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# Respiratory Health of Automobile Workers and Exposures to Metal-Working Fluid Aerosols: Lung Spirometry

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**Background** *Despite substantial evidence that workers exposed to metal-working fluids (MWF) have increased respiratory morbidity, the few studies of chronic effects on lung function have not been conclusive.*

**Methods** *Lung spirometry was measured and both current and past exposures to metal-working fluid (MWF) aerosols were estimated in this cross-sectional cohort of 1,811 male automobile workers. Satisfactory exposure data were available for 1,745 (96%): 239 assemblers (never-exposed to MWF), 487 assemblers (previously exposed), 352 machinists currently exposed to straight oils, 441 to soluble oils, and 226 to synthetic fluids. Operations were classified as either grinding or non-grinding machining.*

**Results** *Current exposure was not found to be associated with either forced expiratory volume in 1 second ($FEV_1$) or forced ventilatory capacity (FVC). Nor was past exposure to water-based fluids (soluble or synthetic MWF) related to pulmonary function. Past exposure to straight oils, however, was significantly associated with FVC. This association was more obvious among older workers and among workers who had never transferred from MWF exposed jobs to assembly.*

**Conclusions** *The magnitude of the association between FVC and lifetime exposure to straight MWF was slightly larger than the estimated cigarette effect, suggesting that the impact of an additional year of exposure to 1 mg/$m^3$ of mineral oil particulate in the thoracic particle size range, has the same impact on FVC as smoking one pack per day for one more year.* Am. J. Ind. Med. 39:443–453, 2001. *© 2001 Wiley-Liss, Inc.*

***KEY WORDS: lung function; machinists; metal-working fluids; automobile workers***

## INTRODUCTION

Metal-working operations require various lubricating and cooling fluids. These fluids commonly comprise straight mineral oils, soluble oil emulsions, or aqueous solutions of synthetic chemicals. Substantial aerosols of these fluids are generated during metal-working procedures. Such aerosols are composed of the diverse chemicals in the particular fluid as well as various contaminants: microbial organisms and their respective toxins; thermal degradation products caused by heat generated during the machining process; tramp oil from the machines themselves and the pumps that circulate the fluids; fine metallic particles created during the

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machining operations; and small amounts of dissolved metals from the tools and work pieces.

Health problems have been long recognized in relation to exposures to metal-working fluids (MWF). Oil folliculitis and irritant dermatitis are common among machinists and skin cancers are caused by dermal contact with mineral oils [IARC, 1984]. Other carcinogenic effects have been examined and a growing epidemiologic literature over the last 20 years now provides evidence that occupational exposure to these complex substances can lead to excess risk of cancer of the larynx and several digestive tract cancers [Acquavella et al., 1993; Bardin et al., 1997; Decoufle, 1978; Eisen et al., 1992, 1994; Jarvholm and Lavenius, 1987; Silverstein et al., 1988; Sullivan et al., 1998; Tolbert et al., 1992].

Adverse nonmalignant respiratory effects have also been found in relation to MWF exposure. In the recently published criteria document for MWF, the National Institute of Occupational Safety and Health (NIOSH) based their recommended exposure limit on the human and animal evidence for nonmalignant respiratory effects, rather than cancer [NIOSH, 1997]. The serious respiratory effects that have been attributed to MWF exposure include nonspecific respiratory symptoms, acute impairment of lung function (as measured by change in forced expiratory volume in one second ($FEV_1$ over a workshift)), asthma and hypersensitivity pneumonitis.

Clinical case reports and surveillance data have linked occupational asthma with inhalation of straight and soluble oils, and synthetic fluids [Hendy et al., 1985; Robertson et al., 1988; Rosenman et al., 1994, 1997], and recent epidemiologic studies support the clinical findings [Eisen et al., 1997; Kennedy et al., 1999; Robins et al., 1997]. Several investigators have reported associations between current exposure to specific types of MWF and respiratory symptoms [Ameille et al., 1995; Järvholm, 1982; Järvholm et al., 1982; Kriebel et al., 1997; Massin et al., 1996; Oxhøj et al., 1982]. Acute effects on pulmonary function have also been observed among workers exposed to variety of different types of MWF [Kennedy et al., 1989; Kriebel et al., 1997; Robins et al., 1997]. Recent clusters of hypersensitivity pneumonitis have further focused concerns about microbial contamination of the water-based fluids [Kreiss and Cox-Gaenser, 1997].

Despite this substantial evidence that populations exposed to MWF have increased respiratory morbidity, the few studies of chronic effects on lung function have not been conclusive [Ameille et al., 1995; Järvholm, 1982; Järvholm et al., 1982; Kreibel et al., 1997; Oxhøj et al., 1982, Sprince et al., 1997]. Most of these studies, however, have been relatively small cross-sectional studies with limited information on past exposure.

This report describes results from the largest cross-sectional study of pulmonary function in a working population exposed to metal-working fluids. The findings reported here are part of a larger evaluation of MWF that included a cohort mortality study as well as assessment of current and past MWF exposures, funded by the United Automobile Workers (UAW) Union and the General Motors (GM) Corporation. We have previously reported that nonspecific respiratory symptoms of cough, phlegm, wheeze, chronic bronchitis and chest tightness, as well as physician diagnosed asthma, were associated with exposures to metal-working fluids in this population [Eisen et al., 1997; Greaves et al., 1997]. We have also previously reported that acute decreases in ventilatory function among a subset of these workers were related to the aerosol exposure levels of metal-working fluids [Kennedy et al., 1989]. The central question this study was designed to answer is whether exposure to specific types of MWF is related to loss in baseline pulmonary function as measured cross-sectionally.

## METHODS

***Study subjects.*** Active workers at three GM sites in Michigan (plants I, II, and III) were selected for a cross-sectional survey on the basis of their current department and job. 'Exposed' machinists were identified as those currently working with one of the three major fluid types: straight oils, soluble oils, or synthetic fluids. (The term 'machinist' is used to describe all workers involved in metalworking operations, including drilling, turning, milling, grinding, boring, broaching and lapping.) 'Unexposed' assembly workers were selected from areas at each site that were separate from machining operations. Because fewer than 5% of machinists were females the study was confined to males.

***Exposure.*** Current as well as past exposures were estimated for each subject. Exposure was characterized by type of fluid, operation, and concentration of "thoracic" particulate.[1] Current exposures to aerosols of metal-working fluids were measured for samples of workers performing diverse machining operations, and exposure levels were determined at each site by department for the various machining operation/metal-working fluid combinations [Greaves et al., 1997; Hallock et al., 1994; Woskie et al., 1994]. Assignments of current exposure levels (expressed in mg/m$^3$) were based on workers' departments and jobs at the time of testing. Cumulative exposures [expressed in (mg/m$^3$)-years] were estimated from workers' job records, previous industrial hygiene measurements, and records of plant

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[1] Aerosol exposures were obtained with two-stage Marple cascade impactors using cut-points of 3.5 and 9.8 μm. The "thoracic" fraction corresponded to particles in the two smaller sized fractions. Details of the size-selective sampling methods and results are reported elsewhere [Hallock et al., 1994; Tolbert et al., 1992; Woskie et al., 1994].

operations and production [Greaves et al., 1997; Hallock et al., 1994].

***Lung function measurements.*** Workers' respiratory health was assessed with the American Thoracic Society questionnaire, plus several supplemental questions, and by lung spirometry [Greaves et al., 1997]. Details of the questionnaire have been published [Greaves et al., 1997], and lung function measurements are described below. The questionnaires and spirometry were administered on site by three trained pulmonary technicians. After being checked for accuracy and completeness, the questionnaire and spirometry data were entered into computerized data bases for subsequent analysis. Pre- and post-shift testing was done on Mondays and Fridays for an acute study of a subset of this population [Kennedy et al., 1989].

Spirometry was performed throughout the workday and workweek with computerized Eagle IIS Spirometry Systems (Warren E. Collins, Braintree, MA). Tests were administered by technicians trained and certified through NIOSH-approved courses. The spirometers were calibrated with a 3-L syringe on three occasions during an 8-hour work period: before, midway through, and at the end of a shift. These water-filled spirometers had excellent stability of calibration, showing less than one percent variability over the entire period of data collection.

Each subject's age, height, and race were recorded, as well as information concerning smoking within an hour of testing or a recent upper respiratory infection. Measurements of maximum expiratory flow–volume curves were obtained with the subject seated and with a nose clip. At least three, and usually five, technically acceptable efforts were obtained for each subject [ATS, 1979]; particular attention was paid to ensure that subjects provided a maximal effort, that spirograms were at least 6 seconds in duration, had a prompt acceleration in flow at the beginning of expiration, and no leakage of gas occurred around the mouthpiece.

Analog volume–time recordings of each expiratory maneuver were traced directly to graph paper on a rotating drum. Volume and time were recorded also electronically with a linear transducer connected to the recording arm of the spirometer; the transducer's signals were digitized by a dedicated microprocessor [Black et al., 1980]. Measurements of the forced expiratory volume in 1 second ($FEV_1$), forced vital capacity (FVC), peak expiratory flow (PEF), maximum mid-expiratory flow (MMEF), and flows at 25, 50, and 75% of FVC were obtained from the spirometer's computer output for each expiratory effort, as well as the duration (in seconds) of the expiratory maneuver [Black et al., 1980].

From each individual's spirometry, the three largest, technically satisfactory values for the $FEV_1$ and FVC were identified and used for subsequent analysis. Variability in an individual's spirometry was calculated from the two largest values obtained for the $FEV_1$ and the FVC; the difference in the two largest values was expressed as a percentage of the maximum value, and assessed with respect to the recommendation that the two largest values for both $FEV_1$ and FVC should be within 5% (or 200 mL, whichever is greater) of their respective maxima. Overall, 4% of workers studied did not meet this repeatability criterion. We had decided a priori, following previous work [Eisen et al., 1984, 1985], that subjects would not be excluded on the basis of lung function repeatability. This practice was subsequently recommended by the American Thoracic Society (ATS, 1987). Thus, we used the maximum values for $FEV_1$ and FVC for each subject throughout these analyses, regardless of whether their tests met the usual repeatability criteria.

Predicted values for $FEV_1$ and FVC, based on age, height, and race, were calculated from prediction equations recently published by Hankinson et al. [1999] based on 7,429 asymptomatic, lifelong nonsmoking participants in the third National Health and Nutrition Examination Survey (NHANES III). Lung function measurements ($FEV_1$, FVC) were expressed as absolute volumes (in liters) and as percentages of the respective predicted values (percent-predicted).

***Statistical Analysis.*** STATA was used for all the statistical analysis [StataCorp, 1997]. The relationships between lung function measurements and exposures to metal-working fluids were first examined graphically to assess the validity of underlying model assumptions. To assess linearity, a nonparametric smoothing technique, LOESS, was used on the raw data [Cleveland, 1979]. This method is a moving average technique that provides a smoothed function of the relationship between variables. The LOESS algorithm was also used to assess adjusted relationships between pulmonary function and exposure, by graphing partial regressions plots to eliminate effects of other covariates in the model.

Linear regression was used to model the exposure–response relationships, adjusting for confounding. The outcomes were simply $FEV_1$ or FVC, measured in liters. In these models, predictors of lung function, i.e., age, height, and race, were included as potential confounders along with smoking, grinding, plant, and exposure. Smoking was measured by packyears. Both current and lifetime MWF exposure to straight, soluble, and synthetic MWF were examined. Current exposure was classified by type of fluid (using three dummy variables, with assembly as the reference group) as well as by thoracic particulate ($mg/m^3$). In addition, particulate level and type were considered together by defining three interaction terms; straight-particulate, soluble-particulate, and synthetic-particulate according to the type of fluid being used in a particular operation. In a similar manner, cumulative exposure was measured first in the aggregate, as ($mg/m^3$)-years of exposure, as well as by combinations of particulate exposure and fluid type, cumulated over time. Dummy variables were defined for type of machining (machining vs. grinding) and plant (I, II, III, with Plant III as the arbitrary reference group). Residuals were examined to assess model fit.

## RESULTS

A total of 1,882 male workers, 86% of the eligible study population, reported for a respiratory evaluation. Among the three study sites, Plant I had a population that was older and comprised mainly black workers; airborne exposures to metal-working fluids were highest on average at this site. Workers at Plant II were predominantly young and white, and had the lowest average exposure levels. Plant III, the site with the smallest number of participants, had a low proportion of black workers, the lowest prevalence of current smokers, and exposure levels that were intermediate between the other two sites [Greaves et al., 1997].

Of the 1,882 participants, the 71 with insufficient current exposure information were excluded from further consideration. Of the remaining 1,811, 41 had technically unsatisfactory lung function tests, leading to their exclusion; a group of 25 assembly workers with no known exposures to metal-working fluids were missing small amounts of their past exposure information such that previous exposure to metal-working fluids could not be ruled out, and they were excluded from the never-exposed group. The analyses of current metal-working fluid exposures and lung function thus were based on 1,745 workers with complete exposure and lung function data: 725 current assemblers (including 492 with past exposure to metal-working fluids), 352 workers currently exposed to aerosols of straight oils, 443 exposed to soluble oils, and 225 exposed to synthetics (Table I). On average, subjects had worked for 12.2 years and had been in exposed machining (or grinding) jobs for 7.0 years.

***Current exposures and lung function.*** When classified by the type of current metal-working fluid exposure, subjects differed with respect to their mean ages and racial mix (Table I). Machinists working with straight or soluble oils were older on average (by 5 to 6 years) than the never-exposed assembly workers or those currently working with synthetic fluids. Machinists working currently with soluble oils, as well as assembly workers who used to work as machinists (mostly in jobs with soluble MWF) had significantly higher proportions of black workers. Patterns of

**TABLE I.** Demographic and Spirometric Characteristics for Auto-Workers Classified by Current Exposure Categories (N = 1,745)*

| | Assembly | | Machinists | | | |
|---|---|---|---|---|---|---|
| | Always | Not always[a] | Straight MWF | Soluble MWF | Synthetic MWF | Total |
| Number | 233 | 492 | 352 | 443 | 225 | 1,745 |
| Race (Black) | 27.0% | 44.5% | 24.4% | 51.7% | 15.5% | 36.2% |
| Age (years) | 35.5 | 38.5 | 41.5 | 40.4 | 35.0 | 38.7 (9.9) |
| | (8.6) | (9.6) | (10.1) | (10.4) | (8.7) | |
| Height (cm) | 174.6 | 174.2 | 174.3 | 175.4 | 174.6 | 174.6(6.5) |
| | (6.7) | (6.5) | (6.5) | (6.5) | (6.1) | |
| Current smoker | 51.5% | 50.2% | 47.2% | 53.3% | 55.6% | 51.2% |
| Never smoked | 30.5% | 29.7% | 23.1% | 24.7% | 24.0% | 26.4% |
| $FEV_1$ (l) | 3.83 | 3.65 | 3.65 | 3.58 | 3.86 | 3.68 (0.77) |
| | (0.74) | (0.77) | (0.76) | (0.76) | (0.75) | |
| $FEV_1$ % predicted[b] | 95.5 | 96.1 | 94.7 | 95.1 | 94.4 | 95.3 (14.3) |
| | (13.6) | (14.2) | (14.5) | (14.6) | (14.0) | |
| FVC (l) | 4.82 | 4.57 | 4.64 | 4.52 | 4.86 | 4.64 (0.87) |
| | (0.88) | (0.89) | (0.86) | (0.85) | (0.83) | |
| FVC % predicted | 97.7 | 97.5 | 96.4 | 97.1 | 96.5 | 97.1 (12.5) |
| | (12.7) | (12.5) | (12.4) | (12.4) | (12.2) | |
| Exposure | 0.11 | 0.11 | 0.43 | 0.55 | 0.41 | 0.32 (0.14) |
| (mg/$m^3$) | (0.02) | (0.02) | (0.26) | (0.17) | (0.07) | |

*Values are means (SD).

[a] Past employment as machinist.

[b] Predicted values from Hankinson et al., 1999.

smoking were similar across exposure groups, although the never exposed group included more never smokers.

Age-, height-, and race-adjusted lung function values showed that, on average, workers in each exposure group had lower $FEV_1$ than the reference group of healthy U.S. males; the mean percent-predicted values for $FEV_1$ were significantly below 100 percent (Table I). This finding was not surprising because the Hankinson prediction equations were based on a population of asymptomatic lifelong nonsmokers. Both adjusted $FEV_1$ and FVC values were slightly lower in all three machinist groups relative to current assembly workers. Among machinists, the average current aerosol exposures in groups exposed to each of the three types of fluid ranged from 0.4 to 0.6 mg/m$^3$ (thoracic fraction). Assembly workers had an average exposure of 0.1 mg/m$^3$ to an unspecified mixture of fluid types.

Graphs of pulmonary function and thoracic particulate indicated that the (crude) relationship was approximately linear. The relationships between lung function ($FEV_1$ and FVC) and current aerosol exposure levels were then examined in linear regression models, adjusting for age, height, race, packyears of smoking, current grinding, and factory. Models were fit first with main effects for thoracic and fluid type and then with the interaction terms. Two different models are presented for each pulmonary function outcome; one including a continuous variable ("MWF aerosol"), defined as the aerosol concentration (in mg/m$^3$), without regard to type and the other with the three terms defined as the aerosol concentration of each of the three specific types of fluid (Table II).

In all these models for current exposure, the demographic characteristics, age, height, and smoking, have the expected associations with $FEV_1$ and FVC. Coefficients for current exposure were uniformly negative in all models, suggesting that workers with higher exposure had lower lung function. None of the exposure terms, however, were statistically significant. Including the three type specific thoracic exposure terms without main effects for thoracic or fluid type also present, constrains the intercepts to be the same, but allows the exposure–response slopes to differ by type. The coefficients for synthetic exposure had the largest negative values, twice as large as the coefficient for straight thoracic and approximately four times that of solubles.

Collinearity was examined in these models for current exposure. The correlations between age and current exposure were low ($r < 0.2$), suggesting only minimal confounding by age. The impact of race on the exposure coefficients was trivial. In order to address the possibility of selective transfer of sicker workers back into assembly jobs, models were fit excluding current assembly workers with past exposure to metalworking fluids (transfers). The results did not change the exposure-response parameter estimates and so are not presented.

***Past exposures and lung function.*** Of the total study population, 42% had been exposed to straight MWF, 78% had been exposed to soluble, and 25% had exposure to synthetics. Among those exposed, the average cumulative exposures to each type of fluid were 4.7 (SD = 10.5) for straight, 5.0 (SD = 8.8) for soluble, and 0.9 (mg/m)$^3$-years

**TABLE II.** Two Regression Models for $FEV_1$ and FVC with Current MWF Exposure (mg/m$^3$) to Any Type of MWF and by Specific Type of MWF (N = 1,742)*

| | $FEV_1$ | | FVC | |
|---|---|---|---|---|
| **Variable** | **Model 1** | **Model 2** | **Model 1** | **Model 2** |
| Age (yrs) | −0.033 (.001)[a] | −0.033 (.001)[a] | −0.031 (.002)[a] | −0.031 (.002)[a] |
| Height (cm) | 0.041 (.002)[a] | 0.041 (.002)[a] | 0.057 (.002)[a] | 0.057 (.002)[a] |
| Race (Black) | −0.488 (0.30)[a] | −0.488 (0.30)[a] | −0.713 (0.33)[a] | −0.713 (0.33)[a] |
| Pack years | −0.007 (.001)[a] | −0.007 (.001)[a] | −0.003 (.001)[a] | −0.003 (.001)[a] |
| Grinding | 0.033 (.047) | 0.037 (0.47) | 0.041 (.052) | 0.047 (.052) |
| Plant I | −0.023 (.045) | −.032 (.048) | −0.049 (.050) | −0.062 (.052) |
| Plant II | −0.054 (.040) | −0.046 (.044) | −0.074 (.044)[b] | −0.065 (.049) |
| Any type (mg/m$^3$) | −0.070 (.067) | — | −0.083 (.074) | — |
| Straight (mg/m$^3$) | — | −0.057 (.071) | | −0.072 (.079) |
| Soluble (mg/m$^3$) | — | −0.031 (.062) | | −0.029 (.068) |
| Synthetic (mg/m$^3$) | — | −0.122 (.110) | | −0.160 (.121) |
| $R^2$ | 0.54 | 0.54 | 0.57 | 0.57 |

*Values are regression coefficients (SE).

[a] $P < 0.01$.

[b] $P < 0.10$.

**TABLE III.** Two Regression Models for $FEV_1$ and FVC with Cumulative Exposure [(mg/$m^3$)-years] to Any Type of MWF and by Specific Type of MWF ($N = 1{,}742$)

| | $FEV_1$ | | FVC | |
|---|---|---|---|---|
| **Variable** | **Model 1** | **Model 2** | **Model 1** | **Model 2** |
| Age (yrs) | −0.033 (.002)[a] | −0.033 (.002)[a] | −0.031 (.002)[a] | −0.031 (.002)[a] |
| Height (cm) | 0.040 (.002)[a] | 0.040 (.002)[a] | 0.057 (.002)[a] | 0.057 (.002)[a] |
| Race (Black) | −0.489 (0.30)[a] | −0.492 (0.30)[a] | −0.717 (0.33)[a] | −0.719 (0.33)[a] |
| Pack years | −0.007 (.001)[a] | −0.007 (.001)[a] | −0.003 (.001)[a] | −0.003 (.001)[a] |
| Plant I | −0.029 (.045) | −.042 (.045) | −0.057 (.049) | −0.071 (.050) |
| Plant II | −0.057 (.041) | −0.067 (.042) | −0.094 (.044)[b] | −0.096 (.047)[b] |
| Any type (mg/$m^3$)-years | −.001 (.001) | — | −0.002 (.002) | — |
| Straight MWF (mg/$m^3$)-years | — | −0.003 (.002) | — | −0.004 (.002)[c] |
| Soluble MWF (mg/$m^3$)-years | — | 0.001 (.002) | — | 0.0004 (.002) |
| Synthetic MWF (mg/$m^3$)-years | — | −0.013 (.010) | — | −0.014 (.011) |
| $R^2$ | 0.54 | 0.54 | 0.57 | 0.57 |

*Values are regression coefficients (SE).

[a] $P < 0.01$.

[b] $P < 0.05$.

[c] $P < 0.10$.

(SD = 2.5) for synthetic. These averages reflect the long-standing use of straight and soluble fluids in automobile manufacturing and the recent introduction of synthetics, as well as their limited use at two of the three factories studied. The correlations among cumulative exposure to the three fluid types were small, +0.06 between straight and soluble, −0.03 between straight and synthetic and −0.003 between soluble and synthetic.

When (mg/$m^3$)-years was measured, regardless of type of fluid, the regression coefficients for total exposure were negative but had large confidence intervals in the models for both $FEV_1$ and FVC (Table III). When stratified by MWF type, the coefficients for straight exposure were stronger, and reached borderline significance in the model for FVC ($P = 0.055$). The magnitude of the effect, −0.004 L/per (mg/$m^3$)-year is approximately the size of the smoking effect (per pack year) on FVC. FVC was lower in plants I and II, relative to Plant III. Models were rerun excluding the 88 subjects with more than 10% of their work history missing. No differences in the exposure parameters were observed, so results based on the full population are reported. In order to examine the underlying assumptions of the linear regression model, the residuals from this FVC model were examined and found to be approximately normal, with no outliers. Based on a partial regression plot, the adjusted relationship between FVC and cumulative exposure to straights was estimated by a smoothing technique and appears to be approximately linear.

The relationship between past exposure and FVC was further examined by exploring the effects of confounding and effect modification. When models were fit separately for each plant (Table IV), the effect of straight exposure was strongest in Plant I, weaker in Plant III, and was not associated with FVC at all in Plant II. Associations with synthetic exposure were uniformly negative in all three plants. When stratified by race, the exposure–response slope was slightly stronger for synthetics among Blacks, and the plant effects were stronger for Whites (Table V). The three plants differed somewhat by their racial composition and by types of MWF used. The study group in Plant I was 66% Black, whereas the proportion of Blacks was just under 20% in the other two plants. Straight MWF was used in all three plants but least often in Plant II. Most of the synthetic exposure occurred in Plant II, and the highest past exposure to soluble MWF was found in Plant I.

We examined the impact of age on the coefficients for cumulative exposure by looking at the correlations among these covariates. The Pearson correlation coefficients between age and lifetime exposure to each of the three types of MWF were 0.28, 0.44, and 0.07 for straight, soluble, and synthetic fluids, respectively. Although these correlations were only moderate, we attempted to disentangle these two

**TABLE IV.** Regression Models for FVC on Cumulative Exposure by Type of MWF Stratified by Plant*

| | Plant I | Plant II | Plant III |
|---|---|---|---|
| Age (years) | −0.290 (.003)[a] | −0.032 (.003)[a] | −0.036 (.006)[a] |
| Height (cm) | 0.052 (.003)[a] | 0.061 (.003)[a] | 0.054 (.057)[a] |
| Race (Black) | −0.666 (.047)[a] | −0.759 (.054)[a] | −0.801 (.114)[a] |
| Pack years | −0.003 (.001)[a] | −0.003 (.001)[b] | −0.002 (.003)[b] |
| Ever grind | 0.042 (.057) | −0.053 (.054) | −0.035 (.079) |
| Straight MWF (mg/m$^3$)-years | −0.005 (.003)[c] | 0.004 (.034) | −0.002 (.004) |
| Soluble MWF (mg/m$^3$)-years | −0.002 (.002) | 0.004 (.010) | 0.011 (.008) |
| Synthetic MWF (mg/m$^3$)-years | −0.022 (.087) | −0.009 (.012) | −0.044 (.044) |
| N | 677 | 820 | 215 |
| $R^2$ | 0.54 | 0.53 | 0.46 |

*Values are regression coefficients (SE).
[a] $P < 0.01$.
[b] $P < 0.05$.
[c] $P < 0.10$.

time related variables by splitting the study group at the median age, and defining two age groups. Separate regression models were fit to the younger and older workers (Table VI). At an $\alpha = 0.10$ significance level, statistically significant associations were observed with both straight and synthetic among older workers. When an outlier detected in a residual plot was removed, however, the parameter estimate for synthetics was closer to zero, and no longer significant. No negative associations were found among the younger workers. There was, however, a positive association with synthetic exposure, providing indirect evidence of selection of healthier young individuals into jobs with synthetic exposure [Eisen, 1995].

**TABLE V.** Regression Models for FVC on Cumulative Exposure, Stratified by Race*

| | White | Black |
|---|---|---|
| Age (years) | −0.032 (.002)[a] | −0.028 (.003)[a] |
| Height (cm) | 0.061 (.003)[a] | 0.049 (.004)[a] |
| Pack years | −0.003 (.001)[a] | −0.001 (.002) |
| Ever grind | −0.036 (.045) | 0.009 (.056) |
| Plant I | −0.109 (.061)[c] | −0.037 (.011) |
| Plant II | −0.112 (.053)[b] | 0.071 (.113) |
| Straight MWF (mg/m$^3$)-years | −0.004 (.003) | −0.004 (.003) |
| Soluble MWF (mg/m$^3$)-years | 0.002 (.004) | −0.003 (.002) |
| Synthetic MWF (mg/m$^3$)-years | −0.009 (.012) | −0.038 (.031) |
| N | 1094 | 618 |
| $R^2$ | 0.51 | 0.42 |

*Values are regression coefficients (SE).
[a] $P < 0.01$.
[b] $P < 0.05$.
[c] $P < 0.10$.

**TABLE VI.** Regression Models for FVC on Cumulative Exposure, Stratified at the Median Age (36)*

| | Younger | Older |
|---|---|---|
| Age (years) | −0.031 (.007)[a] | −0.034 (.003)[a] |
| Height (cm) | 0.063 (.003)[a] | 0.048 (.003)[a] |
| Race (Black) | −0.794 (.048)[a] | −0.625 (.048)[a] |
| Pack years | −0.003 (.002) | −0.002 (.001) |
| Ever grind | −0.024 (.054) | −0.041 (.048) |
| Plant I | −0.073 (.076) | −0.111 (.072) |
| Plant II | −0.107 (.066) | −0.137 (.072)[c] |
| Straight MWF (mg/m$^3$)-years | −0.007 (.015) | −0.004 (.002)[c] |
| Soluble MWF (mg/m$^3$)-years | −0.003 (.012) | −0.0004 (.002) |
| Synthetic MWF (mg/m$^3$)-years | 0.084 (.042)[b] | −0.021 (.011)[c] |
| N | 889 | 823 |
| $R^2$ | 0.48 | 0.47 |

*Values are regression coefficients (SE).
[a] $P < 0.01$.
[b] $P < 0.05$.
[c] $P < 0.10$.

To investigate further HWE due to selective job transfer, we focused on the 492 current assemblers with past exposure (see Table I) to examine the possibility that machinists who were most responsive to MWF exposure might have been more likely to transfer to unexposed

**TABLE VII.** Regression Models for FVC on Cumulative Exposure, for All Subjects and Stratified by Job Transfer Status (Transferred from machining or grinding job to assembly)*

| | All Subjects | Transfers | Non-Transfers |
|---|---|---|---|
| Age (years) | −0.031 (.002)$^{a}$ | −0.032 (.003)$^{a}$ | −0.030 (.002)$^{a}$ |
| Height (cm) | 0.057 (.002)$^{a}$ | 0.059 (.004)$^{a}$ | 0.056 (.003)$^{a}$ |
| Race (Black) | −0.719 (.034)$^{a}$ | −0.744 (0.59)$^{a}$ | −0.707 (.041)$^{a}$ |
| Pack years | −0.003 (.001)$^{a}$ | −0.001 (.002) | −0.003 (.001)$^{a}$ |
| Ever grind | −0.015 (.035) | −0.048 (.067) | −0.007 (.041) |
| Plant I | −0.071 (.050) | 0.012 (.087) | −0.109 (.063)$^{c}$ |
| Plant II | −0.097 (.047)$^{b}$ | −0.038 (.081) | −0.131 (.059)$^{b}$ |
| Transfer status | −0.002 (.032) | | |
| Straight MWF (mg/m$^3$)-years | −0.004 (.002)$^{c}$ | −0.001 (.001) | −0.005 (.002)$^{b}$ |
| Soluble MWF (mg/m$^3$)-years | 0.0004 (.002) | −0.003 (.005) | −0.0004 (.002) |
| Synthetic MWF (mg/m$^3$)-years | −0.014 (.011) | 0.037 (.098) | −0.016 (.011) |
| N | 1712 | 492 | 1220 |
| R$^2$ | 0.57 | 0.60 | 0.56 |

*Values are regression coefficients (SE).

$^{a}P < 0.01$.

$^{b}P < 0.05$.

$^{c}P < 0.10$

assembly jobs. In a model based on all subjects, an indicator term was added to indicate transfer to assembly (Table VII). The negative coefficient suggests that those who transferred to assembly had lower FEV$_1$ at the time of the survey than those who had not transferred, although again the *P*-value was large. Exposure-response models were fit to two subgroups: the 492 transfers and the rest of the population. Among the 1,220 workers who did not transfer from machining or grinding jobs to assembly, the exposure–response parameter for straight exposure was slightly more negative and statistically significant at $\alpha = 0.05$. The association with synthetic exposure, although negative for this group, was not significant.

## DISCUSSION

Exposure to MWF has been recently associated with a variety of respiratory outcomes, including asthma, hypersensitivity pneumonitis, and nonspecific symptoms [Ameille et al., 1995; Eisen et al., 1997; Greaves et al., 1997; Kreiss and Cox-Ganser, 1997; Rosenman et al., 1997]. In addition, across-shift change in lung function has been successfully used to measure short-term respiratory effects of MWF exposure [Kennedy et al., 1989; Kriebel et al., 1997; Robins et al., 1997]. Having documented these pulmonary responses, one might hypothesize an association with annual decline in pulmonary function or with baseline function, as measures of a chronic effect. To date, there have been no longitudinal studies of lung function among workers exposure to MWF. Previous cross-sectional studies of pulmonary function in groups of workers exposed to MWF have reported either no association with exposure, a weak association, or an association found only in a subgroup of the study population [Ameille et al., 1995, Kriebel et al., 1997; Massin et al., 1996; Sprince et al., 1997]. Ameille found an association with FEV$_1$ among smokers. Massin et al. reported a significant association between FEV$_1$ and soluble oil mist which vanished after adjustment for tobacco consumption. The strongest of these studies is Kriebel et al., who found a significant 115 mL decrement in FEV$_1$ among machinists exposed to an average of 0.22 mg/m$^3$ soluble aerosol, relative to assembly. None of these cross-sectional studies included reconstruction of past exposure and there were no reports of a significant association with FVC.

Findings presented here provide evidence of an association between FVC and lifetime exposure to straight MWF. There was little evidence found for associations between FVC and past exposure to the water-based fluids; the regression coefficient for synthetic fluids was three times as large as that for straight fluid with a wide confidence interval. There were no associations with current exposure. FEV$_1$ was not significantly related to any exposure variable, although the magnitude of the regression slopes, −0.003 and −0.013 for cumulative exposure to straight and synthetic fluid, respectively, were almost identical to those in the models for FVC. Based on the health effects literature for metal-working fluids described above, we anticipated that FEV$_1$ would be more sensitive than FVC to the effects of MWF exposure. It may be that the slightly higher significance level of our finding for FVC than $FEV_1$ is due to chance.

The magnitude of the parameter estimate of $-0.004$ L/(mg/m$^3$)-year (95% CI: $-0.006$, $-0.002$) suggests that the effect of being exposed to 1 mg/m$^3$ of straight MWF for 1 year is approximately equivalent to that of smoking one more pack year of cigarettes on FVC. When excluding those who transferred to assembly jobs, the association with a unit change of cumulative straight MWF was slightly stronger than an additional packyear of cigarette smoking, $-0.005$ vs. $-0.003$, respectively. The absence of an association among the previously exposed who had transferred to assembly suggests that the effects of MWF exposure may be reversible in the absence of substantial exposure.

The exposure–response associations observed in a cross-sectional study of active workers might be biased because of misclassification of exposure or outcome, healthy worker selection, or unmeasured confounding. The degree of exposure misclassification in this study was probably less than usual in a study where past exposures are reconstructed. The size-selective sampling method that was used permitted assessment of the 'thoracic' aerosol fraction, which provides a more refined estimate of the aerosol particles likely to penetrate to the lower respiratory tract. Although 'thoracic' and total aerosol levels were correlated in this study, this may not be true for other work environments where the metal-working operations and fluids could lead to very different distributions of particle sizes. Thus, the use of size-specific aerosol samples becomes important when comparing exposure–response information across studies.

With regard to healthy worker selection, we attempted to address one source of bias—that due to sicker workers transferring out of exposed jobs into assembly. When restricted to workers who did not transfer, the strength of the association between FVC and straight exposure increased and became statistically significant ($P < 0.05$). This increase in the magnitude and significance level of the association suggests that the workers who had transferred from machining jobs (and inadvertently truncated their exposure) had biased the earlier results. At the same time, the lack of an exposure–response association among the transfers suggests that the effect of MWF on pulmonary function may not be persistent in the absence of exposure. There is no adequate way, however, in a cross-sectional cohort, to address the potential loss of less healthy workers from among the active workforce. In light of the substantial evidence that synthetic fluids cause a variety of other adverse respiratory outcomes, the absence of positive findings for the water-based fluids in this study may be attributable to HWE.

Previous studies of respiratory symptoms, asthma, and acute lung function changes in this population of automobile workers [Greaves et al., 1997; Kennedy et al., 1989], suggest that each of the major metal-working fluid types can have adverse respiratory effects. Based on these previous findings, the relative toxicity of the principal fluid types appeared to be synthetic fluids showing the highest rates of abnormality, followed by straight oils, and then soluble oils. The present results suggest that lifetime exposure to straight MWF is most strongly associated with a reduction in FVC. A time-weighted average exposure limit of 0.4 mg/m$^3$ of thoracic aerosol has just been recommended by NIOSH (corresponding to a 0.5 mg/m$^3$ recommended exposure limit (REL) for total inhalable particulate). This REL is based on the argument that size-specific aerosol exposure limits may be more appropriate than total aerosol measurements for the protection of respiratory health. The use of size-specific criteria has been recommended by several national and international organizations, including the American Conference of Governmental and Industrial Hygienists [ACGIH, 1994], the French Comité Européen de Normalisation [CEN, 1992], and the Health and Safety Executive of the U.K. [HSE, 1993].

We have noted previously that large numbers of U.S. workers are exposed regularly to aerosols of metal-working fluids, and that the health implications of exposures to these agents may be considerable in terms of respiratory disease [Kennedy et al., 1989]. Since that time the findings of Rosenman et al. [1994, 1997] have given further credence to the view that metal-working fluids are responsible for significant rates of respiratory disease in U.S. industries, while Gannon and Sherwood Burge [1991] have reported similar findings in the heavily industrialized, West Midlands region of the United Kingdom.

Our studies of U.S. automobile workers have shown that roughly 20–30% of individuals currently exposed to these agents experience an acute, transient decrease in lung function [Kennedy et al., 1989]; similar excess prevalence rates were found for cough, phlegm, and wheezing among machinists [Greaves et al., 1997] and for reduction in lung function (as described above). Assuming, conservatively, a rate at the low end of this range (that is, a prevalence of 20%) for machinists experiencing an adverse respiratory effect from metal-working fluid aerosols, and further that the results among automobile workers are generalizable to machinists as a whole, then the possible numbers of adversely affected workers could exceed two million in the United States and more than 20 million worldwide.

If these estimates are approximately accurate, the number of workers affected by aerosols of metal-working fluids would far exceed, for example, the number of coal workers experiencing coal workers' pneumoconiosis, and would qualify metal-working fluids as a major occupational health concern. Unlike coal workers' pneumoconiosis, however, the risks from metal-working fluids are spread across many different industries, both large and small, and the identity of the specific hazard(s) in these fluids is unknown. These features operate against the accurate identification and prevention of work-related respiratory problems associated with metal-working fluid exposures. Further surveillance and experimental data are needed to define the extent to which metal-working fluids contribute to respiratory morbidity and mortality, and to identify the hazardous agents in these fluids. Prospective studies of pulmonary function would allow us to examine the question of chronic effects on lung function better as well as provide information on the sensitivity and specificity of lung function as a surveillance tool for monitoring MWF exposed populations.

Further work is needed also to examine respiratory problems among workers in the many other industries using metal-working fluids. Such work will need to (a) assess the extent and severity of respiratory disease among those exposed currently and in the past to metal-working fluids; (b) examine mechanisms by which possible etiologic agents within these complex mixtures may be causing adverse respiratory effects; (c) define what constitute 'safe' aerosol levels for workers exposed to these various agents; and (d) devise appropriate preventive strategies for reducing workers' exposures to those levels.

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## REFERENCES

Acquavella J, Leet T, Johnson G. 1993. Occupational experience and mortality among a cohort of metal components manufacturing workers. Epidemiology 4(5):428–434.

Ameille J, Pascal W, Choudat D, Ohl G, Vaucouleur JF, Chanut JS, Brouchard P. 1995. Respiratory symptoms, ventilatory impairment and bronchial reactivity in oil-mist exposed automobile workers. Am J Ind Med 27:247–256.

American Conference of Governmental and Industrial Hygienists (ACGIH). 1994. Threshold limit values for chemical substances and physical agents and biological exposure indices (1994–1995): Appendix D: Particle size-selective sampling criteria for airborne particulate matter. Cincinnati, OH:ACGIH. p 43–45.

American Thoracic Society (ATS). 1979. Statement: Snowbird workshop on standardization of spirometry. Am Rev Respir Dis 119:831–838.

American Thoracic Society (ATS). 1987. Standardization of spirometry—1987 update. Am Rev Respir Dis 136:1285–1298.

Bardin J, Eisen EA, Woskie SR, Monson RR, Smith TJ, Tolbert P, Hammond K, Hallock M. 1997. Mortality studies of machining fluid exposure in the automobile industry. V: A case-control study of pancreatic cancer. Am J Ind Med 32:240–247.

Black KH, Petusevsky ML, Gaensler EA. 1980. A general purpose microprocessor for spirometry. Chest 78:605–612.

Cleveland WS. 1979. Robust locally weighted regression and smoothing scatterplots. J Am Stat Assoc 42:121–130.

Comité Européen de Normalisation (CEN). 1992. Workplace atmospheres: size fraction definitions for measurement of airborne particles in the workplace. CEN Standard EN 481. Brussels, Belgium, CEN.

Decoufle P. 1978. Further analysis of cancer mortality patterns among workers exposed to cutting oil mists. J Nat Cancer Inst 61(4):1025–1030.

Eisen EA. 1995. Healthy worker effect in morbidity studies. Med del Lavoro 86;2:127–140.

Eisen EA, Robins JM, Greaves IA, Wegman DH. 1984. Selection effects of repeatability criteria applied to lung spirometry. Am J Epidemiol 120:734–742.

Eisen EA, Oliver LC, Christiani DC, Robins JM, Wegman DH. 1985. Effects of spirometry standards in studies of two occupational cohorts. Am Rev Respir Dis 132:120–124.

Eisen EA, Tolbert PE, Monson RR, Smith TJ. 1992. Mortality studies of machining fluid exposure in the automobile industry. I. A standardized mortality ratio analysis. Am J Ind Med 22:809–824.

Eisen EA, Tolbert PE, Hallock MF, Monson RR, Smith TJ, Woskie SR. 1994. Mortality studies of machining fluid exposure in the automobile industry. III. A case-control study of larynx cancer. Am J Ind Med 26:185–202.

Eisen EA, Holcroft CA, Greaves IA, Wegman DH, Woskie SR, Monson RR. 1997. A strategy to reduce healthy worker effect in a cross-sectional study. Am J Ind Med 31:671–677.

Foe RB, Bigham RS. 1954. Lipid pneumonia following occupational exposure to oil spray. JAMA 155:33–34.

Gannon PFG, Burge SP. 1991. A preliminary report of a surveillance scheme of occupational asthma in the West Midlands. Br J Ind Med 48:579–582.

Greaves IA, Eisen EA, Monson RR, Smith TJ, Pothier L, Kriebel D, Woskie SR, Hallock M, Shallot S. 1997. Respiratory effects of machining fluids. Respiratory symptoms. Am J Ind Med 32:450–459.

Hallock MF, Smith TJ, Woskie SR, Hammond SK. 1994. Estimation of historical exposures to machining fluids in the automotive industry. Am J Ind Med 26:621–634.

Hankinson JL, Odencrantz JR, Fedan KB. 1999. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 159(1):179–187.

Health and Safety Executive (HSE). 1989. General methods for the gravimetric determination of respirable and total inhalable dust. HSE MDHS14 (revised): London, UK:HMSO.

Hendy MS, Beattie BE, Burge PS. 1985. Occupational asthma due to an emulsified oil mist. Br J Ind Med 42:51–54.

International Agency for Research on Cancer (IARC). 1984. Mineral oils (lubricant based oils and derived products): Lyon, France: World Health Organization.

Järvholm B. 1982. Cutting oil mist and bronchitis. Eur J Respir Dis 63 [Suppl. 118]:79–83.

Järvholm B, Lavenius B. 1987. Mortality and Cancer morbidity in workers exposed to cutting fluids. Arch Environ Health 42:361–366.

Järvholm B, Bake B, Lavenius B, Thiringer G, Vokmann R. 1982. Respiratory symptoms and lung function in oil mist-exposed workers. J Occup Med 24:473–479.

Kennedy SM, Greaves IA, Kriebel D, Eisen EA, Smith TJ, Woskie SR. 1989. Acute pulmonary responses among automobile workers exposed to aerosols of machining fluids. Am J Ind Med 15:627–641.

Kennedy SM, Chan-Yeung M, Teschke K, Karlen B. 1999. Change in airway responsiveness among apprentices exposed to metal-working fluids. Am J Respir Crit Care Med 159:87–93.

Kriebel D, Sama SR, Woskie SR, Christiani DC, Eisen EA, Hammond K, Milton DK, Smith M, Virji MA. 1997. A field investigation of the acute respiratory effects of metalworking fluids. I: Effects of aerosol exposures. Am J Ind Med 31:756–766.

Kreiss K, Cox-Ganser J. 1997. Metal-working fluid-associated hypersensitivity pneumonitis: A workshop summary. Am J Ind Med 32:423–432.

Massin N, Bohadana AB, Wild P, Goutet P, Kirstetter H, Toamain JP. 1996. Airway responsiveness, respiratory symptoms, and exposures to soluble oil mist in mechanical workers. Occ Environ Med 53:748–752.

NIOSH. National Institute for Occupational Safety & Health. 1997. Occupational exposure to metalworking fluids. Criteria for a recommended standard. U.S. Department of Health & Human Services. Public Health Service CDC.

Oxhøj H, Andreasen H, Henius U. 1982. Respiratory symptoms and ventilatory lung function in machine shop workers exposed to coolant-lubricants. Eur J Respir Dis 63 [Suppl. 118]: 85–90.

Robertson AS, Weir DC, Burge PS. 1988. Occupational asthma due to oil mists. Thorax 43:200–205.

Robins T, Seixas N, Franzblau A, Abrams L, Minick S, Burge H, Schork MA. 1997. Acute respiratory effects on workers exposed to metalworking fluid aerosols in an automotive transmission plant. Am J Ind Med 31:510–524.

Rosenman KD, Reilly MJ, Watt FC, Kalinowski DJ. 1994. 1993 Annual report of occupational asthma in michigan. Michigan Department of Public Health.

Rosenman KD, Reilly MJ, Kalinowski DJ. 1997. Work-related asthma and respiratory symptoms among workers exposed to metal-working fluids. Am J Ind Med 32:325–331.

Silverstein M, Park R, Marmor M, Maizlish N, Mirer F. 1988. Mortality among bearing plant workers exposed to metalworking fluids and abrasives. J Occup Med 30:706–714.

Sprince N, Thorne PS, Popendorf W, Zwerling C, Miller ER, DeKoster JA. 1997. Respiratory symptoms and lung function abnormalities among machine operators in automobile production. Am J Ind Med 31:403–404.

StataCorp. 1997 Stata statistical software:Release 5.0. College Station TX:Stata Corporation.

Sullivan P, Eisen EA, Woskie SR, Monson RR, Smith TJ, Tolbert P, Hammond K, Hallock M. 1998. Mortality studies of machining fluid exposure in the automobile industry. VI: A case-control study of esophageal cancer. Am J Ind Med 34:36–48.

Tolbert PE, Eisen EA, Pothier LJ, Monson RR, Hallock MF, Smith TJ. 1992. Mortality studies of machining fluid exposure in the automobile industry. II. Risks associated with specific fluid types. Scand J Work Environ Health 18:351–360.

Woskie SR, Smith TJ, Hallock MF, Hammond SK, Rosenthal F, Eisen EA, Kriebel D, Greaves IA. 1994. Size-selective pulmonary dose indices for metal-working fluid aerosols in machining and grinding operations in the automobile manufacturing industry. Am Ind Hyg Assoc J 55:20–29.