FINAL PROGRESS REPORT 9/29/01 to 9/30/06

Research Title: Lung Disease in Chinese Textile Workers

R01 OH02421-13

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ABSTRACT

The proposed study is a competing continuation of R01 OH 02421. This proposal is designed to address unanswered questions regarding the respiratory health of workers chronically exposed to organic dust (specifically cotton dust) and endotoxin. Exposure to gram-negative bacterial endotoxin has been described in laboratory studies as producing acute respiratory symptoms and lung function change. Similar observations have not been reproduced in actual mill settings. To date, no other prospective epidemiologic study has addressed the relative contributions of cotton dust and endotoxin in producing both acute and chronic respiratory effects. In addition, we will examine the long-term effects of *removal* by retirement from exposure on respiratory health status. This is possible because of documented accessibility to workers who have left the workforce. The importance of endotoxin in causing pulmonary effects is important not only in the cotton textile industry, but also in a number multitude of other environments where significant levels of airborne endotoxin are encountered. The study population (closed cohort) that has been followed since 1981 and is unusually well-suited for epidemiologic study due to: low turnover, very low smoking prevalence among women workers, reliable baseline data, a suitable comparison group studied in identical fashion, excellent cooperation among industry officials, union and the collaborative research team, access to subjects who have retired or left the industry in disability, and cost-efficiency. The population included 447 cotton textile and 465 silk textile workers first surveyed in 1981. Follow-up surveys were conducted in 1986, 1992, and 1996, 2001 and 2006 with excellent follow-up. The proposed study is unique because exposure estimates for both dust and endotoxin over a 25-year period allowed assessment of exposure-response relationships for both dust and endotoxin for the full study interval.

SECTION 1

Highlights/Signifcant Findings

The findings have improved our understanding of the relationships between long-term exposure to cotton dust and chronic airway obstruction, which are associated with the occurrence and persistence of byssinosis, and the level of exposure to endotoxin. Moreover, our results suggest that chronic airway obstruction may, to some extent, be reversible after the exposure ceases for those who do not smoke. However, there is a persistent adverse effect of smoking on lung function in retired cotton workers. The data provide additional information in exploring the mechanisms of etiology and pathology of organic dust-related airway disease. On the other hand, the result of comparative dust concentrations from the different samplers indicated that our previous evaluations of dust concentrations in work area and individual exposures might have been underestimated by using VE samplers. Since there is good correlation between VE samples and IOM-personal and IOM-area samples, it is possible to determine more precise individual exposure by calibrating the previously estimated dust levels, and ultimately, to observe a clearer exposure-response relationship to chronic respiratory airway disease.

Translation of Findings
Outcomes/Relevance/Impact

The findings have relevance for worker health in several respects. Firstly, we have identified a cause of chronic airflow obstruction that occurs in the absence of smoking, and is preventable by exposure controls – namely, endotoxin. The effects of endotoxin are additive with smoking among those who do smoke; another opportunity for prevention.
Secondly, we found that cross-shift change in FEV1, and repeated respiratory symptom reporting, both predict long-term loss of lung function. This finding means that monitoring will help with early detection and control of chronic airflow obstruction in exposed workers. Lastly, we found that removal from exposure to cotton dust and its associated endotoxin results in improvement in lung function decline towards normal aging, thus representing the first example of at least partial reversibility for cessation of a chronic occupational exposure.

SECTION II
Scientific Report
a. Specific Aims

The primary objective of this competing continuation is to complete a 20-year longitudinal study of textile workers in Shanghai, China. This study represents the longest prospective cohort study of textile workers ever performed. The follow-up population has been evaluated for exposure and pulmonary effects in 1981, 1986, 1992, 1996, and 2001. The study has allowed us to examine the relationship between acute respiratory responses to cotton dust and long-term change in lung function and to examine cotton dust-associated gram-negative bacterial endotoxin exposure-response relationships. Further study of this cohort in 2001 improved our understanding of the chronic respiratory disease potential of cotton dust and endotoxin. More generally, better understanding of the effects of inhaled endotoxin contribute to assessing risk in a variety of occupational settings where airborne endotoxin exposures have been documented, such as: grain storage and processing, swine confinement buildings, poultry houses, sewage treatment plants, machining operations, biotechnology, and humidified buildings.

The specific aims of this study were:

(1) To estimate 20-year decline in pulmonary function.
   (a) to compare decline in function between cotton and silk textile workers.
   (b) to estimate the relationship between cumulative exposure to cotton dust and endotoxin and decline in lung function among cotton-exposed workers.

(2) To examine the relationship between decline in pulmonary function and the incidence and persistence of respiratory symptoms.

(3) To describe the long-term effects of *removal* by retirement from exposure on respiratory health status. This is possible because of documented accessibility to workers who have left the workforce, and a large proportion of retirees.

(4) To examine the value of cross-shift FEV_1 as a marker for the development and progression of respiratory symptoms or accelerated pulmonary function decline.

b. Results

The results obtained from this study are summarized in three parts: (1) basic information of the 20-year follow-up study; (2) preliminary analysis on environmental assessment; (3) chronic respiratory health effects of long-term exposure to cotton dust.

1. Basic information on the 20-year survey:

In the 20th year survey, a total of 688 (75%) workers from the original cohort of 919 eligible individuals were successfully followed and examined. Additional 62 workers were found to be dead during the follow-up period. The follow-up rate reached 80% if the deceased were excluded (84% in the cotton and 77% in the silk group) (see the follow-up rates over the 20-years in the included table). A major change during last period was that almost all of the workers retired from textile industry due to a closure of the mills. A special effort was made to verify the individual workers' retirement status and dates since the information is paramount for further analysis on the evaluation of exposure-response relationship and the health effects. Demographic features were found, as previously, similar between the two groups at the last survey. A summary of the various survey recruitment success is displayed in the following table:

Table. Follow-Up Rates at Each Survey over the 20-Year Period

Year	Cotton	Silk	Total	Followed rates (%)
1981	447	472	919	
1986	384	403	787	86
1992	394	393	787	86
1996	346	338	684	74
2001	346	342	688	75

2. Environmental Assessment: Analysis on the results of different dust samplers and their correlations:

To provide an assessment of personal exposure level, we collected dust samples using vertical elutriators (VE) and inhalable particle mass personal samplers (IOM sampler) in the fall of 2002. Afterwards, we analyzed dust samples collected from work area and personal exposure, and analyzed endotoxin concentrations. After excluding blank samples, the analyzed dust samples contained 56 full-shift vertical elutriator samples concurrently with 56 IOM-area samples, and 82 IOM-personal samples from different work processes. At the same time, endotoxin was analyzed on 56 full-shift VE dust samples. The level of endotoxin was highest in drawing and carding (4289Eu/m^3 and 4050 Eu/m^3, respectively), and lowest in spinning and waving (53 Eu/m^3 and 89 Eu/m^3, respectively). A comparison of the dust concentrations from the different samplers revealed that IOM-personal samplers, followed by IOM-area samplers, obtained the highest values. The lowest values of dust concentrations were provided by VE (see the figure showing the dust concentrations from different samplers). A correlation analysis of mean dust concentrations at each work process indicated that there was a significant correlation between the IOM-area samples and VE samples ($r = 0.70$, $p < 0.01$), and between the IOM-personal samples and VE samples ($r = 0.58$, $p < 0.05$).

3. Chronic respiratory health effects of long-term exposure to cotton dust – A twenty-year follow-up study in cotton textile workers.

To determine the magnitude of the chronic respiratory effect in the cotton workers, including lung function and respiratory symptoms, and evaluated the roles of exposure to dust and endotoxin, we conducted data analysis on the 20-year follow-up study. We found that 32% of cotton workers reported byssinosis at least once over the observation time. Cotton workers had more persistent respiratory symptoms (both specific and nonspecific) in comparison with silk workers. More importantly, cotton workers had substantially greater annual declines in FEV_1 and FVC over 20-year period. The rate of decline in FEV_1 over the last 5-years was not different from that over 20-years, but in males, smokers tended to have a greater loss and nonsmokers had a smaller loss over the last 5-years, suggesting an improvement of airway obstruction in the nonsmoking male cotton workers after the exposure was stopped. The annual loss of FEV_1 tended to be greater with increasing reporting frequency of byssinosis over time. The level of exposure to endotoxin, rather than exposure to dust, was negatively related to the longitudinal changes in lung function. Furthermore, higher levels of exposure to endotoxin were associated with a greater annual loss in FEV_1 and FVC, indicating a trend of exposure-response relationship. A copy of the paper is attached in the appendix.

Publications

Xiao-Rong Wang, Lei-Da Pan, Hong-Xi Zhang, Bi-Xiong Sun, He-Lian Dai, and David Christiani. A Follow-Up Study of Respiratory Health of Non-Smoking Newly Hired Female Textile Workers. American Journal of Industrial Medicine 41:111-118, 2002.

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Program Director/Principal Investigator (Last, First, Middle): Christiani, David C.

Inclusion Enrollment Report

This report format should NOT be used for data collection from study participants.

Study Title: Lung Disease in Chinese Textile Workers

Total Enrollment: 688 **Protocol Number:** P10175

Grant Number: R01 OH002421

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	0	0	0	**
Not Hispanic or Latino	395	293	0	688
Unknown (individuals not reporting ethnicity)				
Ethnic Category: Total of All Subjects*	395	293	0	688 *
Racial Categories				
American Indian/Alaska Native				
Asian	395	293	0	688
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More Than One Race				
Unknown or Not Reported				
Racial Categories: Total of All Subjects*	395	293	0	688 *

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)

Racial Categories	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More Than One Race				
Unknown or Not Reported				
Racial Categories: Total of Hispanics or Latinos**	0	0	0	0 **

* These totals must agree.
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