

# Epidemiologic Investigation of Respiratory Morbidity at a Nylon Flock Plant

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**Background** *A cluster of biopsy-confirmed interstitial lung disease among workers at a nylon flock plant led to a request for National Institute for Occupational Safety and Health investigators to conduct a health hazard evaluation.*

**Methods** *Part of the overall evaluation, reported here, involved a cross-sectional medical survey of current employees. The survey consisted of a questionnaire, spirometry and diffusing capacity testing, and chest radiograph.*

**Results** *Workers assigned to production and maintenance jobs reported frequent eye and throat irritation, respiratory symptoms, and systemic symptoms (i.e., generalized aches and fevers). Most reported improvement when away from work. Frequent respiratory/systemic symptom prevalence was significantly associated with departmental category, with days and hours worked per week, and with working on a flocking range. Compared to asymptomatic workers, symptomatic workers had similar mean ratios of forced expiratory volume in one second to forced vital capacity, but lower mean percent of predicted values for both forced vital capacity and diffusing capacity. All acceptable chest radiographs were classified as category 0 for small opacities.*

**Conclusions** *Findings of this study, along with those from studies reported elsewhere, implicate occupational exposure to flock-associated dust as a significant respiratory health hazard at this plant. Am. J. Ind. Med. 38:628–638, 2000. Published 2000 Wiley-Liss, Inc.†*

**KEY WORDS:** *occupational lung disease; interstitial lung disease; pneumonitis; nylon; flock; textiles*

## INTRODUCTION

In early 1996, the National Institute for Occupational Safety and Health (NIOSH) received a request to investigate respiratory illness among workers at a plant in Rhode Island that produces flock and upholstery fabric coated with nylon flock. The request specified that two workers had been recently diagnosed with interstitial lung disease (ILD), initially thought to be hypersensitivity pneumonitis (HP). Both had been evaluated by a local occupational medicine

specialist who suspected that their illness was work-related, restricted them from work at the plant, and urged the company to request NIOSH assistance. Several additional workers were subsequently diagnosed with similar disease [Kern et al., 1998; Kern et al., 2000]. This report presents results of a cross-sectional respiratory morbidity survey conducted at the Rhode Island plant. NIOSH investigators also conducted an industrial hygiene assessment of this plant [Burkhart et al., 1999] and preliminary toxicological studies of airborne dust collected from this plant and related materials [Porter et al., 1999].

## Plant Description

Flock (predominantly nylon and a much lesser amount of polyester flock) is produced at the plant in a continuous process. “Tow”—a loose bundle composed of tens of thousands of thin continuous filaments, each approximately

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10–20  $\mu\text{m}$  in diameter—is coated with a flock finish containing tannic acid, an ammonium ether of potato starch, and a fatty alcohol derivative before being cut by high-speed rotary cutters, dried, milled to break up flock that fuses during cutting, screened for size, and bagged as flock. Some tow is dyed before being made into flock.

Flocked upholstery fabric is produced at the plant in a continuous, roll-to-roll, process. A viscous acrylic latex adhesive is applied as a thin coating to cotton-polyester backing fabric. Flock, sometimes with a desiccant silicate powder mixed in to prevent clumping, is applied to this adhesive-coated fabric by sifting it and allowing it to fall through an electrostatic field that aligns the flock so that it embeds end-on into the adhesive. After heat-curing of the adhesive, the flocked fabric may be subjected to mechanical embossing, screen printing with water-based ink, or otherwise finished, depending on customer specifications.

Between process runs that differ with respect to flock texture (e.g., length and/or diameter) or color, residual flock is cleaned from the affected production line. This is accomplished by what the workers refer to as a “blow-down,” an extremely dusty process that involves the use of compressed air to clear loose, settled flock—at times, several inches thick—from the equipment, walls, and floor. The frequency of blow-downs varies with the production schedule; on occasion, several blow-downs may be performed per shift.

At the time of the NIOSH medical survey, 170 workers were employed in continuous operations, 7 days a week. Many employees worked more than 5 days per week and more than 8-hour workdays. During the standard workweek, workers are typically assigned to a specific job/work station. On weekends, these same employees may be assigned to other jobs.

The workers least exposed to the production areas are those who work in the offices and in shipping and warehousing operations. However, few workers in these less-exposed groups can be considered unexposed to air contaminants in the production areas. Most offices are in the production building, and although served by an independent heating, ventilating and air conditioning system, the office area was under negative pressure with respect to the production area, resulting in substantial air movement through doorways and passageways. Also, some office workers and many warehouse/shipping workers spend at least some part of their workday in the production areas of the plant. Single-use respirators were used by some workers in various production areas of the plant.

A more complete description of the plant process is available elsewhere [NIOSH, 1998].

## METHODS

In mid-1996, we conducted a cross-sectional survey, which included a standardized questionnaire, spirometry testing, diffusing capacity testing, and chest radiograph. Current employees were invited to participate in any or all components of the survey on a voluntary basis, and signed informed consent was obtained from every participant.

We designed a computer-assisted [Dean et al., 1995] survey questionnaire (available from the authors) after reviewing index case medical records and after open-ended interviews with index cases and several flocking range workers. The questionnaire focused on symptoms (Table I) and medical conditions, as well as on demographics, work assignments, and smoking history. Participants were asked how many days they currently worked each week and how

**TABLE I.** Questions Used to Ascertain Frequent Symptoms Among Employees at a Nylon Flock Plant, Rhode Island

Irritation symptoms	
Throat irritation	Do you frequently have throat irritation?
Eye irritation	Do you frequently have eye irritation?
Respiratory symptoms	
Shortness of breath	Do you frequently have shortness of breath?
Cough	Do you frequently have a dry cough?
Wheeze	Do you frequently have a wheezing or whistling in the chest?
Chest tightness	Do you frequently have chest tightness?
Phlegm	Do you frequently have a cough with phlegm?
Systemic symptoms	
Fevers	Do you frequently have fever?
Generalized aches	Do you frequently have aches all over your body, similar to when you have the flu?
For positive responses to each of the above questions, follow-up included	Does it improve when away from work?

many hours they worked each workday; each worker's responses to these two questions were multiplied to determine number of hours worked per week.

Spirometry, using equipment and procedures conforming to standard guidelines [American Thoracic Society, 1995a], generated measurements of forced expiratory volume in one second (FEV<sub>1</sub>), forced vital capacity (FVC), and the FEV<sub>1</sub>/FVC ratio for analysis. We calculated predicted values for FEV<sub>1</sub> and FVC using published reference equations [Knudson et al., 1983], multiplying the values predicted by the equations by 0.85 to obtain predicted values for blacks [Hankinson, 1986].

Testing for lung diffusing capacity using carbon monoxide as a test gas (DL<sub>CO</sub>) conformed to standard guidelines [American Thoracic Society, 1995b], except that we did not ask smokers to refrain from smoking prior to testing. However, we did adjust each individual's carbon monoxide (CO) backpressure for concentration of CO measured in expired gas immediately prior to testing. For each individual tested, we obtained a maximum of five trials to obtain two DL<sub>CO</sub> values within 5% of one another, and took the mean DL<sub>CO</sub> from the two acceptable trials as the individual's test result, expressing it as a percent of predicted value [Miller et al., 1983].

Standard posteroanterior chest radiographs were taken in the NIOSH mobile examination trailer and sent to two NIOSH-certified B readers who, without knowledge of participants' ages, occupations, symptoms, or smoking histories, independently classified each film according to the current international classification system for pneumoconiosis [ILO, 1980]. For any of the films on which the first two readers disagreed on small opacity profusion, we obtained an additional independent classification from a third B reader. We analyzed the consensus or median small opacity profusion classification for each film.

We used Epi Info software [Dean et al., 1995] to analyze results of the medical survey. Based on question-

naire responses regarding job assignment, each survey participant was assigned to one of two departmental categories: Office/Warehouse/Shipping or Production/Maintenance. For categorical symptom data, prevalence ratios (PRs) and confidence intervals (CIs) were calculated to compare the results of designated subgroups of workers. For continuous pulmonary function data, mean values were compared using Student's *t*-test, or if variances differed, using the nonparametric Kruskal-Wallis test.

## RESULTS

### Demographics and Reported Exposures

Of 170 current workers, 151 (89%) completed the questionnaire. The median age of all participants was 39 years (range: 18 to 71). A large majority (89%) were males. Most (72%) were white, 16% were Hispanic, 9% were non-Hispanic black, 3% were Asian/Pacific Islander, and 1% reported their race as "other." Overtime was commonplace; 129 (85%) reported working more than five days per week, and 26 (17%) reported working seven days per week. Table II shows data on age, tenure at the plant, number of days and hours worked per week, reported exposures, and smoking by departmental category. The most obvious differences were that Office/Warehouse/Shipping workers were about half as likely as Production/Maintenance workers to report ever working on the flocking range or ever participating in a blow-down. Nevertheless, these two exposures were reported by about one-third of Office/Warehouse/Shipping workers (data not shown).

### Symptoms and Medical Conditions

Responses to questions regarding frequent symptoms (with onset after hire at the plant) are summarized by departmental category in Table III. Not shown in Table III,

**TABLE II.** Tenure, Number of Days and Hours Worked per Week, Flocking Range Exposure, Blow-Down Exposure, and Smoking Status by Departmental Category—Questionnaire Responses of Current Employees at a Nylon Flock Plant, Rhode Island

		Office/Warehouse/Shipping (n = 32)	Production/Maintenance (n = 119)
Age (years)	mean	43.1	39.2
Tenure (years)	mean	8.9	8.1
Days worked per week	mean	5.6	6.1
Hours worked per week	mean	52.3	54.3
Flocking range (ever)	%	37.5	68.9
Blow-down (ever)	%	34.4	77.3
Current smoker	%	28.1	33.6
Never smoker	%	25.0	30.3
Pack-years	mean	19.7	22.6

**TABLE III.** Number, Percent, and Prevalence Ratios for Frequent Symptoms and for Frequent Symptoms That Improve Away From Work by Departmental Category—Questionnaire Responses of Current Employees at a Nylon Flock Plant, Rhode Island

Symptom	Office/Warehouse/Shipping (n = 32)		Production/Maintenance (n = 119)		PR <sup>a</sup>	95% CI
	n	%	n	%		
Irritation						
Eye	0	—	37	31.1	∞	—
Improves <sup>b</sup>	0	—	31	26.1	∞	—
Throat	1	3.1	28	23.5	7.5	1.1–53
Improves <sup>b</sup>	0	—	19	16.0	∞	—
Respiratory						
Shortness of Breath	5	15.6	42	35.3	2.3	1.0–5.2
Improves <sup>b</sup>	1	3.1	20	16.8	5.4	0.8–39
Cough	3	9.4	38	31.9	3.4	1.1–10
Improves <sup>b</sup>	2	6.3	23	19.3	3.1	0.8–12
Chest tightness	4	12.5	41	34.5	2.8	1.1–7.1
Improves <sup>b</sup>	1	3.1	24	20.2	6.5	0.9–46
Wheeze	4	12.5	25	21.0	1.7	0.6–4.5
Improves <sup>b</sup>	1	3.1	14	11.8	3.8	0.5–28
Phlegm	5	15.6	38	31.9	2.0	0.9–4.8
Improves <sup>b</sup>	1	3.1	22	18.5	5.9	0.8–42
Systemic						
Fevers	1	3.1	6	5.0	1.6	0.2–13
Improves <sup>b</sup>	0	—	5	4.2	∞	—
Generalized aches	1	3.1	30	25.2	8.1	1.1–57
Improves <sup>b</sup>	0	—	21	17.6	∞	—

<sup>a</sup>PR = Prevalence ratio, based on office/warehouse/shipping workers as reference.

<sup>b</sup>Specified frequent symptom improves when away from work.

the median reported duration for each of these frequent symptoms ranged from 6 to 18 months, and there were no significant differences in prevalence by smoking status.

Frequent eye irritation with onset after hire was reported by over 30% of Production/Maintenance workers, compared to none of the Office/Warehouse/Shipping workers. Over 25% of Production/Maintenance workers reported frequent eye irritation that improved when away from work. Likewise, frequent throat irritation with onset after hire was reported by over 20% of Production/Maintenance workers, compared to less than 5% of Office/Warehouse/Shipping workers (PR = 7.5, 95% CI = 1.1–53). Frequent throat irritation that improved when away from work was reported by 16% of Production/Maintenance workers, but by none of the Office/Warehouse/Shipping workers.

With respect to respiratory symptoms, over 30% of Production/Maintenance workers reported frequently experiencing shortness of breath, cough, chest tightness, and phlegm, and over 20% reported frequently experiencing wheeze. This is reflected in high prevalence ratios for these

frequent respiratory symptoms among Production/Maintenance workers (relative to Office/Warehouse/Shipping workers), which ranged up to 3.4 (95% CI = 1.1–10) for cough. Even higher prevalence ratios, ranging from 3.1 to 6.5, were observed for frequent respiratory symptoms that improve when away from work.

With respect to systemic symptoms, six of the 119 Production/Maintenance workers reported frequent fevers with onset since hire, and five of these six reported that their frequent fevers improved when away from work (Table III). The only Office/Warehouse/Shipping worker who reported frequent fevers also reported both working on the flocking range and blow-down exposure. Frequent generalized aches with onset since hire were reported by 25% of Production/Maintenance workers, compared to less than 5% of Office/Warehouse/Shipping workers (PR = 8.1; 95% CI = 1.1–57). Nearly 18% of Production/Maintenance workers, compared to none of the Office/Warehouse/Shipping workers, reported frequent generalized aches that improve when away from work.

More than half of the participants reported at least one of the preceding frequent systemic and/or respiratory symptoms with onset after hire, including 64.7% (77 of 119) Production/Maintenance workers and 28.1% (9 of 32) Office/Warehouse/Shipping workers (PR = 2.3; 95% CI = 1.3–4.1). As shown in Table IV, several factors were associated with having one or more of these symptoms with onset after hire. Symptom prevalence was substantially higher among workers who had ever participated in blow-downs and, even moreso, among workers who had ever worked on the flocking ranges. Among Production/Maintenance workers, symptom prevalence increased significantly with days worked per week ( $\chi^2_{\text{trend}} P = 0.015$ ) and hours worked per week ( $\chi^2_{\text{trend}} P = 0.012$ ); a similar, though not statistically significant, trend for hours worked per week was seen among Office/Warehouse/Shipping workers. In contrast, there were no apparent symptom prevalence trends related to tenure at the plant among workers in either departmental category. Also, smoking status was not significantly associated with symptoms (Table IV), nor were age, race, or sex (data not shown).

Among Production/Maintenance workers, 13 (11%) reported having had physician-diagnosed pneumonia in the past five years while employed at the plant, compared to only 1 (3%) of Office/Warehouse/Shipping workers (Table V). Likewise, Production/Maintenance workers were more than twice as likely as Office/Warehouse/Shipping workers to report having had two or more flu-like illnesses during the preceding year (Table V). Also, Production/Maintenance workers were three times as likely as Office/Warehouse/Shipping workers to report having had two or more attacks of shortness of breath with wheeze during the preceding two years and nearly four times as likely to report a physician diagnosis of asthma (Table V).

### Pulmonary Function Testing

Among the 151 workers who completed questionnaires, 145 performed spirometry and 110 participated in diffusing capacity testing. Restriction (defined as FVC < lower limit of normal with FEV<sub>1</sub>/FVC > lower limit of normal) was observed in 8 of 113 (7.1%) Production/Maintenance workers compared to 1 of 32 (3.1%) Office/Warehouse/Shipping workers (PR = 2.3; 95% CI = 0.3–17). Low diffusing capacity (defined as < 80% of predicted value) was observed in 12 of 91 (13.2%) of Production/Maintenance workers compared to 1 of 19 (5.3%) of Office/Warehouse workers (PR = 2.5; 95% CI = 0.4–18).

Among all participants, mean percent predicted values of DL<sub>CO</sub> ( $P < 0.02$ ) and FVC ( $P < 0.07$ ), but not of FEV<sub>1</sub>/FVC, were lower among those with at least one frequent systemic and/or respiratory symptom compared to those without (Table VI). Stratifying by smoking status (Table VI), this same pattern of pulmonary function test results asso-

ciated with symptom status remained evident and statistically significant among ever-smokers, but not among never-smokers. Therefore, after excluding never-smokers, we repeated the analyses for which results are shown for all participants in Table IV. Symptom prevalence among all smokers was significantly associated with departmental category, days worked per week, hours worked per week, participation in blow downs, ever working on a flocking range, and departmental category (data not shown). Furthermore, the prevalence ratios for each of these factors among smokers alone remained similar in magnitude to those shown in Table IV.

### Radiography

All 143 interpretable films (out of 145 taken) were classified as having a small opacity profusion of major category 0, and only 3 of these were classified as minor category 0/1.

### DISCUSSION

This cross-sectional medical-epidemiological survey was motivated by the occurrence of a cluster of an interstitial lung disease (ILD) reported in detail elsewhere and referred to as “flock worker’s lung” by Kern and colleagues [Davidoff, 1998; Kern et al., 1998; NIOSH, 1998]. Most cases diagnosed among workers at this plant were diagnosed in 1996, a year during which active case finding was undertaken, but other cases were diagnosed later and one case, identified retrospectively, had been diagnosed in 1985 [Kern et al., 1998, 2000]. Among all diagnosed cases from this plant, duration of employment before symptom onset ranged from less than one year to 31 years (median 6 years). Chronic and progressive shortness of breath and cough that preceded diagnosis by several months to several years were the prominent symptoms in nearly all cases. However, several affected individuals described other respiratory symptoms (e.g., productive cough, wheezing) and systemic symptoms (e.g., episodes of mild fever and generalized aches). In some cases, including one worker whose workstation had been enclosed to prevent dust from escaping to contaminate other parts of the plant, systemic symptoms were quite notable [NIOSH, 1998]. In all diagnosed cases, substantial clinical improvement in both symptoms and other clinical abnormalities occurred over a period of weeks to months following removal from the workplace or reassignment to non-production areas [Kern et al., 1998, 2000].

Importantly, a cluster of ILD was independently reported among workers at a very similar nylon flock plant in Canada [Lougheed et al., 1995]. The specific etiology for the disease cluster in Canada was not identified, although the investigators speculated that the illness—severe enough

**TABLE IV.** Number, Percent, and Prevalence Ratio for Reporting At Least One Frequent Systemic or Respiratory Symptom (With Onset After Hire) by Various Factors—Questionnaire Responses of Current Employees at a Nylon Flock Plant, Rhode Island

≥ 1 Frequent systemic and/or respiratory symptom<sup>a</sup> (with onset after hire at the plant)

Factor	Office/Warehouse/Shipping					Production/Maintenance				
	n	%	PR <sup>b</sup>	95% CI <sup>c</sup>	$\chi^2_{trend}$	n	%	PR <sup>b</sup>	95% CI <sup>c</sup>	$\chi^2_{trend}$
Smoking status										
Never	2	25.0	—	—	—	22	61.1	2.4	0.7–8.4	—
Ever	7	29.2	1.2	0.3–4.5		55	66.3	2.7	0.8–8.9	
Tenure at plant (years)										
< 3	3	30.0	—	—	$\chi^2 = 0.07$	22	53.7	1.8	0.7–4.8	$\chi^2 = 1.9$
3–10	3	30.0	1.0	0.3–3.8	$P = 0.79$	25	73.5	2.5	0.9–6.5	$P = 0.17$
> 10	3	25.0	0.8	0.2–3.3		30	68.2	2.3	0.9–6.0	
Days worked per week										
< 5	3	18.8	—	—	$\chi^2 = 1.0$	2	33.3	1.8	0.4–8.2	$\chi^2 = 5.9$
6	5	38.5	2.1	0.6–7.0	$P = 0.33$	56	62.2	3.3	1.2–9.3	$P = 0.015$
7	1	33.3	1.8	0.3–11.9		19	82.6	4.4	1.6–12.4	
Hours worked per week										
< 45	3	20.0	—	—	$\chi^2 = 2.2$	2	33.3	1.7	0.4–7.6	$\chi^2 = 6.3$
45–65	3	25.0	1.3	0.3–5.1	$P = 0.13$	61	62.9	3.1	1.1–8.8	$P = 0.012$
> 65	3	60.0	3.0	0.9–10.4		14	87.5	4.4	1.6–12.2	
Blow-down (ever)										
No	4	19.0	—	—	—	15	55.6	2.9	1.1–7.5	—
Yes	5	45.5	2.4	0.8–7.1		62	67.4	3.5	1.5–8.6	
Flocking range (ever)										
No	3	15.0	—	—	—	21	56.8	3.8	1.3–11.2	—
Yes	6	50.0	3.3	1.0–10.9		56	68.3	4.6	1.6–13.1	

<sup>a</sup>Shortness of breath; cough; chest tightness; wheeze; phlegm; fevers; and generalized aches.

<sup>b</sup>PR = Prevalence ratio, based on group with '—' as reference for each factor.

<sup>c</sup>95% CI = Upper and lower limits of 95% confidence interval for prevalence ratio.

**TABLE V.** Number and Percent of Respondents Reporting Other Medical Conditions by Departmental Category—Questionnaire Responses of Current Employees at a Nylon Flock Plant, Rhode Island

	Office/Warehouse/Shipping (n = 32)		Production/Maintenance (n = 119)			
	n	%	n	%	PR	95% CI
Pneumonia <sup>a</sup>	1	3.1	13	10.9	3.5	0.5–25
Flu-like illnesses <sup>b</sup>	4	12.5	35	29.4	2.4	0.9–6.1
Asthma <sup>c</sup>	1	3.1	14	11.8	3.8	0.5–27
Attacks of SOB with wheeze <sup>d</sup>	3	9.4	33	27.7	3.0	1.0–9.0

<sup>a</sup>Pneumonia diagnosed by a physician since hire and in last five years.

<sup>b</sup> ≥ 2 such illnesses during the preceding year.

<sup>c</sup>Asthma diagnosed by a physician.

<sup>d</sup> ≥ 2 attacks during the preceding two years.

to require prolonged mechanical ventilation in one of the affected workers—might have been caused by inhalation of mycotoxin relating to observed fungal contamination of the adhesive used at the plant [Lougheed et al., 1995]. However, despite removal of the contaminated adhesive and measures taken to prevent fungal growth in stored adhesive, several additional cases of this respiratory illness subsequently occurred among workers at the plant in Canada [Eschenbacher et al., 1999].

Additional sporadic cases of clinically similar work-related ILD have recently occurred in workers from other nylon flock plants, and it is now clear that this work-related disease presents with a wide-range of severity and that more severe cases are generally—though perhaps not always—histopathologically distinctive [Boag et al., 1999; Eschenbacher et al., 1999; Kern et al., 2000]. Effective prevention depends on an understanding of the epidemiology—including, to the extent possible, the etiology—of this disease.

One purpose of our cross sectional survey was to help screen current workers for possible ILD; to this end, more than half of those participating in the NIOSH survey made their survey results available for review by the clinical occupational medicine specialist who first identified the disease cluster among workers at the Rhode Island plant and has since published clinical details of eleven diagnosed cases from this plant [Kern et al., 1998, 2000].

The major purposes of our survey were to quantify and characterize respiratory morbidity—including subclinical morbidity—among current workers at the Rhode Island plant and to identify work-related factors associated with the observed morbidity. Frequent respiratory and systemic symptoms that may represent mild ILD, as well as physician-diagnosed pneumonia and repeated flu-like illnesses that may represent misdiagnosed ILD, were all more prevalent among Production/Maintenance workers than among

Office/Warehouse/Shipping workers, the latter group being generally less exposed to production areas of the plant. Work-relatedness of excess morbidity ascertained in our survey is supported by the preceding observations, by the frequent report of improvement in symptoms when away from work (particularly among workers more exposed to the production areas of the plant), and by the association of symptom prevalence with work on the flocking ranges, blow-down exposures, and amount of exposure as reflected by days and hours worked per week.

Pulmonary function testing results served to validate the relevance of frequent respiratory/systemic symptoms reported by workers at this plant. The finding that mean FVC and DL<sub>CO</sub> values, but not mean FEV<sub>1</sub>/FVC ratio values, were generally lower among those with at least one of these symptoms compared to asymptomatic workers is consistent with a restrictive interstitial disease process rather than an obstructive airways disease process. The strength of this finding among ever-smokers, but not among never-smokers, together with the preponderance of ever-smokers among the physician-diagnosed cases of ILD at this plant [Kern et al., 1998, 2000], suggests that affected smokers may be especially susceptible to functional impairment. A modifying effect of smoking remains uncertain, however, as an association between smoking and symptoms was not evident in our analysis shown in Table IV.

The apparent excesses of production-related asthma and attacks of shortness of breath with wheezing suggest the possibility that occupational exposures in the plant may also be associated with airways disease, either as a manifestation of the underlying disease, as in inhalational ILD caused by other agents [Redlich, 1996], or independent of it. This warrants further investigation with assessment of airways hyperreactivity in relation to symptoms, other physiologic measurements, and exposure. Airways irritation seems

**TABLE VI.** Comparison of Mean Pulmonary Function Results by Symptom Status and Smoking Status—Current Employees at a Nylon Flock Plant, Rhode Island

		$\geq 1$ Frequent systemic and/or respiratory symptom <sup>a</sup> (with onset after hire at the plant)		
		Yes	No	P <sup>b</sup>
All				
DL <sub>CO</sub> (% predicted)	mean	94.0	100.9	0.02
	SD	15.1	13.4	
	n	68	42	
FVC (% predicted)	mean	99.1	103.2	0.07
	SD	13.3	13.6	
	n	84	61	
FEV <sub>1</sub> /FVC (X 100)	mean	80.0	80.2	0.86
	SD	6.5	6.5	
	n	84	61	
Never-smokers				
DL <sub>CO</sub> (% predicted)	mean	98.3	103.1	0.31
	SD	14.3	11.9	
	n	19	14	
FVC (% predicted)	mean	102.1	102.0	0.97
	SD	12.5	14.7	
	n	23	19	
FEV <sub>1</sub> /FVC (X 100)	mean	79.8	80.8	0.69
	SD	8.4	7.5	
	n	23	19	
Ever-smokers				
DL <sub>CO</sub> (% predicted)	mean	92.3	99.8	0.04
	SD	15.2	14.2	
	n	49	28	
FVC (% predicted)	mean	98.0	103.8	0.03
	SD	13.6	13.2	
	n	61	42	
FEV <sub>1</sub> /FVC (X 100)	mean	80.1	79.9	0.89
	SD	5.6	6.1	
	n	61	42	

<sup>a</sup>Shortness of breath; cough; chest tightness; wheeze; phlegm; fevers; generalized aches.<sup>b</sup>Probability that means are the same for those with and for those without symptoms.

highly plausible in a setting where workers experience such high prevalences of frequent eye and throat irritation that improve when away from work.

The lack of any clear interstitial abnormalities on radiographic evaluation of these active flock workers is not surprising. In fact, among clinically-diagnosed cases from this plant, nearly one half have presented with normal chest radiographs; and, in mild cases, radiographic abnormalities may be subtle, even on high-resolution computerized tomograph (HRCT) scans [Kern et al., 1998, 2000; Eschenbacher et al. 1999]. Limited sensitivity of standard

chest radiographs and HRCT scans has been similarly demonstrated in hypersensitivity pneumonitis [Lynch et al., 1992].

Despite relatively high participation rate, this cross-sectional epidemiologic study was limited by low power, resulting from the relatively small size of the workforce available for study at this plant. Another study limitation relates to ascertainment of exposure; no personal dust sampling was done [NIOSH, 1998]. Within departmental categories, individual exposures may vary substantially, but information obtained in the questionnaire did not permit

optimally distinguishing important differences. Air sampling by NIOSH industrial hygienists indicated that flocking rooms and blow-downs were associated with particularly high dust exposures, exceeding the OSHA permissible exposure limit for respirable particulates not otherwise regulated [NIOSH, 1998; Burkhart et al., 1999]. However, our questionnaire ascertainment of blow-down and flock room exposures were, in retrospect, admittedly crude. We could not distinguish between workers with frequent blow-down exposure and those with rare blow-down exposure, and we could not distinguish workers who worked specifically in the flocking rooms from those who worked elsewhere on the flocking range.

Another possible limitation of this study results from a healthy worker survivor effect [Arrighi and Hertz-Picciotto, 1994] and transfer effect [Eisen, 1995] common to cross-sectional studies. These effects are typically associated with a tendency for workers who are most highly exposed (and most likely to be adversely affected by exposure) to either leave the workforce or to transfer to a job with less exposure. In fact, before our survey of current workers was carried out, workers already diagnosed with ILD were no longer working at the plant [Kern et al., 1998; NIOSH, 1998].

The major overall impact of the study limitations discussed above would probably be a relative underestimation of associations between adverse health effects and departmental category or other factors (e.g., flocking range work, blow-down exposure, etc.). Nevertheless, our survey contributes to other evidence that nylon flock-associated dust is likely responsible for excess morbidity among workers at this plant.

Risk factors evident in the results of this epidemiologic investigation have implications for prevention. Exposure to flock-associated dust should be reduced and controlled by severely limiting use of blow-downs, filtering exhaust streams of process cyclones used to pneumatically transport loose flock within the plant, controlling dust in flocking rooms and at bagging stations, administratively restricting work hours, and requiring effective personal respiratory protection in high dust areas. Based on findings of microscopic examination of respirable dust and nylon flock from this plant [Burkhart et al., 1999], it seems likely that more attention to careful sharpening, honing, and alignment of the blades in the rotary cutters may also prove effective as a strategy to limit generation of respirable nylon fragments during flock production.

Continuous nylon filaments are commercially manufactured with diameters as small as about 10  $\mu\text{m}$ . Because even very short segments of such filaments would not be considered respirable in size, little relevant research has been done to assess respiratory toxicity of nylon particles and employers in the flock industry have not been concerned with potential respiratory toxicity of nylon. However, respirable nylon particles—some of them elongated in

shape and exceeding 5, 10, and even 15  $\mu\text{m}$  in length—were found to be present in respirable dust samples collected from the air in the Rhode Island plant, apparently generated during cutting and/or subsequent processing of nylon flock [Burkhart et al., 1999].

Animal studies have clearly documented respiratory toxicity associated with nylon particles. Respirable fragments of nylon, even without flock finish, cause a very intense acute inflammatory response following a one-time instillation into rat lungs [Porter et al., 1999]. Guinea pigs inhalationally exposed several times a day to pulverized nylon for 325 days have developed ILD [Pimentel et al., 1975]. From these animal studies, alone, it is clear that airborne nylon particulate has substantial potential respiratory toxicity when inhaled. In addition, although not providing detailed exposure or work process information, one published paper has reported nylon fiber inclusions within lesions seen in lung biopsies of two individuals with interstitial lung disease who had worked in the textile industry for 10 or more years [Pimentel et al., 1975]. Clinical pathologists have not observed fibers in routine microscopic evaluations of biopsy tissue from nylon flock workers with interstitial lung disease [Boag et al., 1999; Eschenbacher et al., 1999].

Nylon is not the only component of airborne respirable dust collected in the Rhode Island plant. In animal studies, respirable dust collected from the air in the flocking rooms and flock screening rooms at the plant appeared to be even more toxic than nylon fragments alone [Porter et al., 1999]. Moreover, when airborne dust from the Rhode Island plant was washed in water, the extract also induced substantial acute inflammatory response following intratracheal instillation. These findings provide reason to be concerned about potential respiratory toxicity not only of the nylon fragments themselves, but also of flock finish carried on the surface of these fragments or broken off the surface of flock during processing. Tannic acid is one major component of flock finish. Condensed tannins have been shown to influence alveolar macrophage function [Rohrbach, 1994], to induce epithelial cell changes [Cloutier and Rohrbach, 1986], and to cause an inflammatory response when inhaled [Kilburn et al., 1973]. Inhaled tannin-containing dusts may, therefore, play a role in human disease [Lauque et al., 1988]. However, the hydrolyzable tannins used in flock finish may not have toxicity equivalent to condensed tannins, and no epidemiological studies adequate to document adverse effects of tannin inhalation have been done [Lacey et al., 1994]. Less evidence exists regarding potential respiratory toxicity of potato starch, another component of flock finish. Occupational exposure to dust in the potato starch industry has been associated with asthmatic effects in workers; microbial contaminants and/or potato proteins are suspected specific causative agents [Hollander et al., 1994]. No relevant published information is available on the fatty alcohol

component of flock finish used at the Rhode Island plant. The desiccant powder, a silicate sometimes mixed in with the flock, seems an unlikely cause because there was no evidence of mineral particulate in lung biopsies of workers from this plant [Boag et al., 1999; Eschenbacher et al., 1999]. Moreover, this powder is apparently not used at all the flock plants where clinical cases have occurred.

Based upon the total evidence, we conclude that respirable dust generated during nylon flock production and processing, including respirable nylon fragments, represents the most likely cause of the excess respiratory morbidity we observed and the ILD cases reported by others among workers at this plant [Kern et al., 1998, 2000]. Strategies to protect the health of workers employed at the Rhode Island plant should emphasize primary prevention of illness through reduction of worker exposure to dust at the plant by a combination of work practice and process changes, engineering and administrative controls, and (as needed) personal protective equipment. In addition, an appropriately designed medical screening program could prove useful for secondary prevention through early detection of disease in individual workers, permitting appropriate action to reduce the risk of clinically significant occupational disease in individuals with mild symptoms before objective clinical test results become abnormal. Screening data can underpin ongoing surveillance efforts to identify risk factors and document efficacy of exposure controls.

Ongoing epidemiological studies now being conducted by NIOSH investigators at several other flock plants should provide a better understanding of the quantitative association between respiratory morbidity and flock-associated dust, and animal inhalation studies now being planned should provide a more definitive understanding of the toxicity of respirable nylon particulate.

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## REFERENCES

- American Thoracic Society. 1995a. Standardization of spirometry—1994 update. *Am J Respir Crit Care Med* 152:1107–1136.
- American Thoracic Society. 1995b. Single-breath carbon monoxide diffusing capacity (transfer factor)—recommendations for a standard technique. *Am J Respir Crit Care Med* 152:2185–2198.
- Arrighi HM, Hertz-Picciotto I. 1994. The evolving concept of the healthy worker survivor effect. *Epidemiol* 5:189–196.
- Boag AH, Colby TV, Fraire AE, Kuhn C III, Roggli VL, Travis WD, Vallyathan V. 1999. The pathology of interstitial lung disease in nylon flock workers. *Am J Surg Pathol* 23:1539–1545.
- Burkhart J, Piacitelli C, Schwegler-Berry D, Jones W. 1999. Environmental study of nylon flocking process. *J Toxicol Environ Health, Part A*, 57:1–23.
- Cloutier MM, Rohrbach MS. 1986. Effects of endotoxin and tannin isolated from cotton bracts on the airway epithelium. *Am Rev Respir Dis* 134:1158–1162.
- Davidoff F. New disease, old story. 1998. *Ann Intern Med* 129:327–328.
- Dean AG, Dean JA, Coulombier D, Brendel KA, Smith DC, Burton AH, Dickler RC, Sullivan K, Fagan RF, Arner TG. 1995. Epi Info, version 6: a word processing, database, and statistics program for public health on IBM-compatible microcomputers. Atlanta: Centers for Disease Control and Prevention.
- Eisen E. 1995. Healthy worker effect in morbidity studies. *Med Lav* 86:125–138.
- Eschenbacher WL, Kreiss K, Loughheed MD, Pransky GS, Day B, Castellon RM. 1999. Nylon flock-associated interstitial lung disease: clinical pathology workshop summary. *Am J Respir Crit Care Med* 159:2003–2008.
- Hankinson JL. 1986. Pulmonary function testing in the screening of workers: guidelines for instrumentation, performance, and interpretation. *J Occup Med* 28:1081–1092.
- Hollander A, Heederik D, Kaufmann H. 1994. Acute respiratory effects in the potato processing industry due to a bioaerosol exposure. *Occup Environ Med* 51:73–78.
- ILO. 1980. Guidelines for the use of ILO international classification of x-rays of pneumoconioses, 1980 edition. Geneva, International Labour Office, 1980. Occupational Safety and Health Series, No. 22 (rev.).
- Kern DG, Crausman RS, Durand KTH, Nayer A, Kuhn C. 1998. Nylon flock worker's lung: chronic interstitial lung disease in the nylon flocking industry. *Ann Int Med* 129:261–272.
- Kern DG, Kuhn C, Ely EW, Pransky GS, Mello CJ, Fraire AE, Muller J. 2000. Flock worker's lung: broadening the spectrum of clinicopathology, narrowing the spectrum of suspected etiologies. *Chest* 117:251–259.
- Kilburn KH, Lynn WS, Tres LL, McKenzie WR. 1973. Leukocyte recruitment through airway walls by condensed vegetable tannins and quercetin. *Lab Invest* 28:55–59.
- Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. 1983. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis* 127:725–734.
- Lacey J, Auger P, Eduard W, Norn S, Rohrbach MS, Thorne PS. 1994. Tannins and mycotoxins. *Am J Indus Med* 25:141–144.
- Lauque DE, Hempel SL, Schroeder MA, Hyatt RE, Rohrbach MS. 1988. Evaluation of the contribution of tannin to the acute pulmonary inflammatory response against inhaled cotton mill dust. *Am J Pathol* 133:163–173.
- Loughheed MD, Roos JO, Waddell WR, Mundt PW. 1995. Desquamative interstitial pneumonitis and diffuse alveolar damage in textile workers. *Chest* 108:1196–1200.
- Lynch DA, Rose CS, Way D, King TE Jr. 1992. Hypersensitivity pneumonitis: sensitivity of high-resolution CT in a population-based study. *Am J Roentgenol* 159:469–472.
- Miller A, Thornton JC, Warsaw R, Anderson H, Teirstein AS, Selikoff IJ. 1983. Single breath diffusing capacity in a representative sample of the population of Michigan, a large industrial state. *Am Rev Respir Dis* 127:270–277.

- NIOSH. 1998. Health hazard evaluation report: Microfibres, Inc., Pawtucket, Rhode Island. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 96-0093.
- Pimentel JC, Avila R, Lourenco AG. 1975. Respiratory disease caused by synthetic fibers: a new occupational disease. *Thorax* 30:204-219.
- Porter DW, Castranova V, Robinson VA, Hubbs AF, Mercer RR, Scabilloni J, Goldsmith T, Schwegler-Berry D, Battelli L, Washko R, Burkhart J, Piacitelli C, Whitmer M, Jones W. 1999. Acute inflammatory reaction in rats after intratracheal instillation of material collected from a nylon flocking plant. *J Toxicol Environ Health, Part A*, 57:25-45.
- Redlich CA. 1996. Pulmonary fibrosis and interstitial lung diseases. In: Harber P, Schenker MB, Balmes JR, editors. *Occupational and environmental respiratory disease*. St. Louis, MO: Mosby-Yearbook, Inc., p 216-227.
- Rohrbach MS. 1994. Modulation of macrophage function by condensed tannin. *Am J Indus Med* 25:97-99.