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Work Area Measurements as Predictors of Personal Exposure to Endotoxin and Cotton Dust in the Cotton Textile Industry

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Objectives: To determine if work area measurements of endotoxin and/or cotton dust obtained from the vertical elutriator (VE) can be used to predict levels of personal endotoxin exposure as measured by the Institute of Occupational Medicine (IOM) inhalable dust sampler in the cotton textile industry.

Methods: Fifty-six work area cotton dust samples were collected from 14 areas and 82 personal cotton dust samples were collected from 41 workers in three textile mills (Mills A, B and C) in Shanghai, China. Cotton dust concentrations were determined gravimetrically from sample filters, of which endotoxin concentrations were determined using a kinetic chromogenic modification of the limulus amoebocyte lysate assay. Linear regression models were used to determine the association between log IOM personal endotoxin concentration and log VE area endotoxin concentration.

Results: Median cotton dust and endotoxin concentrations measured from VE area samples in the three mills were 0.36 mg m^{-3} and 1280.76 endotoxin units per cubic meter (EU m^{-3}), respectively, compared to 1.74 mg m^{-3} and 2226.83 EU m^{-3} from IOM personal samples. Excluding samples from weaving processes, we observed linear associations between VE area measures of endotoxin and IOM personal endotoxin concentrations; VE area concentration of endotoxin explained 83 and 89% of the total variation in IOM personal endotoxin concentration for Mills A and B, respectively (Mill A: $R^2 = 0.83$, $P < 0.0001$; Mill B: $R^2 = 0.89$, $P < 0.0001$). Although area measures of cotton dust was also a significant predictor of person endotoxin, the model explained less of the variance in personal endotoxin measurements.

Conclusions: Specific to the conditions of the textile mills investigated in this study, work area measurements of endotoxin, but not cotton dust, may be reasonable proxies for personal levels, at least for rank-ordering exposures.

Keywords: cotton dust; endotoxin; exposure assessment; occupational exposure; Shanghai textile workers

INTRODUCTION

Occupational exposure to cotton dust can cause acute respiratory responses such as chest tightness and bronchorestriction (Merchant *et al.*, 1973) and respiratory disease including byssinosis (Schilling *et al.*, 1955). The association between long-term exposure to cotton dust and chronic airway disease remains unclear, although several longitudinal studies indicate that long-term exposure may lead to chronic respiratory disease and excessive loss of pulmonary function (Beck *et al.*, 1982; Zuskin *et al.*, 1991; Glindmeyer *et al.*, 1994; Christiani *et al.*, 2001; Wang *et al.*, 2005).

In response to high rates of byssinosis in the cotton textile industry, the Occupational Safety and Health Administration (OSHA) subsequently mandated exposure limits for cotton dust exposure without knowledge of a specific causative agent in the cotton dust

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(OSHA, 1978). For specific work areas, personal exposure limits (PELs) for dust exposure were set at 0.20 mg m^{-3} for yarn and washing and 0.5 mg m^{-3} for slashing and weaving. Since then, experimental and observational studies identified bacterial endotoxin, present in cotton dust, as a major causative agent contributing to airway inflammation and obstruction (Castellan *et al.* 1984; Rylander *et al.* 1989; Christiani *et al.*, 2001). The most recent follow-up of a 25-year prospective cohort study of cotton textile workers in Shanghai, China, also found that chronic loss in lung function was more strongly associated with cumulative exposure to endotoxin than to cotton dust (Wang *et al.*, 2005).

No regulatory standard currently exists for endotoxin exposure but 'no observed effect levels' (NOEL) for endotoxin for various health endpoints have been proposed, ranging from 50 to several hundred endotoxin units per cubic meter (EU m^{-3}) (Heederik and Douwes, 1997; Douwes *et al.*, 2003). In the cotton textile industry, endotoxin concentrations may vary by stage in cotton processing; a meta-analysis utilizing endotoxin measurements from different studies of the cotton textile industry observed highest mean levels of endotoxin concentration in the opening and carding operations followed by a gradual reduction through later stages in processing (Lane *et al.*, 2004). Mean endotoxin concentrations for opening and carding (378 and 396 ng m^{-3}, respectively) from the meta-analysis were well above the recommended range in NOEL's for endotoxin (Lane *et al.*, 2004).

If airborne endotoxin is more responsible for cotton dust-related health effects than cotton dust itself, it is important to evaluate how well personal exposure to endotoxin can be determined from work area sampling. Work area sampling is the conventional method for monitoring occupational exposure to cotton dust, although lack of personal sampling data presents a potential source for exposure misclassification. However, recent UK studies suggest that personal breathing zone sampling for cotton dust is possible using the Institute of Occupational Medicine (IOM) total dust sampler (Niven *et al.* 1992; Ogden *et al.*, 1993; Niven *et al.*, 1998). These studies have shown a strong correlation between byssinosis prevalence and cumulative exposure to dust, but only weak correlations with current exposure as measured by a personal sampling technique (Niven *et al.*, 1992, 1998).

In the USA, the OSHA PEL is based on work area sampling with a vertical elutriator (VE) that uses particle fractionation ($\leq$15 μm in aerodynamic equivalent diameter) (Lynch, 1970; OSHA, 1978, 9). Many international studies have adopted OSHA's approach for measuring cotton dust exposure. However, personal exposure of inhalable dust may be as much as 4.5 times the equivalent area measurement (Astrakianakis *et al.*, 2006). If the work shift includes job task variation for workers, then a personal breathing zone sampling method would be preferable to measure exposure. However, if dust and endotoxin levels are fairly uniform within the work area, then a work area sampling method should provide accurate exposure estimates. Furthermore, if there is a relationship between the work area and personal levels of exposure, it would be possible to refine exposure estimates of inhalable dust (and associated endotoxin) from work area sampling and detailed work history for use in epidemiological studies.

Investigators from the University of Washington in Seattle assembled a very large cohort, examining cancer incidence among workers in the cotton textile industry in Shanghai (Camp *et al.*, 2003; Wernli *et al.*, 2003). An exposure validation study was carried out in three of the participating mills; work area (VE) and personal sampling methods (IOM inhalable dust sampler) were used for measuring cotton dust and endotoxin. The primary objective of this analysis was to determine if work area measurements of endotoxin and/or cotton dust obtained from the VE can be used to predict levels of personal endotoxin and/or cotton dust exposure as measured by the IOM inhalable dust sampler. To make a direct comparison of work area and personal samples with the same sampling instrument, work area sampling was also performed with the IOM inhalable dust sampler. Secondary and tertiary objectives were to investigate whether work area measurements of cotton dust can be used as predictors of personal exposure and whether cotton dust concentration can be used as predictors of endotoxin exposure, respectively.

METHODS

Study sites, work processes and sample size

Personal and work area sampling were performed in three textile mills (Mills A, B and C) from the Shanghai area in November 2002 (Astrakianakis *et al.*, 2006). These mills participated in another ongoing study of cancer incidence among cotton textile workers (Camp *et al.*, 2003). Work area and personal samples were collected in 14 processes from the three mills combined, in processes common in yarn preparation and weaving. In Mills A and B, personal and work area sampling were conducted for the following processes: opening, carding, drawing, roving, combing and spinning. The weaving process was sampled in Mill A and Mill C, which was a weaving-only facility.

Work area and personal sampling were performed in separate morning (AM) and afternoon (PM) shifts for each process. Four work area samples were collected for each process, with two during the morning and afternoon each. Thus, a total of 56 work area samples were collected in the three mills. Three workers per process were concurrently monitored

during the AM and PM shifts, providing a total of six personal samples for each process. On average, two work area and three personal samples were collected during each shift for each process in each mill. With exception is the opening process of Mill A where only two workers were sampled, giving a total of 82 personal samples collected in the three mills.

Sampling instruments

Detailed description about the sampling instruments and strategy is provided in Astranakianakis *et al.* In brief, VEs (General Metal Works, Inc., Cleveland, OH, USA) were used to collect area samples of airborne cotton dust for each process at a fixed location, relevant to the work done and representative of that specific process. The VE is >1 m in length and is designed for area sampling. The flow rate for the VE (7.4 ± 0.2 l min^{-1}) is set to give upward velocity such that particles >15 μm in aerodynamic diameter will fall out of the jet stream in a separation chamber; respirable particles ≤15 μm remaining in the jet stream were collected onto a 37-mm filter cassette (Astrakianakis *et al.*, 2006).

IOM inhalable dust samplers (SKC, Inc., Houston, TX, USA) were used to collect personal airborne cotton dust. The IOM sampler was placed within the worker's breathing zone and the workers who wore the samplers were in close proximity to the area samplers (<5 m). The IOM samplers operate at a flow of 2.0 l min^{-1} through a single 15-mm orifice and collect particles approximating the inhalable particulate fraction, and the majority of particles entering the cassette were collected on a 25-mm filter. Earlier studies have reported the need to remove long cotton fibers or lint pad, referred to as 'fly', from the filter to measure dust concentration which is more biologically relevant. For this study, we fitted a dome-shaped stainless steel screen with 2-mm openings over the IOM cover cap to prevent protrusion of fly onto the filter. Filters were replaced after ∼3 h (at midday) and pump flows were checked midway during sampling for each shift (Astrakianakis *et al.*, 2006).

Sampling duration lasted ∼3 h for each AM and PM shifts. Synthetic fibers were produced in each of the mills, so VE's were placed in cotton-only areas and distant from synthetic fiber production. The IOM sampler was also used to collect area samples—the IOM sampler was placed next to the VE—so that a direct comparison between personal and area measurements could be made with the same sampling instrument (Astrakianakis *et al.*, 2006).

Laboratory analysis

Filters were pre-weighed at the University of Washington in Seattle and hand carried to and from Shanghai. On return, filters were kept refrigerated at 4°C until analysis which occurred within 60 days upon return. For quality control, a field blank was set aside for each sampler. Five filters for each sampler were also maintained as laboratory blanks. The net gravimetric mass (in milligrams) for dust was calculated as the post-weight minus pre-weight value corrected for change in field blank mass and change in laboratory blank mass. Airborne cotton dust concentration was reported in mg m^{-3} (Astrakianakis *et al.*, 2006).

After post-weighing, VE filters were shipped to the University of British Columbia (UBC) and the IOM (area and personal) filters were shipped to National Institute of Occupational Safety and Health (NIOSH) for endotoxin analysis. The findings from the VE endotoxin analysis at UBC have been reported previously (Astrakianakis *et al.*, 2006). The extracts from the VE samples analyzed at UBC were split into duplicate aliquots and subsequently shipped to NIOSH for endotoxin analysis.

At NIOSH, IOM personal and area filters were placed in 50-ml conical centrifuge tubes and extracted with 10 ml water. The samples were vortexed between 30 and 60 s before being placed on a rocker for 60 min and finally centrifuged at 2200 rpm at 4°C for 10 min. All equipment and dilution water used were pyrogen free and sterile. The VE aliquots were stored at 4°C until ready for analysis. The NIOSH laboratory, following Nieuwenhuijsen *et al.* (1999), used a kinetic chromogenic modification of the limulus amoebocyte lysate (LAL) assay for quantifying endotoxin concentration (BioWhittaker Kinetic QCL). Endotoxin was tested for original concentration and its 5-fold serial dilution at 37°C. Positive and negative controls and five standard concentrations (0.005, 0.05, 0.5, 5.0 and 50.0) were included with each lot of samples. The endotoxin activity of the sample (EU per filter) was calculated relative to the assay standard where the R^2 of the standard curves was >0.97 for all lots of samples. Airborne endotoxin concentration was reported in EU m^{-3}. The protocol for endotoxin analysis at UBC, which followed Thorne (2000), is comparable to NIOSH and is summarized in more detail in Astrakianakis *et al.* All comparisons described in this document are with respect to VE and IOM endotoxin measurements obtained from NIOSH.

Statistical analysis

Data analysis was performed with SAS V 9.1 (SAS Institute, Cary, NC, USA 2002–2003). To compare area concentrations with personal concentrations, the mean of the two area concentrations cotton dust and endotoxin measurements were assigned to the three personal samples from the same shift (AM, PM) and process. Using linear regression (PROC REG), IOM personal concentration of cotton dust and endotoxin was modeled as a function of VE area cotton

dust and endotoxin concentration, respectively. All variables were naturally log transformed, and a simple linear model for cotton dust or endotoxin took this form:

$$\log(\text{IOM personal}) = \beta_0 + \beta_1(\log(\text{VE area})) + \varepsilon.$$

Similarly, IOM personal concentration was modeled as a function of IOM area concentration. In addition, to compare endotoxin and cotton dust measurements, we modeled endotoxin concentration as a function of cotton dust measurements for all sampling techniques (IOM personal, VE area, IOM area). Outliers with studentized residuals $\geq |3|$ were excluded from all models.

All models were adjusted for effect of mill; dummy variables were created to distinguish the effects of Mills A, B and C, using Mill A as the reference. To evaluate for effect modification by mill, we excluded samples from weaving in Mills A and C and created a covariate called MILLB, thus making an effective comparison between Mills A and B where Mill A is the reference group. If the interaction term was statistically significant ($P < 0.05$), models were stratified by mill.

RESULTS

The median cotton dust and endotoxin concentrations in the three mills from VE area measurements were 0.36 mg m^{-3} and 1280.76 EU m^{-3}, respectively, compared to concentrations of 1.74 mg m^{-3} and 2226.83 EU m^{-3}, respectively, measured from IOM personal measurements. Area sampling using the IOM sampler also underestimated personal exposure to cotton dust and endotoxin; median IOM area cotton dust and endotoxin concentrations were 0.67 mg m^{-3} and 1289.83 EU m^{-3}, respectively.

Concentrations by sampling technique, mill and work processes

A summary of area and personal cotton dust and endotoxin concentrations by work process and sampling technique for each mill is provided in Table 1. Similar trends are observed for geometric mean levels of area cotton dust and endotoxin concentrations in Mills A and B. Area cotton dust levels were higher in the early stages of processing for Mills A (opening and carding) and B (carding and drawing). Area endotoxin concentrations were also higher in the

Table 1. Geometric mean cotton dust and endotoxin concentration by sampling technique and work processes in Mills A, B and C

	Cotton dust concentration (mg m^{-3})			Endotoxin concentration (EU m^{-3})		
	VE area[a] ($n = 4$)	IOM area[b] ($n = 4$)	IOM personal[c] ($n = 6$)	VE area[a] ($n = 4$)	IOM area[b] ($n = 4$)	IOM personal[c] ($n = 6$)
	GM (GSD)[d]	GM (GSD)[d]	GM (GSD)[d]	GM (GSD)[d]	GM (GSD)[d]	GM (GSD)[d]
Mill A process						
Opening[e]	0.52 (1.18)	0.95 (1.03)	1.56 (1.79)	582.88 (2.50)	293.90 (1.09)	791.87 (1.15)
Carding	0.37 (1.72)	1.16 (1.28)	5.22 (1.91)	2697.36 (2.75)	1957.48 (1.43)	5381.85 (2.14)
Drawing[f]	0.39 (1.32)	0.61 (1.10)	1.66 (1.33)	2225.24 (1.53)	1937.86 (1.43)	3662.27 (1.93)
Combing	0.22 (1.16)	0.33 (2.04)	1.58 (1.29)	1554.27 (1.49)	885.14 (2.49)	2045.36 (1.81)
Roving	0.31 (1.20)	0.36 (1.53)	1.14 (1.34)	1322.83 (1.23)	1044.51 (1.58)	2114.69 (1.57)
Spinning	0.15 (1.48)	0.42 (1.75)	1.11 (1.11)	42.25 (1.85)	50.02 (2.27)	87.89 (2.29)
Weaving	0.40 (1.14)	0.80 (1.65)	1.81 (1.21)	58.41 (1.16)	36.79 (1.81)	73.42 (1.19)
Entire mill	0.31 (1.61)	0.58 (1.84)	1.75 (1.84)	562.21 (5.57)	418.93 (5.56)	893.18 (5.83)
Entire mill (no weaving)	0.30 (1.66)	0.54 (1.86)	1.75 (1.93)	819.97 (4.74)	651.96 (4.29)	1388.13 (4.60)
Mill B process						
Opening	0.44 (1.24)	1.00 (1.68)	3.47 (1.68)	578.31 (2.31)	870.23 (1.37)	1935.61 (1.28)
Carding	0.53 (1.43)	1.30 (1.71)	2.46 (1.24)	4235.97 (1.65)	3672.61 (1.67)	4064.77 (1.21)
Drawing	0.54 (1.20)	1.38 (1.19)	2.67 (1.13)	6139.54 (1.14)	4555.74 (1.27)	6316.29 (1.18)
Combing	0.23 (1.03)	0.23 (2.39)	1.41 (1.21)	1167.41 (1.33)	1525.16 (1.19)	3435.58 (1.24)
Roving	0.41 (1.13)	1.12 (1.47)	2.14 (1.25)	3308.84 (1.26)	3878.91 (1.30)	1715.64 (9.60)
Spinning	0.12 (1.68)	0.57 (1.21)	1.46 (1.46)	56.50 (1.42)	3878.91 (1.30)	239.71 (1.36)
Entire mill	0.33 (1.85)	0.80 (2.19)	2.15 (1.52)	1219.06 (5.32)	1611.69 (3.18)	2031.13 (3.98)
Mill C process						
Weaving	0.26 (2.08)	0.59 (1.50)	1.00 (1.37)	84.40 (2.77)	102.83 (1.60)	100.2 (2.13)

[a]Work area samples collected with VE sampler (AM shift $n = 2$, PM shift $n = 2$).
[b]Work area samples collected with IOM inhalable dust sampler (AM shift $n = 2$, PM shift $n = 2$).
[c]Personal samples collected with IOM inhalable dust sampler (AM shift $n = 3$, PM shift $n = 3$).
[d]GM, geometric mean; GSD, geometric standard deviation.
[e]$n = 4$ for personal in opening process (Mill A).
[f]$n = 5$ for personal in drawing process (Mill A, dust only).

carding and drawing operations. Lower area dust and endotoxin concentrations were observed in the spinning and combing operations. Endotoxin and cotton dust concentrations from the personal samples were higher in the carding and drawing operations. Similar to the area samples, lower personal dust and endotoxin concentrations were observed in the spinning or combing operations. Excluding samples from the weaving process in Mill A, median area and personal endotoxin and cotton dust concentrations were not significantly different between Mills A and B with exception to personal cotton dust concentration (Kruskal–Wallis $P = 0.01$).

Associations between personal and area measurements of endotoxin exposure

There was evidence of effect modification by mill on the association between IOM personal and VE/IOM area endotoxin concentration; the interaction term MillB* (area endotoxin concentration) was statistically significant for each area sampler ($P = 0.0001$ for VE area, $P = 0.02$ for IOM Area). Thus, we stratified the linear regression models by mill, summarized in Table 2 and in Fig. 1a and b.

The association between IOM personal and VE area endotoxin concentration was statistically significant and IOM personal and VE area endotoxin concentrations were highly correlated (Mill A: $R^2 = 0.83$, $P < 0.0001$; Mill B: $R^2 = 0.89$, $P < 0.0001$); much of the total variance in IOM personal endotoxin concentration could be explained by VE area endotoxin concentration in both mills. Similarly, the association between IOM personal and IOM area endotoxin concentration was statistically significant and much of the total variance in IOM personal endotoxin concentration could be explained by IOM area endotoxin concentration in both mills (Mill A: $R^2 = 0.77$, $P < 0.0001$; Mill B: $R^2 = 0.89$, $P < 0.0001$). The intercepts in VE area models for Mills A and B (Table 2) indicate significant systematic underestimation of IOM personal concentration by 1.07 and 3.15 log EU m^{-3} in Mills A and B, respectively, when using VE area measurements; intercepts in IOM area models for Mills A and B were not statistically significant ($P > 0.05$). The parameters for log area concentration were much closer to 1.00 for IOM area than VE area (Table 2), indicating change in log IOM personal endotoxin concentration more closely approximated change in log IOM area than log VE area endotoxin concentration.

Associations between area and personal measurements of cotton dust exposure

Similar to endotoxin, the association between IOM personal and area cotton dust concentration was statistically significant for both area samplers ($P < 0.0001$ for VE area and IOM area), after adjusting for Mills B and C (Table 2). Unlike endotoxin, however, the models failed to explain most of the variance in IOM personal cotton dust concentration (VE area: $R^2 = 0.37$; IOM area: $R^2 = 0.44$) (Table 2). The intercepts in both models indicate that there was significant underestimation of log IOM personal cotton dust concentration by 1.03 and 0.74 log EU m^{-3} when using VE area and IOM area measurements, respectively. Parameters for log area cotton dust concentration were further away from 1.00 than for endotoxin (Table 2). When Mills B and C were left out of the model, parameters for intercept and log area cotton dust concentration changed slightly, but the R^2 for each model was reduced moderately (VE area: $R^2 = 0.24$; IOM area: $R^2 = 0.33$). Outliers that were excluded from endotoxin and cotton dust models summarized in Table 2 did not change the parameters for intercept, log area cotton dust concentration and R^2 of their respective models considerably.

Associations between endotoxin and cotton dust concentrations

The results of the linear regression models describing the association between endotoxin and cotton dust concentration by sampling technique are summarized in Table 3. The association between endotoxin and cotton dust concentration from IOM personal samples, adjusted for Mills B and C, was statistically significant ($P = 0.0002$), but much of the total variance in IOM endotoxin concentration was unexplained ($R^2 = 0.38$). The association between endotoxin and cotton dust concentrations from IOM area samples was marginally statistically significant ($P = 0.07$). Consistent with a previous analysis (Astrakianakis *et al.*, 2006), we observed a significant association between VE area endotoxin and cotton dust concentrations, adjusting for Mills B and C; total variance in endotoxin concentration explained in this model with VE area dust measurements was moderately higher compared to models with other sample types ($R^2 = 0.49$, $P < 0.0001$).

Table 4 summarizes the between sample type comparison of IOM personal endotoxin and VE area or IOM area cotton dust concentrations. Adjusting for Mills B and C, VE area cotton dust concentration was a significant predictor of IOM personal endotoxin concentration ($P < 0.0001$), but the majority of total variance in IOM personal endotoxin concentration was not explained by VE area cotton dust concentration and Mills B and C ($R^2 = 0.42$). In contrast, the association between IOM area cotton dust and IOM personal endotoxin concentrations was not statistically significant ($P = 0.24$). The goodness of fit of both models was reduced considerably when excluding Mills B and C (VE area: $R^2 = 0.23$; IOM area: $R^2 = 0.03$).

Table 2. Association between log IOM personal concentration and log work area concentrations of endotoxin and cotton dust

	Sampling technique											
	Endotoxin[a]								Cotton dust[a]			
	VE area				IOM area				VE area (n = 80)[e,f]		IOM area (n = 80)[e,g]	
	Mill A (n = 34)[b,c]		Mill B (n = 35)[b]		Mill A (n = 34)[b,d]		Mill B (n = 35)[b]					
	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value
Intercept	1.07 (0.51)	0.04	3.15 (0.28)	<0.0001	0.79 (0.44)	0.08	0.96 (0.61)	0.13	1.03 (0.13)	<0.0001	0.74 (0.07)	<0.0001
Log work area[h]	0.92 (0.07)	<0.0001	0.65 (0.04)	<0.0001	0.95 (0.06)	<0.0001	0.97 (0.09)	<0.0001	0.44 (0.09)	<0.0001	0.42 (0.07)	<0.0001
Mill B[i]	—	—	—	—	—	—	—	—	0.22 (0.09)	0.02	0.12 (0.09)	0.17
Mill C[i]	—	—	—	—	—	—	—	—	−0.43 (0.18)	0.02	−0.52 (0.16)	0.002
R^2 statistic	0.83		0.89		0.77		0.89		0.37		0.44	

[a]Units for endotoxin and cotton dust concentrations are expressed in log EU m^{-3} and log mg m^{-3}, respectively.
[b]Samples from weaving processes in Mills A and C were excluded from the endotoxin analysis.
[c]Outlier (x = 8.162 log EU m^{-3}, y = 2.846 log EU m^{-3}) was excluded from this model.
[d]Outlier (x = 8.384 log EU m^{-3}, y = 2.846 log EU m^{-3}) was excluded from this model.
[e]One observation missing IOM personal cotton dust measurement.
[f]Outlier (x = 2.825 log mg m^{-3}, y = −0.9143 log mg m^{-3}) was excluded from this model.
[g]Outlier (x = 2.825 log mg m^{-3}, y = 0.3606 log mg m^{-3}) was excluded from this model.
[h]Beta coefficient represents change in log IOM personal concentration per unit change in log work area concentration.
[i]Mill A is reference.

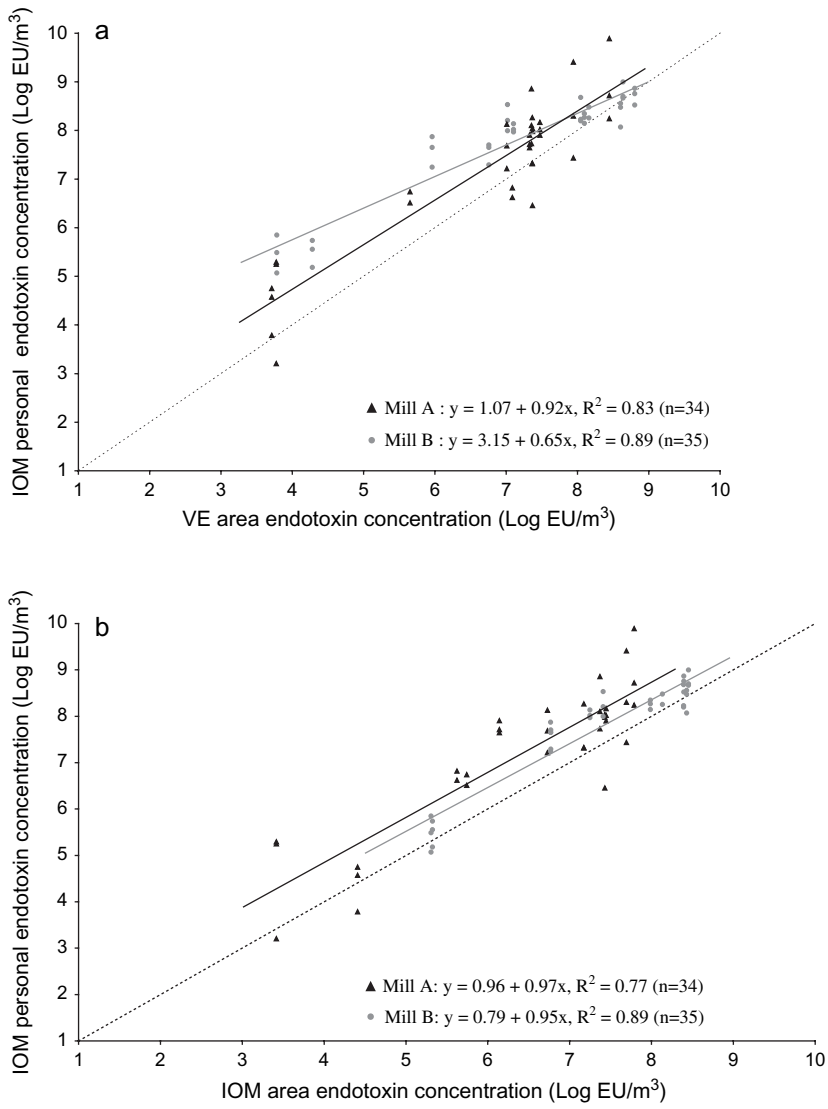

Fig. 1. (a) IOM personal versus VE area endotoxin concentration by mill. Samples from weaving processes in Mills A and C were excluded from this analysis. Outlier ($x = 8.162$ log EU m^{-3}, $y = 2.846$ log EU m^{-3}) was excluded from this model. (b) IOM personal versus IOM area endotoxin concentration by mill. Samples from weaving processes in Mills A and C were excluded from this analysis. Outlier ($x = 8.384$ log EU m^{-3}, $y = 2.846$ log EU m^{-3}) was excluded from this model.

DISCUSSION

Exposure validation, in the context of occupational epidemiologic research, is necessary to increase our understanding of the exposure of interest with potential to improve and refine personal exposure estimates. The primary objective of this study was to evaluate whether VE area endotoxin measurements can be used to predict levels of personal endotoxin concentration measured using the IOM inhalable dust sampler among workers in the Chinese cotton textile industry. Although VE area measurements underestimated personal exposure to endotoxin, we observed strong correlations between VE area and IOM personal measurements for endotoxin. We observed similarly strong correlations for IOM area measurements. Our findings suggest that work area measurements of endotoxin can be used to estimate personal exposure in linear regression models, independent of area sampling instrument.

Because multiple sampling techniques were carried out, analyses were performed to evaluate other validations of cotton dust and endotoxin exposures. In contrast with endotoxin exposure, we observed a much weaker association between area and personal measurements for cotton dust, suggesting area cotton dust measurements are weak predictors of personal exposure, and that use of area measurements of

Table 3. Association between log endotoxin concentration[a] and log cotton dust concentration by sampling technique

	Sampling technique					
	IOM personal ($n = 80$)[b,c]		IOM area ($n = 56$)		VE area ($n = 56$)	
	β (SE)	*P* value	β (SE)	*P* value	β (SE)	*P* value
Intercept	6.09 (0.27)	<0.0001	6.27 (0.30)	<0.0001	8.52 (0.45)	<0.0001
Log cotton dust (log mg m^{-3})[d]	1.12 (0.29)	0.0002	0.51 (0.28)	0.07	1.88 (0.32)	<0.0001
Mill B[e]	0.80 (0.31)	0.01	1.22 (0.39)	0.003	0.65 (0.36)	0.08
Mill C[e]	−1.49 (0.61)	0.02	−1.38 (0.74)	0.07	−1.52 (0.70)	0.03
R^2 statistic	0.38		0.32		0.49	

[a]Units for endotoxin concentration are expressed in log EU m^{-3}.
[b]One observation missing IOM personal cotton dust measurement.
[c]Outlier ($x = 2.846$ log mg m^{-3}, $y = 0.9100$ log mg m^{-3}) was excluded from this model.
[d]Beta coefficient represents change in log endotoxin concentration (log EU m^{-3}) per unit change in log cotton dust concentration (log mg m^{-3}).
[e]Mill A is reference group.

Table 4. Association between log IOM personal endotoxin concentration[a] and log work area cotton dust concentration

	Sampling technique			
	VE area ($n = 81$)[b]		IOM area ($n = 81$)[c]	
	β (SE)	*P* value	β (SE)	*P* value
Intercept	8.52 (0.41)	<0.0001	6.97 (0.27)	<0.0001
Log work area cotton dust (log mg m^{-3})[d]	1.45 (0.30)	<0.0001	0.32 (0.27)	0.24
Mill B[e]	0.84 (0.30)	0.01	0.86 (0.35)	0.02
Mill C[e]	−1.94 (0.57)	0.001	−2.19 (0.64)	0.001
R^2 statistic	0.42		0.26	

[a]Units for personal endotoxin concentration are expressed in log EU m^{-3}.
[b]Outlier ($x = -0.8168$ log EU m^{-3}, $y = 2.846$ log EU m^{-3}) was excluded from this model.
[c]Outlier ($x = 0.4237$ log EU/m^3, $y = 2.846$ log EU m^{-3}) was excluded from this model.
[d]Beta coefficient represents change in log IOM personal endotoxin concentration (log EU m^{-3}) per unit change in log work area cotton dust concentration (log mg m^{-3}).
[e]Mill A is reference group.

endotoxin to estimate personal exposure may be subject to less measurement error than cotton dust. Weaker associations were also observed between cotton dust and endotoxin measurements for each sample type (IOM personal, IOM area, VE area). Similarly, VE area and IOM area dust concentrations were weakly associated with IOM personal endotoxin concentration although the results suggest that VE area cotton dust concentration (rather than IOM area) may be a better predictor for IOM personal endotoxin concentration. This observation has practical merit assuming that airborne endotoxin is the more causative agent associated with cotton dust-related health effects and assuming that VE area dust sampling is likely the common practice for monitoring airborne endotoxin exposure in the cotton textile industry.

There are possible explanations for the contrast in findings between endotoxin and cotton dust regarding the agreement between personal and work area measurements, of which three will be discussed. First, endotoxin levels observed in this study varied much more strongly than cotton dust levels. Thus, while it is expected that the analytical and sampling error combined is expected to be greater for measurement of endotoxin than cotton dust concentration, the effect of the larger error is probably minimal because of the wide variation in endotoxin measurements. Secondly, endotoxin could spread further more uniformly throughout the work area than cotton dust, under the assumption that smaller particles fall at a slower rate than larger particles and if endotoxins mainly present on smaller particles. However, this dispersion pattern for endotoxin may be dependent on workplace and work process. A third possible explanation for different findings between endotoxin and cotton dust may be sampling method for airborne cotton dust. Studies in the UK have reported the presence of non-respirable fly contamination of cotton dust samples collected with the IOM inhalable dust sampler (Niven *et al.*, 1992, 1998). For this study, we fitted a stainless steel screen over the IOM cover cap which should have prevented most fly contamination. However, it is possible that IOM samples of

cotton dust still may have contained fly, which may or may not be contaminated with endotoxin. If fly during early cotton processing stages (where airborne cotton dust and endotoxin levels are higher) is less likely to be contaminated with endotoxin, then the correlation between personal cotton dust and endotoxin measurements could be reduced. Alternatively, area cotton dust and endotoxin concentrations were measured using the VE, which relies on particle fractionation and should prevent fly contamination of the dust filters (Neefus *et al.*, 1977). However, earlier studies have shown that particles >15 μm could be trapped in the jet stream, so measurement error may also occur with use of VEs for airborne cotton dust sampling (Claassen, 1979; Robert, 1979).

There are other sources of variation that may explain the observed findings of this study, such as task and operations performed which are known to affect endotoxin and cotton dust concentrations. An earlier UK study with a much larger sample size (305 area samples and 252 personal samples) found the correlation between area and personal measurements of cotton dust to vary by work process (Niven *et al.*, 1992). Previous studies in the Chinese cotton textile industry have also shown that the correlation between endotoxin and cotton dust concentrations to vary by work process (Olenchock *et al*., 1990; Christiani *et al.*, 1993; Astrakianakis *et al.*, 2006).

This study had insufficient power for a stratified analysis by work process, but we performed a multilevel analysis comparing personal and work area measurements accounting for clustering by work area and worker (data not shown). The parameters for intercept and log work area concentration generally did not vary considerably with those presented in Table 2. However, the standard errors in the multilevel models were inflated as expected. The results from this subsequent analysis suggest that work process may affect the variance in estimated correlation between personal and work area measures. Other factors may influence the variation in endotoxin and cotton dust concentrations and they include raw materials used, production rate, exhaust ventilation, instrument-to-instrument variability and instrument error. However, adjustment for mill in our models may account for some of the variation explained by these unmeasured factors. This study was also cross-sectional; thus seasonality, relevant for endotoxin, was not taken into account.

Finally, endotoxin concentration in this study was measured in one laboratory, directly for IOM samples and indirectly for VE samples. Measurement of endotoxin concentration may also be affected by other factors including storage time, temperature, humidity, cotton source and LAL batch/lot number (Chun *et al.*, 2006). Because endotoxin concentration for VE samples was measured in two different laboratories, we used this opportunity to make an interlaboratory comparison (data not shown). The mean difference in EU per filter between the two laboratories was 1411.3 EU per filter ($P < 0.001$), with a correlation observed between measurements reported at UBC and NIOSH ($r = 0.835$). However, a stronger correlation was observed when we examined log EU m^{-3} ($r = 0.937$), as expected given the log-normal distribution of the measurements; results from both laboratories were within the expected variance of the analytical method. Thus, we expect that use of duplicate aliquots of the VE samples for this study to represent a minor source of variation.

CONCLUSIONS

Without supplementary information to evaluate other sources of variation in cotton dust and endotoxin levels, it would be difficult to generalize the findings from this study to the cotton textile industry at large. However, specific to the conditions of the mills investigated for this study, work area measurements appear to be reasonable proxies of personal exposure to endotoxin, at least for rank-ordering exposures, whereas cotton dust is not nearly as good a proxy. And when supplemented with detailed work history, work area measurements of endotoxin could be applied in estimation of exposure–response relationships for epidemiologic studies.

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