AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 46:104–111 (2004)

Spray-Painting and Chronic Airways Obstruction

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Background *The aim was to investigate the respiratory response of HDI-based paint aerosol within the context of the protection afforded by current exposure guidelines.*
Methods *A cross-sectional study of 240 painters spraying polyurethane enamels was undertaken at four aircraft maintenance plants. Questionnaire and spirometric data were related to gravimetric measures of cumulative total and respirable paint aerosol (TPA and RPA) and estimated isocyanate in total and respirable aerosols (TIA and RIA).*
Results *Average cumulative exposures in mg/m^3-years ± SD were 159.0 ± 115.2 TPA, 19.1 ± 13.8 RPA, 15.8 ± 11.5 TIA, and 1.9 ± 1.4 RIA. After adjusting for smoking and asthma symptoms, higher exposures were associated with statistically significant reduction in expiratory flowrates. Significant smoking-related reductions were also observed, without exposure interactions.*
Conclusions *These results suggest important respiratory effects from exposures to spray paint aerosols at levels generally in compliance with existing standards for otherwise unregulated particulates and for the isocyanate component of the paint.* Am. J. Ind. Med. 46:104–111, 2004. *© 2004 Wiley-Liss, Inc.*

KEY WORDS: isocyanate exposure; spray-paint; cross-sectional; lung function; chronic obstructive pulmonary disease

INTRODUCTION

Spray painting contaminates workplace air with an aerosol of inhalable paint ingredients in the form of particles and vapors. Spray painters therefore work in a potentially hazardous environment where the level of risk depends on the intensity of exposure and the toxicities of the materials used. The preferred coatings for the surface of aircraft and automobiles are 1,6-hexamethylene diisocyanate (HDI)-based polyurethane enamels, which are resistant to abrasion and ultraviolet radiation. These high-performance industrial paints are usually solvent-based [U.S. Department of Health and Human Services, 1984], often ‘‘two-part catalyzed,’’ and contain di- or poly-isocyanates.

The di- and poly-isocyanates have complex respiratory toxicity. Toxic effects include respiratory irritation, asthma, hypersensitivity pneumonitis, and asymptomatic accelerated loss of lung function [Musk et al., 1988]. Some studies show that even exposure to relatively low concentrations of isocyanates is associated with decreased lung function [Diem et al., 1982; Tornling et al., 1990]. Generally, isocyanate-induced occupational asthma can occur in as many as 5–10% of exposed workers [Malo et al., 1999]. In susceptible individuals, occupational asthma is diagnosed on the basis of

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Contract grant sponsor: AAMC-CDC; Contract grant number: MM0056-02/02; Contract grant sponsor: DOD.

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Accepted 10 May 2004
DOI 10.1002/ajim.20054. Published online in Wiley InterScience (www.interscience.wiley.com)

exposure-related symptoms and temporary reductions of lung function in response to exposures. Accelerated loss of lung function related to isocyanate exposure is initially asymptomatic, not related to the presence of isocyanate asthma, and susceptibility appears to be general [Diem et al., 1982].

In painters, occupational exposure to isocyanates is associated with increased occurrence of respiratory health problems, mainly asthma [Seguin et al., 1987]. However, paint aerosol is a heterogeneous material presenting a mixed exposure potential. Exposure standards or guidelines apply to certain specific paint aerosol components, such as specific solvents, pigments, or other additives. The most commonly used isocyanate in polyurethane paint formulations is HDI, and more specifically its trimeric oligomers, HDI-biuret and HDI-isocyanurate. The American Conference of Governmental Industrial Hygienists (ACGIH) has adopted a Threshold Limit Value (TLV) of 5 ppb (0.035 mg/m^3) for HDI. The National Institute for Occupational Safety and Health (NIOSH) has established recommended exposure limits (RELs) for HDI of 5 ppb (0.035 mg/m^3) as an 8-hr time-weighted average limit and 20 ppb (0.14 mg/m^3) as a ceiling limit. Occupational exposures to HDI and its trimers are not specifically regulated under federal OSHA standards, though Oregon state OSHA has set guidelines of 0.5 mg/m^3 as a time-weighted average limit, and 1 mg/m^3 as a short-term exposure limit for HDI trimers. Currently, there is little quantitative exposure-response data on which to support more stringent guidelines.

The present study was conducted at four aircraft maintenance plants. The aim was to investigate respiratory response to HDI-based paint aerosol in the context of the protection afforded by currently applicable exposure guidelines; a specific focus was on lung function. Lung function, questionnaire, and environmental data were collected in 1991, in what was to be the initial phase of a planned longitudinal study. Military operations, and the reductions in force following the Gulf War, rendered the planned follow-up unfeasible and hence the cross-sectional results are presented only.

MATERIALS AND METHODS

Population

Spray-painters at four US Air Force aircraft maintenance facilities (Air Logistic Centers) were recruited for this cross-sectional health survey. These facilities had large hangars where assorted maintenance activities were conducted by 576 workers from a variety of trades that included a large number of spray-painters. We asked all spray-painters to participate in the survey, and a total of 240 spray-painters signed the consent form and completed the questionnaire and lung function test.

Pulmonary Function Testing and Questionnaire

Pulmonary function testing and a medical, smoking, and occupational questionnaire that included time in spray painting activities and current use of respiratory protection (air-purifying cartridge respirators and air-supplied respirators) were administered by trained personnel (NIOSH Spirometry Course # 002 presented by one of the investigators, HWG) using a computerized system designed to collect such data from remote facilities [Glindmeyer and Lissak, 1984]. This system employs a computer with a resident questionnaire and an on-line 8-L dry rolling-seal volumetric spirometer. Validation of the accuracy of this spirometric system [Nelson et al., 1990] has shown that it complied with ATS spirometric test criteria [Ferris, 1978; Gardner et al., 1987]. A 3-L calibrating syringe was used for daily calibration. Testing was conducted in the standing position with nose clips and height was measured without shoes. Spirometric test results were taken from at least three acceptable tests with good initial effort (extrapolated volume less than 5% of the FVC, with distinct superimposable forced expiratory flow-volume curves) [Glindmeyer et al., 1987], good continued effort for at least 7 s, and repeatable FEV_1 and FVC values within 5% or 100 ml. The analyses used the largest FEV_1 and FVC, the FEV_1/FVC computed from the largest values, and the forced expired flow from 25 to 75% of the FVC (FEF_{25-75}) computed from the test with the largest sum of FEV_1 and FVC. Quality assurance [Glindmeyer et al., 1987] of the spirometric tests was done by one of the investigators (HWG).

Percent predicted lung function values were computed using race-specific (Caucasian and African-American) reference values estimated from equations that included age and age squared term. The reference equations were developed from blue-collar never-smokers who denied occupational inhalant exposures, and whose lung function was tested on the same type of equipment with the same data reduction and quality assurance procedures as was used in the present study [Glindmeyer et al., 1995].

We also utilized the percent predicted values noted above to determine the percentage of workers falling into the following categories of COPD as defined by the GOLD committee [Pauwels et al., 2001] and updated in 2003 [Fabbri and Hurd, 2003].

- Stage 0 (at risk) = chronic symptoms (cough, sputum production) with normal spirometry;
- Stage I (mild COPD) = $FEV_1/FVC < 70\%$, $FEV_1 \geq 80\%$ predicted with or without chronic symptoms;
- Stage II (moderate COPD) = $FEV_1/FVC < 70\%$, $50\% \leq FEV_1 < 80\%$ predicted with or without chronic symptoms;

- Stage III (severe COPD) = $FEV_1/FVC < 70\%$, $30\% \leq FEV_1 < 50\%$ predicted with or without chronic symptoms; and
- Stage IV (very severe COPD) = $FEV_1/FVC < 70\%$, $FEV_1 < 30\%$ predicted.

Pack-years, defined as the number of packs of cigarettes smoked per day times number of years smoked, was computed from questionnaire data for all current and ex-cigarette smokers. For 17 subjects with missing pack-years, the average estimate of pack-years for a given age, race, and sex group was substituted.

Exposure Estimates

Each plant was visited twice for exposure monitoring, with each visit being conducted over a period of about 1 week. Monitoring activities consisted of personal sampling of overspray aerosol during application of polyurethane paint. Measured exposures thus represent task-based time-weighted averages (TWA), rather than shift-based (8-hr) TWA. During the sampling visits, data were collected on various factors of interest for exposure characterization, including the type of spray equipment utilized, aircraft type and plane parts being painted, type of paint and or primer applied, and type and use of respiratory protective equipment.

Total and respirable aerosol samples were collected via personal monitoring using pre-weighed 25-mm Teflon filters, 1 μm pore size (Millipore FA), contained in 3-piece polystyrene cassettes. Total aerosol samples were collected by operating the filter cassette in the open-face mode at a nominal flow rate of 2 L/min. Respirable samples utilized the same filter cassette type, but were preceded by a cyclone pre-separator (SKC, Model 225-01-01) to remove the non-respirable fraction. These samples were collected at a flow rate of 1.9 L/min. The total and respirable filter sampling devices were mounted on each side of the worker's upper chest, in the breathing zone.

After collection, the filter samples were reweighed following humidity conditioning over saturated sodium dichromate and the total or respirable particulate concentration determined. Subsequently, the "worst case" isocyanate group concentration in each sample was estimated using an algorithm that determines the expected percentage of isocyanate group in the dry paint aerosol based on the composition of the paint as determined from the Material Safety Data Sheets and paint formula for the actual paint in use at the time of the sampling. The algorithm is as follows:

$$\%\,\text{Isocyanate group} = \left[\frac{(w_a)(S_a)(\rho_a)}{(w_p)(S_p)(\rho_p) + (w_a)(S_a)(\rho_a)}\right] \times f_{NCO} \times 100$$

where: w_a = weighting factor for number of parts activator (isocyanate component) used in the paint formulation

- S_a = % solids by weight of the activator
- ρ_a = density of the activator
- S_p = % solids by weight of the polyol component
- ρ_p = density of the polyol component
- w_p = weighting factor for number of parts polyol
- f_{NCO} = (# of isocyanate groups) (42 g/mole isocyanate group)/(molecular weight of the isocyanate compound).

This calculation makes the following assumptions: the non-solids content of the polyol and activator components completely volatilizes from the collected sample; the isocyanate is the only solids component in the activator; and the paint is mixed in the proportions indicated by the instructions.

Each plant had paint hangars in which entire aircraft or parts on the aircraft were painted, as well as more traditional paint booths for painting small parts detached from the aircraft. Samples were collected at each plant from workers in both types of painting operation. Two-way analysis of variance was performed on the log-transformed exposure data using plant and operation as the treatment variables in order to ascertain whether there were significant differences between the plants and operations and to evaluate the merits of various levels of detail in potential exposure groupings [Heederik and Attfield, 2000; Werner and Attfield, 2000]. There were no statistically significant differences in either total or respirable aerosol exposure between hangar and booth painting operations nor were there any significant interactions between plant and operation. Between the plants, there was no significant difference in respirable aerosol exposure levels; however, there was a significant difference in total aerosol exposure ($P = 0.034$, see Table I for mean values). Exposures within each plant were therefore averaged across all hangar and booth operations, but plant was maintained as a separate exposure correlate. Here, the arithmetic mean was calculated and used as the exposure measure for each plant rather than the geometric mean. It has become generally accepted that the arithmetic mean is preferable to the geometric mean in calculating exposure dose for log-normally distributed exposure profiles in that the body integrates varying exposure in a linear fashion, and health effects models that are linear in nature are biased when using geometric mean exposure [Seixas et al., 1988; Crump, 1998]. Plant exposure was multiplied by each individual's time in spray-painting (determined by questionnaire) to estimate individual cumulative aerosol exposure for the study subjects at their respective plants.

For each study subject, cumulative exposures in total paint aerosol (TPA), respirable paint aerosol (RPA), estimated isocyanate in total aerosol (TIA), and estimated isocyanate in respirable aerosol (RIA) were computed by

TABLE I. Personal Exposure Monitoring Results for Spray Painting Activities

		% Isocyanate group in paint aerosol	Total aerosol [TPA] (mg/m^3)		Isocyanate Group in total aerosol [TIA] (mg/m^3)		Respirable aerosol [RPA] (mg/m^3)		Isocyanate group in respirable aerosol [RIA] (mg/m^3)	
Facility	**N**	**Mean ± SE**	**Mean ± SE**	**Geom. mean/[a]GSD**	**Mean ± SE**	**Geom. Mean/GSD**	**Mean ± SE**	**Geom. Mean/GSD**	**Mean ± SE**	**Geom. Mean/GSD**
Plant 1	43	11.8 ± 0.1	8.5 ± 0.8	6.8/2.2	1.0 ± 0.1	0.80/2.3	1.0 ± 0.1	0.6/4.3	0.12 ± 0.02	0.07/4.4
Plant 2	43	12.0 ± 0.2	14.5 ± 1.5	9.8/2.9	1.7 ± 0.2	1.2/2.9	1.4 ± 0.2	1.0/2.5	0.17 ± 0.02	0.12/2.4
Plant 3	38	8.7 ± 0.4	9.7 ± 1.2	7.2/2.3	0.92 ± 0.15	0.59/2.7	1.6 ± 0.4	0.6/5.7	0.15 ± 0.05	0.05/6.5
Plant 4	28	11.3 ± 0.0	6.7 ± 0.9	5.3/2.1	0.76 ± 0.10	0.60/2.1	1.8 ± 0.3	0.8/6.9	0.20 ± 0.03	0.09/6.9
Overall	152	11.0 ± 0.2	10.1 ±0.6	7.3/2.5	1.2 ± 0.1	0.79/2.6	1.4 ± 0.1	0.8/4.5	0.16 ± 0.01	0.08/4.8

[a] Geometric standard deviation.

combining years spent in painting activities with the concentration value for the respective contaminant, taken as the arithmetic mean averaged across the plant in which the subject worked. The number of years spent in painting activities was obtained from questionnaire response.

All data were collected in compliance with Tulane University's Institutional Review Board human subjects criteria.

Statistical Methods

We used the multiple linear regression analysis to relate percent predicted FEV_1, FVC, FEV_1/FVC, and FEF_{25-75} to each exposure variable, while adjusting for race, smoking status (never smoker, ex-smoker, current smoker), pack-years, current use of respiratory protection, and the symptom complex of shortness of breath with wheeze. Exposure variables investigated by the regression analysis were cumulative exposure indices (TPA, RPA, TIA, RIA) and years of spraying (while taking into account plant differences). Potential confounding variables were selected out of the regression model if they were not statistically significant at the $P < 0.05$ probability level and did not significantly alter the association between pulmonary function and exposure. Because age was significantly correlated with cumulative exposure indices and years of spray painting, adjustment for age was done by using percent predicted lung function values [Glindmeyer et al., 1995].

Furthermore, we used multiple logistic regression [Kleinbaum et al., 1998] to relate the prevalence of chronic obstructive lung disease to exposure variables, while adjusting for the confounding variables. The dichotomous COPD outcome variables reflected increasing severity of COPD as defined above. The exposure and confounding variables included in the regression model were the same as those used with the lung function outcomes described above.

The symptom complex of shortness of breath with wheeze, used as a surrogate variable for asthma, was adjusted for in all the regression models.

RESULTS

The cumulative exposure estimates were based on a total of 152 sets of personal exposure monitoring samples collected at the four plants and summarized in Table I. The data appeared to be log-normally distributed. The overall geometric means/geometric standard deviations (GSD) were 7.3 mg/m^3/2.5 and 0.8 mg/m^3/4.5, for total and respirable aerosol, respectively. The overall arithmetic means ± stanstandard errors (SE) were 10.1 mg/m^3 ± 0.6 and 1.4 mg/m^3 ± 0.1, for total and respirable aerosol, respectively. The collected samples contained an average ± SE estimated isocyanate group percentage of 11.0 ± 0.2%, with arithmetic means ± SE for isocyanate group in total aerosol and isocyanate group in respirable aerosol of 1.2 mg/m^3 ± 0.08 and 0.16 mg/m^3 ± 0.01, respectively. Plant 2 had the highest exposures to total and respirable aerosol, % isocyanate, and isocyanate group in total aerosol.

Table II presents demographic and cumulative exposure data by plant. There were 240 painters of mean age of 40.3 years, of whom approximately 93% were men and 22% were African-Americans. Approximately 30% were never smokers, 23% ex-smokers, and 47% current smokers. The mean years spray-painting for the study population was 10.3, ranging from 8.5 to 11.0 years across plants. The results show that the workers in Plant 2 had highest cumulative exposure as well as highest measurements of exposure in comparison to the other plants.

Table III shows, for increasing levels of cumulative respirable aerosols (levels are based on approximate population quartiles), mean age, mean lung function (in percent of predicted value ± standard error), percentages in COPD

TABLE II. Demographic, Smoking, and Exposure Statistics, by Plant

	Plant number				Total
Characteristic	**1**	**2**	**3**	**4**	
No. of workers	65	108	41	26	240
Mean age ± SD	38.5 ± 8.5	43.0 ± 9.4	38.5 ± 8.0	36.1 ± 8.5	40.3 ± 9.2
% Male	92.3	91.7	95.1	96.2	92.9
% African American	33.9	20.4	19.5	0	21.7
Smoking status % or pack-years					
Never smoker	30.8	30.6	34.2	15.4	29.6
Ex smoker	20.0	31.5	9.8	15.4	22.9
Current smoker	49.2	38.0	56.1	69.2	47.5
Pack-years[a] ± SD	15.9 ± 23.5	16.5 ± 18.1	17.0 ± 20.3	13.3 ± 16.0	16.2 ± 19.9
Exposure years or mg/m^3-years					
Spray-painting ± SD	10.9 ± 8.2	11.0 ± 8.0	8.7 ± 5.2	8.5 ± 5.4	10.3 ± 7.4
Cum. TPA ± SD	91.9 ± 69.4	159.0 ± 115.2	84.6 ± 50.1	56.9 ± 36.1	117.0 ± 96.6
Cum. TIA ± SD	10.9 ± 8.2	19.1 ± 13.8	7.3 ± 4.3	6.4 ± 4.1	13.5 ± 11.7
Cum. RPA ± SD	11.1 ± 8.4	15.8 ± 11.5	13.8 ± 8.1	15.0 ± 9.5	14.1 ± 10.1
Cum. RIA ± SD	1.3 ± 1.0	1.9 ± 1.4	1.2 ± 0.7	1.7 ± 1.1	1.6 ± 1.2

[a] Missing pack years: plant 1 (5 subjects), plant 2 (1 subject), plant 4 (11 subjects).

(GOLD) categories, and percent with shortness of breath and wheeze. The association between increasing age and increasing cumulative exposure is shown as expected, and there appears to be an association between increasing exposure and both reduced lung function, elevated levels of COPD, and increasing percentages of workers reporting symptoms.

Table IV presents results from the multiple linear regression models with percent predicted lung function as an outcome variable. Regression coefficients, their SE and two-sided significance level are reported for each independent exposure variable. The effect of current versus never smoking was observed for all lung function tests, and was significant for FEV$_1$, FEV$_1$/FVC, and FEF$_{25-75}$. Because we used the percent predicted lung function, neither age, sex, or race were statistically significant nor had they an effect on the estimated regression coefficients for exposure, and were thus selected out of the regression models. The estimated coefficients for smoking status were similar (within 10%) regardless of the exposure variable, and are presented only for Model I that included total particulate as an exposure variable. None of the regressions were significant for those having, vs. those lacking, the symptom complex of shortness of breath with wheeze, which might indicate asthma. The only significant effect was observed for FVC, and this had no effect on the significance of exposure. The pack-years variable was significant only for FEF$_{25-75}$, while the exposure indices remained significant. Interactions between smoking status and exposure indices were not statistically significant. All of the four cumulative exposure indices were significantly associated with decreased FEV$_1$, FEV$_1$/FVC, and FEF$_{25-75}$. Current use of respiratory protection was not associated with lung function (results not shown). Years spray painting was associated with decreased FEV$_1$ and FEF$_{25-75}$ while the plant effect was adjusted for. In this analysis, Plant 2 was used as a comparison group because it had the largest number of workers and highest exposures.

Although there was some increased trend in the prevalence of COPD in relation to cumulative respirable aerosol exposure (see Table III), the multiple logistic regression relating the probability of COPD to the cumulative exposure or years of spray painting failed to detect significant associations, for any severity of COPD (results not shown). However, smoking status and pack-years were always statistically significant. No significant differences in the probability of COPD were found between plants, nor was there a significant effect of race, or current use of respiratory protection. Interactions between smoking categories and exposure indices were investigated, with no significance observed.

DISCUSSION

At the time this study was conducted, there was essentially exclusive use of polyurethane paints on aircraft at the participating plants. The earliest documented date of use of polyurethane paints at the plants was 1981, although it is likely that these paints were used with increasing frequency sometime prior to that date. The study population had on average about 10 years of continuing exposure to isocyanate-containing paint overspray, and many of the study subjects

TABLE III. Age, Smoking, Lung Function, COPD Risk, and Symptoms, by Cumulative Respirable Paint Aerosol and Isocyanate

Respirable aerosol level (mg/m^3-years)	N	Mean age ± SE	% Curr smoker	Mean FEV_1% Pred ± SE	Mean FVC % Pred ± SE	Mean FEV_1/FVC % Pred ± SE	Mean FEF25–75% Pred ± SE	COPD categories (%) Stage 0 at risk	COPD categories (%) Stage I mild	COPD categories (%) Stage II + mod or Sev	SOB & wheeze (%)
Respirable Paint Aerosol (RPA)											
0.5–5.8	66	37.0 ± 1.1	51.2	95.0 ± 2.1	97.3 ± 1.7	97.3 ± 1.0	90.2 ± 3.8	6.1	6.1	3.0	4.6
6.1–14.1	58	38.3 ± 1.1	46.6	94.5 ± 1.6	96.3 ± 1.5	98.1 ±0.8	91.0 ± 2.9	8.6	5.2	1.7	1.7
14.2–20.5	56	40.7 ± 1.1	42.9	92.5 ± 1.7	96.7 ± 1.8	95.7 ± 1.2	84.1 ±3.5	16.1	14.3	10.7	5.4
21.1–57.6	60	45.4 ± 1.2	48.3	90.6 ± 1.7	94.0 ± 1.7	96.3 ± 0.8	81.5 ± 3.5	11.7	10.0	1.7	8.3
Respirable isocyanate aerosol (RIA)											
0.1–0.7	66	37.0 ± 1.1	51.5	95.0 ± 2.1	97.3 ± 1.7	97.3 ± 1.0	90.3 ± 3.8	6.1	6.1	3.0	4.6
0.7–1.4	58	38.1 ±1.1	50.0	95.2 ± 1.6	97.8 ± 1.5	97.3 ± 0.8	89.7 ± 3.1	10.3	6.9	3.5	3.5
1.4–2.4	55	40.0 ± 1.1	41.8	91.3 ± 1.6	94.2 ± 1.6	97.0 ± 1.0	85.5 ± 3.3	14.6	12.7	7.3	3.6
2.4–6.9	61	46.2 ± 1.2	45.9	90.9 ± 1.8	94.9 ± 1.7	95.9 ± 1.0	81.6 ± 3.6	11.5	9.8	3.3	8.2

had exclusive exposure to polyurethane paint during their tenure at the plants.

Measured exposures to paint aerosols in this study were generally in compliance with federal OSHA standards for particulates not otherwise regulated [OSHA PEL = 15 mg/m^3 total particles; 5 mg/m^3 respirable particles]. However, in 86% of samples, measures of estimated isocyanate group in total aerosol were above the short-term Oregon state OSHA standard for HDI trimers of 1 mg/m^3 (0.26 mg/m^3 as isocyanate group). Carlton and England [2000], measured HDI monomer and oligomers during spray-painting in some of the same facilities investigated in the study described herein which was originally conducted in 1991. This later study showed HDI monomer levels to be low compared to exposure limits, with averages being 0.1 and 2.4 ppb for 8-hr TWA and task (spray-painting) TWA, respectively. While peak HDI trimer levels measured in 2000 were also frequently higher than the short-term Oregon state OSHA standard, 8-hr time-weighted levels were almost all within the 0.5 mg/m^3 TWA standard. Carlton et al., used a technique similar to that described in this paper for estimating isocyanate, based on the paint formulation (total aerosol mass method or TAMM), and also used a specific analytic technique (ISOCHEK® sampler) not available at the time of our 1991 study. In this later study, 54 TAMM samples and 56 ISOCHEK samples yielded respective mean concentrations of 3.75 and 2.27 mg/m^3 for HDI trimer, with ranges of 0.22 to 17.3 and <0.01 to 5.77 mg/m^3, respectively. These mean values, when converted to isocyanate-group concentrations, are equal to 1.0 and 0.6 mg/m^3, respectively. These values compare favorably to our observed overall mean of 1.2 mg/m^3 for estimated isocyanate group in total aerosol.

Our finding of exposure-related adverse effects on lung function suggests that the current standards for spray painting aerosols exposure levels may not be protective, particularly in light of the fact that actual worker exposures were reduced by frequent use of respiratory protective equipment. Furthermore, the assigned cumulative exposures, based on measurements during spray-painting tasks only, rather than full shift measurements, may be overestimated. However, as we were unable to obtain historical data on the frequency, rate, or duration of actual aircraft painting tasks prior to the study, or on changes in engineering controls and work practices, the exposures might also be underestimated.

Statistically significant reductions in lung function were demonstrated using continuous outcome variables for lung function. These variables remained significant after adjustment for asthma-like respiratory symptoms, which in the absence of information on the presence of work-related asthma, represented diagnosed and undiagnosed asthma. However, because post-bronchodilator spirometry was not conducted, some of the reduction in lung function may have been due to bronchospasm. This effect was, however, mini-

TABLE IV. Effects of Smoking and Exposure Type on % Predicted Lung Function

Model	Smoking[a] and cumulative exposure	Regression coefficients for % predicted lung function ($\beta \pm$ SE)			
		FEV1	FVC	FEV1/FVC	FEF25−75
I	Current vs. never	−5.10 ± 2.06[b]	−2.07 ± 1.90	−3.37 ± 1.10[c]	−10.83 ± 3.95[c]
	Ex-smoker vs. never	1.02 ± 2.50	1.09 ± 2.30	−0.02 ± 1.33	1.89 ± 4.78
	TPA (mg/m^3-years)	−0.03 ± 0.01[c]	−0.01 ± 0.01	−0.01 ± 0.005[b]	−0.06 ± 0.02[c]
II	RPA (mg/m^3-years)	−0.22 ± 0.09[b]	−0.13 ± 0.08	−0.10 ± 0.05[b]	−0.50 ± 0.17[c]
III	TIA (mg/m^3-years)	−0.21 ± 0.08[c]	−0.11 ± 0.07	−0.10 ± 0.04[b]	−0.51 ± 0.15[c]
IV	RIA (mg/m^3-years)	−2.00 ± 0.76[c]	−1.20 ± 0.70	−0.83 ± 0.41[b]	−4.41 ± 1.46[c]
V	Years of spray painting	−0.31 ± 0.12[b]	−0.20 ± 0.11	−0.12 ± 0.07[d]	−0.66 ± 0.23[c]
	Plant 1 vs. plant 2	−0.17 ± 2.17	−0.26 ± 1.99	−0.33 ± 1.16	0.73 ± 4.15
	Plant 3 vs. plant 2	2.71 ± 2.57	2.06 ± 2.35	0.39 ± 1.37	4.88 ± 4.92
	Plant 4 vs. plant 2	0.59 ± 3.06	−2.04 ± 2.80	2.61 ± 1.63	10.20 ± 5.86

[a] Regression coefficients for smoking status are presented only for the first model (I). The estimates for smoking were similar, or showed a similar pattern, when the other exposure variables were included in the models (II−V) instead of total particulate.
[b] Significant at probability level $P < 0.05$.
[c] Significant at $P < 0.01$.
[d] Significant at $P < 0.10$.

mized in the data analysis by adjusting for symptoms of shortness of breath with wheeze, which did not alter the significance of the exposure effect.

For the dichotomous (present/absent) outcome variables of COPD of increasing severity, there was some exposure-response trend with cumulative exposure. However, this trend dropped off in the last exposure category, suggesting that there may be healthy worker survivor effect present in those with highest exposure.

In models relating spirometric health outcomes to retrospective exposures, the modeling is complicated by the fact that cumulative exposure, age and pack-years of smoking are all time-related, and are thus potentially collinear. In this analysis, correlations between the exposure indices and age, as well as between the number of years spray-painting and age, ranged from 0.42 to 0.50, and all were statistically significant (at $P < 0.001$ probability level). In this situation, models incorporating both age and exposure can provide imprecise estimates of the model coefficients for the collinear variables. In addition, in small sample sizes of exposed subjects, the effect of age can take on the effect of exposure. To avoid this problem, we chose to incorporate the age adjustment directly into the dependent variable, by using percent predicted spirometric outcomes.

Workers studied in the setting of this research—large government facilities with relatively sophisticated health and safety programs—would be expected to show fewer exposure effects than workers in more typical painting venues, e.g., auto body shops. However, recent and current exposure standards for spray-painting aerosols exposure levels did not appear to be fully protective in our study. This suggests the need for reductions in exposure levels in spray-painting operations, which might be effected through improvements in both engineering controls and paint formulations. It should also be remembered that the measured exposures were to a complex mixture, and adverse effects may have been derived from components other than isocyanates.

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