize the effect of spurious high level samples, which occasionally occur and may be due to worker "tampering" of samples. Within the database, all workers were given a personalized occupational exposure estimate of both cotton dust and endotoxin, which was determined by individual sampling or by specific occupational coding during the study period.

Questionnaire

All questionnaires were a modified version of the Medical Research Council respiratory questionnaire.[7] The questionnaire, initially used in English as part of epidemiological studies in the United Kingdom with additional questions for upper respiratory tract and ocular symptoms,[8] was directly translated into Turkish. Blind reverse translation was performed by different translators and reviewed by the original UK investigators to verify accuracy of translation. Baseline demographic questions were added to determine age, sex, work history, past work history, smoking habits, and past allergy symptoms. Follow-up questionnaires were used to detect any change in occupational group or mill of work, the development of new work-related symptoms, and changes in smoking habits. Lower respiratory tract symptoms (LRTS) are defined as cough, phlegm, chest tightness, wheeze, and shortness of breath. Upper respiratory tract symptoms (URTS) are defines as ocular or nasal irritation. Symptoms were defined as work-related if symptoms were reported as occurring after the individual first started at work, or as being worse on shift or as being better when the worker was on days off. Workers were classified as current-, ex-, or nonsmokers according to their baseline questionnaire response, but later reclassified if they took up smoking or subsequently stopped.

Lung Function Testing

Lung function tests were performed pre-shift and at least 6 hours into the shift by a single trained technician. A Vitalograph Series-S dry wedge bellows spirometer (Vitalograph Ltd, Buckingham, UK) was used throughout, and tests were performed according to the American Thoracic Society criteria.[9] A minimum of three tests were performed or continued until a minimum of three tests with less than 5% variability were obtained.

Values were calculated as percent predicted lung function using Polgar[10] equations or European Summary Equations.[11] For all subjects aged 18 and younger the Polgar equations were used. European summary equations were used for all subjects older than 18, assuming no change in predicted lung function in workers aged 18 to 25.

Any worker who presented with a baseline lung function of less than 80% predicted was excluded from the study.

Tests were performed at the start of the test week in question on the first shift, before work was commenced, and repeated at the end of the first shift and last shift of that working week. If a worker was initially tested on a morning shift, all subsequent shifts were performed when the worker rotated back to that shift. All workers had tests on either early or late day shifts. Cross–first-shift and cross-week lung function change was calculated from obtained values at each time point.

Longitudinal change in lung function over the course of the study was calculated by comparing preshift lung function at baseline with the preshift lung function at each subsequent time point.

Acute Airway Response

Acute airway response was defined on the basis of one of two possible variable changes:

- Across–first-shift change = [(pre–first-shift FEV_1 − post first shift FEV_1)/pre–first-shift FEV_1] × 100.
- Across-week change = [(pre–first-shift FEV_1 − post–last-shift FEV_1)/pre–first-shift FEV_1] × 100.

If either one of these values exceeded 5%, it was classified as an acute airway response.

Skin Tests

All workers were invited to participate in skin testing at the baseline time point only. A trained nurse performed and assessed all tests. Skin tests were performed to detect 10 common aeroallergens (cat, dog, *Dermatophagoides pteronyssinus*, cockroach, grass pollen, tree pollen, artemisia, *Aspergillus*, *Alternaria*, and *Cladosporium*). Any skin weal of 3 mm greater than that of the negative control was used to define the presence of atopy.

Statistical Analysis

Because endotoxin is not normally distributed, it was classified as either high (>260 EU/m^3), medium (140–260 EU/m^3) or low (<140 EU/m^3), dust concentrations were included as a continuous variable. For each symptom and the presence of an acute airway response, person-time incidences were calculated. To investigate the factors associated with the presence of work-related respiratory symptoms and acute airway responses, a Cox proportional hazards analysis was used. Since there was a strong correlation between dust concentrations and endotoxin levels, two models were performed to investigate the impact of each environmental variable separately. The backward elimination method was used. Hazard ratios and 95% confidence intervals were calculated. A P value of <0.05 was considered significant.

Survival curves of the work-related upper (WR-URTS) and lower (WR-LRTS) respiratory symptoms were obtained using Kaplan-Meier analysis.

Longitudinal decline in FEV_1 was calculated at 12 months, and factors related to decline were investigated by linear regression analysis.

TABLE 2
Personal Cotton Dust and Endotoxin Concentrations in Mills and Occupation Groups

	Personal Cotton Dust			Endotoxin		
	Samples (*n*)	Concentration* (mg/m^3)	IQR	Samples (*n*)	Concentration* (EU/m^3)	IQR
Total	572	2.01	1.05–3.48	191	191	91–394
Mill						
1	297	2.55	1.34–4.25	86	275	153–462
2	89	1.83	0.85–3.44	36	198	128–391
3	186	1.55	0.79–2.54	69	97	56–244
Occupation groups						
Open and card attendant	17	3.49	2.25–6.72	5	2135	348–4064
Draw/speed frame operative and comber	110	1.74	1.12–2.8	29	407	228–1572
Spinner	170	2.49	1.27–4.04	56	150	71–321
Porter in spinning	45	2.37	1.32–3.47	13	263	129–595
Doffer	55	1.74	0.91–3.05	21	142	88–300
Winder	66	2.04	0.77–4.77	24	129	71–337
Bobbin carrier in winding	50	1.02	0.64–2.01	15	128	56–191
Cleaner and quality control staff	29	2.56	1.46–5.37	14	202	151–397
Packing operatives	16	1.16	0.77–1.86	9	26	11–98
Waste room operatives	14	8.57	5.39–36.05	5	5857	1053–9607

*Median.
IQR indicates interquartile range (25th–75th percentile).

TABLE 3
Frequency of Work-Related Symptoms and Acute Airway Response in Follow-Up Time Points and Person-Time Incidence Rates

	1st Week (*n* = 157)	1st Month (*n* = 135)	3rd Month (*n* = 115)	6th Month (*n* = 99)	12th Month (*n* = 84)	Person-Time Incidence Rate
WR-LRTS, *n* (%)	5 (3.2)	12 (8.9)	18 (15.7)	4 (4.0)	6 (7.2)	0.38
Cough	3 (1.9)	4 (3.0)	11 (9.6)	3 (3.0)	3 (3.6)	0.25
Phlegm	3 (1.9)	10 (7.4)	16 (13.9)	4 (4.0)	4 (4.8)	0.31
Chest tightness	—	—	2 (1.7)	—	—	0.02
Shortness of breath	—	1 (0.7)	—	—	1 (1.2)	0.02
Wheezing	1 (0.6)	2 (1.5)	—	—	—	0.02
WR-URTS, *n* (%)	47 (29.9)	56 (41.5)	49 (42.6)	31 (31.3)	34 (40.5)	2.30
Nasal irritation	28 (17.8)	33 (24.4)	31 (27.0)	20 (20.2)	22 (26.2)	1.17
Ocular irritation	32 (20.4)	40 (29.6)	36 (31.3)	20 (20.2)	24 (28.6)	1.45
Acute airway response, *n** (%)	61 (45.2)	35 (27.1)	21 (18.3)	29 (29.9)	21 (25.9)	2.74

*n = 135, 129, 115, 97, and 81, respectively.
WR-LRTS indicates work-related lower respiratory symptoms; WR-URTS, work-related upper respiratory symptoms.

Results

The demographic features of the study population (n = 157) are presented in Table 1. Almost half the workers at baseline were in the 17 to 18 age group, and hence the need for lung function regression equations for young individuals. There was an even male-female distribution, one third were current smokers, and the prevalence of atopy in the 125 who agreed to undergo skin testing was 21%. Table 1 also presents the demographic features of those workers who left employment at the mill within the first year (leavers) and those workers who continued in employment throughout the study period of 12 months (active workers). There were no significant differences between the two groups, except for a borderline significant trend for active workers to be more likely to be never smokers; 71.4% versus 58.9% in leavers (P = 0.06).

The environmental exposures witnessed in the study are given in Table 2. Endotoxin and dust concentrations were higher in mill 1 than the other mills and, as typically known from previous studies, were higher in waste, open, and card room workers when compared with other occupations in the mill. It is of note that the interquartile range exceeds the occupational exposure standard set in the United Kingdom for all occupations with the exception of packing, while waste operatives are exposed to 3 times the advisory levels.

The prevalence of work-related respiratory symptoms at each time point, including the prevalence of measurable acute airway responses,

TABLE 4
Risk Factors of Work-Related Respiratory Symptoms and Acute Airway Response (Cox Hazard Analyses)

	Model I				Model II			
Dependent Variables	Independent Variables	β	*P*	HR (95% CI)	Independent Variables	β	*P*	HR (95% CI)
WR-LRTS	Smoking				Smoking			
	Never and ex-smokers				Never and ex-smokers			
	Current smokers	1.02	0.004	2.77 (1.37–5.58)	Current smokers	1.05	0.004	2.86 (1.41–5.83)
	Endotoxin level				Dust concentration (1 mg/m^3)	0.23	0.002	1.26 (1.09–1.46)
	Low							
	Medium	1.06	0.034	2.88 (1.09–7.62)				
	High	1.03	0.038	2.81 (1.06–7.45)				
WR-URTS								
Ocular irritation	Smoking				Smoking			
	Never and ex-smokers				Never and ex-smokers			
	Current smokers	0.48	0.040	1.61 (1.02–2.55)	Current smokers	0.61	0.012	1.84 (1.14–2.98)
	Endotoxin level				Dust concentration (1 mg/m^3)	0.12	0.018	1.12 (1.02–1.24)
	Low							
	Medium	0.60	0.030	1.82 (1.06–3.13)				
	High	−0.01	0.981	0.99 (0.56–1.77)	Mill			
					1			
	Irritation at start				2	0.63	0.033	1.88 (1.05–3.37)
	No				3	−0.04	0.880	0.96 (0.57–1.63)
	Yes	0.66	0.024	1.61 (1.09–3.45)				
Nasal irritation*								
Acute airway response	Male				Male			
	Female	0.41	0.044	1.51 (1.01–2.24)	Female	0.41	0.044	1.51 (1.01–2.24)

*All independent variables entered the model but none of them were significant.
WR-LRTS indicates work-related lower respiratory symptoms; WR-URTS, work-related upper respiratory symptoms.

are presented in Table 3. Symptoms appear to peak at 3 months with a fall off in symptom reporting after this time. In comparison, acute airway responses were measured most frequently in the first week (45.2%) and were least frequent at 3 months, when symptoms were most common (18.3%). Work-related chest tightness (an integral symptom of byssinosis) was only reported by two workers at the third month, whereas upper respiratory tract symptoms were frequently seen (30% to 40% of workers at all time points).

Table 4 presents the Cox proportional model analysis of factors predictive of work-related respiratory symptoms. Lower and upper respiratory tract symptoms are presented separately. Two models are reported so that a direct comparison of the impact of dust and endotoxin can be perceived. Current smoking (hazard ratio [HR] 2.8 in each model) predicts the presence of LRTS. For endotoxin, either medium or high concentration is associated with a higher hazard when compared with low-exposure workers (HR = 2.9, 2.1 respectively; $P < 0.05$). For dust, the HR is 1.26 for each 1 mg/m^3 increase in dust exposure ($P < 0.005$).

For ocular symptoms, current smokers were more likely to report symptoms (HR = 1.6, 1.8 respectively; $P < 0.05$). Medium (but not high) endotoxin exposure (HR = 1.8; $P < 0.05$) and higher levels of dust-exposed workers (HR = 1.12; $P < 0.05$) reported symptoms.

Nasal irritation had no predictive factors. Acute airway response was only predicted by female status (HR = 1.5; $P < 0.05$).

Longitudinal decline in FEV_1 at 12 months in those workers who stayed in the study was 66 mL (standard error = 37) as a group mean (Table 5). In the univariate analysis, there were large differences for those younger than 16 years (rise of 84 mL/yr), compared with those 17 to 18 years old (loss of 116 mL/yr; $P <$ 0.05) and those older than 19 years

TABLE 5
Longitudinal Change in FEV_1 During the First Year of Occupation by Several Characteristics

	FEV_1 Change at 12 Months* (mL)	
	Mean (SE)	*P*†
All	−65.5 (37.2)	0.082
Male	15.6 (59.8)	0.792
Female	−148.7 (40.2)	0.001
Age groups		
15–16 yr	84.0 (76.1)	0.281
17–18 yr	−116.5 (50.7)	0.028
≥19 yr	−180.0 (50.3)	0.002
Smokers	−128.5 (72.2)	0.091
Nonsmokers	−43.4 (43.4)	0.322
Atopic	−63.4 (48.3)	0.209
Nonatopic	−66.0 (45.4)	0.151
Symptomatic‡	−124.2 (48.1)	0.013
Asymptomatic	26.5 (55.5)	0.637
Across-shift fall in FEV_1§		
≥5%	−74.6 (60.1)	0.226
<5%	−60.8 (47.4)	0.106
Across-week fall in FEV_1§		
≥5%	−165.3 (62.8)	0.013
<5%	27.3 (39.3)	0.491

*Difference calculated as (FEV_1 value at 12th month — baseline FEV_1 value).
†Paired *t* test.
‡Respiratory symptoms reported during the first 3 months.
§Falls recorded during the first month.

TABLE 6
Risk Factors for the Longitudinal Change in FEV_1 During the 12 Months of Occupation (Linear Regression Analysis)

Independent Variables*	Standardized Coefficient, β	*P*
Age (yr)	2.5	0.016
Work-related symptoms†	2.3	0.026
Cross-week Δ FEV_1‡	2.6	0.012

*Variables included into the model are age, sex, smoking, cross-shift change in FEV_1 (Δ FEV_1), cross-week Δ FEV_1, work-related symptoms, atopy, dust, and endotoxin exposure levels.
†Any work-related symptom developed during the first 3 months of occupation.
‡Having more then 5% cross week drop in FEV_1 during the first month of occupation.

(loss of 180 mL/yr; $P < 0.005$). Women (−148 mL/yr), when compared with men (+16 mL/yr), were more susceptible ($P = 0.001$). Those with symptoms within the first 3 months and those who demonstrated across-week falls in FEV_1 in the first month also demonstrated greater impacts. There was a borderline trend for smokers, but not for atopic status at baseline.

Table 6 presents the linear regression analysis of factors predictive of lung function decline in survivors at 1 year. Older age (odds ratio [OR] = 2.5; $P < 0.05$), work-related symptoms reported in the first 3 months (OR = 2.3; $P < 0.05$), and across-week acute airway responses demonstrated in the first month (OR = 2.6; $P < 0.05$) were all independent predictors of loss of lung function at 12 months.

Figure 1 demonstrates the survival curves for workers experiencing upper or LRTS at one time within the study. There is a visibly different pattern, with 77% of workers reaching 12 months without experiencing work-related respiratory tract symptoms at one time.

Finally, Fig. 2 presents the changing pattern of cross-week and cross–first-shift FEV_1 response in workers throughout the study. The data are presented as absolute values in order to highlight the magnitude of the mean change over time. This is most obviously expressed for across-week change, which average 140 mL in the first week, but improves to only 20 mL across the week at the end of 12 months.

Discussion

This study has investigated the development of work-related symptoms and acute airway responses in workers exposed to cotton dust for the first time. During the study, there was a high intensity of recording symptoms and of investigating changes in lung function across the week and across the shift. The study has also incorporated a high-intensity exposure assessment protocol, allowing us to believe that the exposure estimates are very representative and individualized.

We encountered a number of problems and weaknesses within our initial study design. First, the population was very young, which has given us a problem in determining representative predictor equations for lung function. We ended up using Polgar equations up to the age of 18 and European summary equations, using a minimum age of 25, in the calculation for those aged 18 to 25. These assumptions are not ideal but gave us the best fit with normality at baseline.

The study was performed in three mills in close proximity of each other in a relatively deprived area in Turkey, with an expected high labor turnover. Initially, we had also planned to study leavers, but found it impossible to invite participation of workers on the day they left or subsequently. Those who responded told us that they usually left for personal reasons or problems with manage-

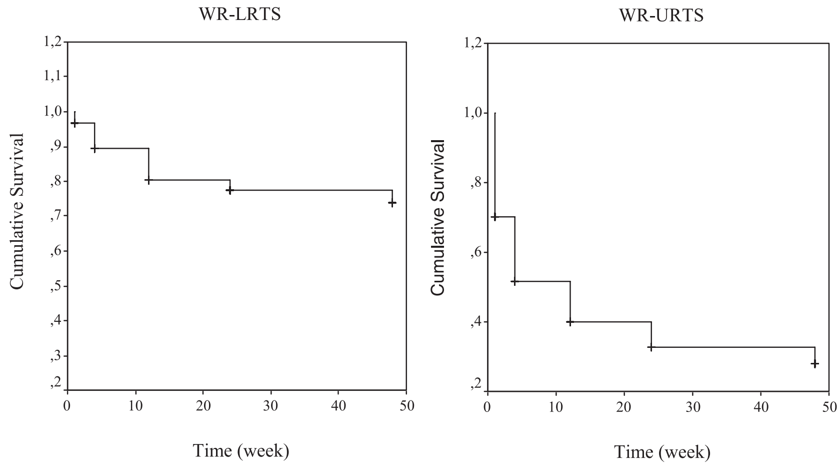

Fig. 1. Cumulative survival function of being symptom-free (WR-LRTS and WR-URTS) based on the Kaplan-Meier survival analyze. WR-LRTS indicates work-related lower respiratory tract symptoms; WR-URTS, work-related upper respiratory tract symptoms.

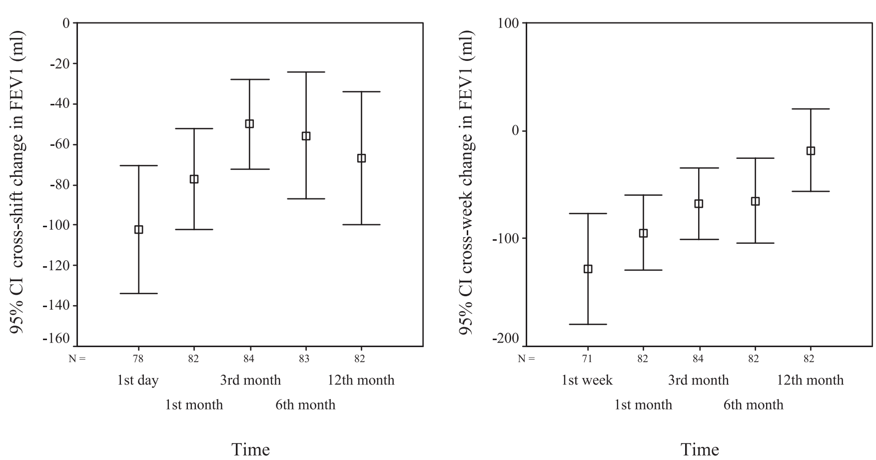

Fig. 2. Mean values and 95% CI of cross-shift and cross-week changes in FEV_1 throughout the follow-up.

ment, and it is possible that our findings on leavers in this very high turnover setting is confounded by socioeconomic factors.

It has been considered previously and other studies have reported that some workers find the environment of cotton spinning mills intolerable and leave for health reasons.[1] It has been suggested partly because of the low prevalence of atopy found in cross-sectional studies that atopic workers may be more likely to select out of this challenging environment because of the high level of particularly fungal allergens encountered. One of the aims of this study was to examine this possibility, but as we have previously reported, we have not found evidence to support this theory.[4] In the current analysis, atopy did not have any predictive impact on the development of symptoms, acute airway responses, or lung function decline over the first 12 months. Atopy as a cause of chronic symptoms was not found in a study from the United Kingdom,[12] but has been reported to be associated with early lung function decline by other investigators.[13]

Of potential health predictors of leaving, only the presence of work-related lower respiratory tract symptoms (WR-LRTS) at 3 months influenced leaving at any time point in the study.[4] The finding of our earlier analysis may be reflected against the finding in this study that this is the time of peak prevalence of LRTS. Significant effects at this time point may have occurred, because the greater prevalence influenced the power to demonstrate the effect. Alternatively, 3 months may represent a critical period of work duration during which workers reflect on the balance of benefits (work) against impact (symptoms).

The initial increase of LRTS to 3 months followed by a fall in reporting may have several explanations:

1. It may simply reflect questionnaire fatigue, with workers less likely to report effects they still experienced (against this argument is the evidence that such an effect of reduced reporting is not seen for the upper respiratory tract symptoms);
2. It may be caused by a "healthy worker effect," with the workers leaving, diluting the remaining population of symptomatic individuals; or
3. Alternatively, it may represent a genuine tolerating effect after continued exposure. The latter implies that the individual develops a relative resistance to the effects of ongoing exposure at the same level. Such an effect is recognized on repeat exposure to endotoxin, and therefore has biological plausibility.

Our findings mirror the findings from the earlier study of Wang et al, who found that many symptoms reported at 3 months were not recorded at 1 year in their population.[3]

URTS have been reported frequently in previous cross-sectional studies of cotton workers. The prevalence of upper respiratory tract symptoms in this study is comparable with those seen in the United Kingdom, in Lancashire cotton spinners.[8] This study has suggested that these symptoms occur very early in the working life of people exposed to cotton spinning (even within the first week), and while they are a significant health problem we did not find that they influenced leaving the working environment.[4] The symptoms are related to the occupations with medium endotoxin exposure, but are correlated with increasing dust exposure. These occupations are the later processes such as spinning and winding, when endotoxin has been partially removed from cotton, but large particle fibers remain in abundance.[5]

A recent study by Wang et al reported that symptoms suggestive of byssinosis are rare in the workers after early exposure.[3] Our data support this finding, with only two reports of work-related chest tightness and neither of these fulfilled the criteria used for a definition of chronic byssinosis. This is not surprising, as cross-sectional studies have demonstrated that byssinosis is rare in workers with less than 15 years experience of work in the cotton spinning industry.[14]

In terms of determining risk factors for LRTS, we found that smoking (not surprisingly) and endotoxin or dust exposure predicted symptoms. It is difficult to try to separately tease out the impact of dust or endotoxin separately, because, however handled (grouped into tertile or analyzed as continuous data), they are very closely correlated. This study has not been designed or powered to determine which of these exposure indices is most important for the development of health effects.

Intriguingly, exposure did not predict either acute airway response or decline in lung function at 12 months. The former factor was only related to female gender after multivariate analysis, and although we can not comment on the plausibility of this finding, it implies that the female airways are more susceptible to the acute effects of cotton dust and/or its contaminants.

For this study, we used across-shift change in FEV_1 at an absolute change of 5% as a cutoff for an acute response. This level is of doubtful clinical significance and is at the level of minimum detection. It could be argued that we should have used a larger fall (either 8% or 10%), but unfortunately, within the scope of the size of this study, falls of this magnitude were rare and therefore all power to determine an influencing effect was lost. There is some internal validation of using this level, as certainly for across-week changes, it became highly predictive of the 12-month decline of lung function. Those with across-week acute responses (defined at the 5% level) lost 165 mL/yr, while those without such an acute across-week response had a mean rise in lung function of 27 mL/yr. There is good previous evidence that acute changes in lung function can predict longer-term decline.[15–18] The across-week acute airway response remained as a predictor in the multivariate analysis and was independent of the effect of LRTS.

It is also worth noting that the number of acute airway responses became smaller as the study progressed, and the mean across-shift and across-week FEV_1 change diminished markedly over the 12 months of the study. We do not believe that this was caused by the healthy worker effect because our previous study showed no impact of acute responses on the individuals leaving the mill.[4] This again implies that there is the development of tolerance and it is perhaps a little too easy to suggest that this may be caused by developing tolerance to endotoxin exposure and has been seen in previous studies.[19–21]

Conclusions

We have demonstrated in this study of workers naive to cotton dust exposure that symptoms and acute airway responses develop early after first exposure, and if there is any tolerance effect, it develops in those workers who remain to 12 months employment. Current smoking and increasing exposure predict the development of WR-LRTS, while early symptoms and acute airway changes across the working week predict the loss of lung function seen at 12 months of continued employment.

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