

# EPIDEMIOLOGY -- RESPIRATORY EFFECTS PLENARY SESSION

## Session Arranger / Moderator:

**JAMES B. D'ARCY, PhD, CIH**, Staff Research Scientist, General Motors Corporation

## Discussants:

**CHARLES BRADFORD**, Director of Health & Safety, IAMAW

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**WILLIAM E. LUCKE, PhD**, Manager, Regulatory Affairs, Cincinnati Milacron

**GREGORY R. WAGNER, MD**, Director, Division of Respiratory Disease Studies, NIOSH

## Technical Presenters:

**SUSAN M. KENNEDY, PhD**, Director, Occupational Hygiene Programme, University of British Columbia  
*TWO YEAR LONGITUDINAL CHANGES in AIRWAY RESPONSIVENESS  
AMONG YOUNG MACHINISTS*

**THOMAS G. ROBINS, MD, MPH**, Professor, University of Michigan School of Public Health  
*ACUTE RESPIRATORY EFFECTS of MACHINING FLUID AEROSOLS:  
EVIDENCE for a ROLE of BACTERIA*

**DAVID KRIEBEL, ScD**, Associate Professor, University of Massachusetts, Lowell  
*FIELD INVESTIGATION of the ACUTE RESPIRATORY EFFECTS of  
MACHINING FLUIDS*

**KENNETH D. ROSENMAN, MD**, Professor of Medicine, Michigan State University  
*OCCUPATIONAL ASTHMA and RESPIRATORY SYMPTOMS AMONG  
WORKERS EXPOSED to MACHINING FLUIDS*

**DAVID J.P. BASSETT, PhD**, Chairman, Occupational & Environmental Health, Wayne State University  
*REVIEW of ACUTE RESPIRATORY HEALTH EFFECTS*

# EPIDEMIOLOGY -- RESPIRATORY EFFECTS

## PLENARY SESSION

Session Arranger / Moderator:

**JAMES B. D'ARCY, PhD, CIH, General Motors**

**Mr. DAVID FELINSKI, AAMA:** Good afternoon, and welcome back from lunch. It is now my privilege and pleasure to introduce the Session Arranger for this afternoon's session.

James B. D'Arcy received his Bachelors and Masters Degrees in Chemistry from Oakland University, his Doctorate in Industrial Health from the University of Michigan, and is Board certified in the comprehensive practice of Industrial Hygiene.

Dr. D'Arcy joined General Motors in 1978 as a Staff Research Scientist at the Research and Development Center in Warren Michigan. His Program Manager responsibilities for the Department of Automotive Safety and Health Research include research on health effects of automobile manufacture and use; internal consultation on industrial hygiene concerns and indoor air quality investigations; the design and development of environmental test chambers; and the development of aerosol generation systems.

Dr. D'Arcy is Chairman of the AAMA Metalworking Fluids Task Group, and is an active member of numerous Professional Scientific Societies such as the American Academy of Industrial Hygiene, the American Association for Aerosol Research, the American Association for the Advancement of Science, the American Chemical Society, the American Conference of Governmental Industrial Hygienists, the American Industrial Hygiene Association, the American Public Health Association, the Michigan Industrial Hygiene Association and Sigma Xi.

The author of numerous publications in the scientific literature, and recipient of the Warren A. Cook Award, Dr. D'Arcy's current research interests include Engineering controls for worker exposures; Health effects of new industrial processes; Expert systems for

dissemination of occupational health expertise; Biological exposure indices; and Inhalation toxicology.

Dr. D'Arcy, the Session is yours.

**Dr. JAMES D'ARCY, General Motors:**

Thank you David. I think this afternoon's session is going to be a pretty lively session, and I think we should be able to defeat the postprandial dip that typically happens after lunch. We have five presentations here this afternoon, and because of the time constraints, we'll hold questions until the discussion session, so to assure that the first speakers get challenged as much as the last speakers, you may want to jot down your early questions so you don't forget them when the time comes. Yesterday we heard quite a bit about the epidemiology among the workers that are using these metal removal fluids about cancer, a very long latency period type of disease, a very serious disease. This morning we heard about the respiratory irritancy of some of these materials in laboratory animals, and this afternoon, we are going to focus on epidemiology among the workers of different respiratory conditions including this same type of irritancy, we believe, that you heard about in animal models this morning. Now this was first reported in a paper by Kennedy, *et al* in 1987, and Dr. Kennedy is going to be our first speaker this afternoon. Dr. Kennedy is from the University of British Columbia and she's going to be speaking about a longitudinal study she is doing. The title of it is - "Two year longitudinal changes in airway responsiveness among young machinists", and as far as I know this is one of the only, if not the only longitudinal study of this important health area. Dr. Kennedy.

## Two-Year Longitudinal Change in Airway Responsiveness Among Young Machinist Apprentices.

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### ABSTRACT

To investigate potential early pulmonary responses to machining fluid exposure, we enrolled 1st year machinist apprentices (and apprentices in 3 other trades for comparison) into an 8 y prospective study. We report here on results after 2 years of follow-up. We obtained complete follow-up data for 82 machinists and 159 controls. The majority of machinists worked in shops with less than 10 machinists. Testing was performed at the training school, not the worksite. Tests (both occasions) included a respiratory questionnaire, am and pm spirometry, methacholine challenge testing, and allergy skin prick tests. Detailed exposure information (employers, type and duration of each machine-coolant task, ventilation systems, respiratory protection) was collected at the initial and final tests and by telephone at approximately 6 month intervals between tests. Representative full shift personal monitoring for 'total aerosol mass' was conducted for specific machine-coolant combinations at 13 different shops (n = 80 samples). Exposure concentrations ranged from non-detectable to 3.65 mg/m<sup>3</sup>, with a mean value of 0.46 mg/m<sup>3</sup>. Worksites and jobs with mixed coolant exposures tended to have higher aerosol concentrations (mean 0.72 mg/m<sup>3</sup>) than either soluble fluid alone (mean 0.25 mg/m<sup>3</sup>) or synthetic fluid alone (mean 0.44 mg/m<sup>3</sup>). Baseline levels of bronchial responsiveness did not differ between groups; the average change in bronchial responsiveness over the two years was approximately double in machinists compared to other apprentices (p=0.05). A marked increase in bronchial responsiveness (defined as greater than one 'doubling dose' difference in PC<sub>20</sub> between tests) was found in 30% of workers with ≥ 300

days of machining fluid exposure compared to 7% of the remainder (p=0.01). A moderate increase in bronchial responsiveness was more likely among machinists working with a mixture of fluid types and among the small number of machinists working mainly with computer controlled machines with synthetic fluids (p < 0.05, for differences among all groups). Increased bronchial responsiveness was associated with synthetic fluid exposure in those who quit the machining trade between surveys. No cases of obvious occupational asthma were noted during this study.

### INTRODUCTION

Previous studies have suggested that exposure to metal working fluids may lead to an acute reduction in lung function which can be detected over the course of one work shift. In a previously published report by one of the authors<sup>(1)</sup> a cross-shift reduction in FEV<sub>1</sub> of 5% or greater was found in 23% of machinists working in automobile parts manufacture compared to 10% of assembly workers in the same plants (p<0.05). Although an exposure response trend was seen (with increasing prevalence of an acute response associated with increasing exposure level), no differential effect was seen for different classes of machining fluids; that is, the effect appeared to be of similar magnitude for each of straight oils, soluble oil emulsions, and synthetic fluids. Although an acute cross-shift change in FEV<sub>1</sub> is not, by itself, evidence of lung impairment, studies in other industries have shown that cross-shift FEV<sub>1</sub> decline is predictive of increased risk for chronic airflow obstruction.<sup>(2)</sup> Case reports have also been published which show clear evidence that the development of specific occupational

asthma is associated with components of metalworking fluids in some workers.<sup>(3,4)</sup>

To further investigate the potential relationship between metalworking fluid exposure and the development of respiratory morbidity we initiated an 8 year prospective study of newly apprenticed machinists with the objective of identifying the risk factors for, and early natural history of, the development of both acute and chronic respiratory obstruction, including asthma, which may be associated with exposure to metalworking fluids. We report here results after 2 years of follow-up.

### **SUBJECTS and METHODS**

In British Columbia, Canada, all newly apprenticed machinists in any industry are required to attend classes at the BC Institute of Technology for 4 weeks every year for each of four years of their apprenticeship. Each class consists of approximately 20 students. We invited all students in each first year apprenticeship class over a two year period to participate in this study. Any apprentice who had been employed in a machining job for more than 6 months was excluded. A total of 116 machinists agreed to participate (participation rate: 91%). The comparison group included 240 apprentices, similarly recruited, from construction painting, insulation, and electrician classes (participation rate 83%). As we were interested in the new development of asthma and other acute non-asthmatic pulmonary responses, subjects with current asthma (n=10) were excluded from further analysis.

Questionnaires were administered by a trained interviewer and included a detailed current and past respiratory symptoms questionnaire (an expanded version of the American Thoracic Society questionnaire for use in epidemiologic studies) and a detailed history of current and past work practices and exposures. Allergy skin prick tests were conducted using three common environmental antigens (house dust mite, mixed Pacific grasses, cat epidermal antigen) and positive and negative controls (histamine and saline, respectively). The wheal diameter was read at 15 minutes and a positive test was recorded if the

wheal diameter was 3 mm or more larger than the saline control. Spirometry was performed first thing in the morning and at the end of the afternoon on a classroom day and on a workshop day, using a dry rolling seal spirometer (S & M Instruments Ltd, Doylestown PA), with subjects seated and wearing noseclips. The same two trained technicians conducted all tests. A minimum of 3 acceptable forced expiratory maneuvers were obtained from each subject and the maximum FEV<sub>1</sub> and FVC were used for analysis. Bronchial hyperresponsiveness was measured by methacholine challenge performed on a separate day, after all spirometry had been performed. Subjects were rescheduled if they reported a recent upper respiratory tract infection. The methacholine challenge test protocol followed the tidal breathing method with normal saline and methacholine concentrations from 0.01 to 64 mg/ml being nebulized into a face mask for 2 minutes. A forced expiratory maneuver was performed at 30 seconds and 3 minutes following each concentration and the lowest FEV<sub>1</sub> recorded. The test was terminated when FEV<sub>1</sub> fell to 20% of the lowest post saline level or the maximum concentration was reached. The linear slope of the least squares regression line from the relationship between FEV<sub>1</sub> and methacholine concentration was calculated and the concentration associated with a 20% drop in FEV<sub>1</sub> (PC<sub>20</sub>) determined by linear interpolation or extrapolation.

Following the baseline testing, each participant was contacted by telephone at approximately 6 month intervals to obtain additional information about the current work and exposures. A spreadsheet was completed during the telephone interview which identified each type of machining task performed, the type of coolant or lubricant used, the nature of controls present (e.g., ventilation, respiratory protection, enclosure), and the proportion of time spent at the task.

When the study subjects attended at the technical school for their third year class (i.e. approximately 2 years after the baseline testing), all testing procedures conducted at baseline were repeated. Subjects who had left the trade or were unable to attend follow-up apprenticeship classes

were located and invited for retesting at our clinic. A number of subjects were unable to attend the clinic as they had moved away and several of these were tested in their home towns using a mobile pulmonary laboratory.

## RESULTS AND DISCUSSION

We obtained complete baseline data for 95 machinists and 191 controls and complete follow-up data for 82 machinists and 159 controls. The major source of missing data was the methacholine challenge test as this was the most difficult to schedule. There were no significant differences in baseline characteristics between those who were tested at follow-up and those who were not.

As most of the machinists worked in shops with less than 10 machinists and the worksites were distributed widely throughout the province, it was not possible to conduct exposure monitoring at all worksites. Therefore, representative full shift personal monitoring for 'total aerosol mass' was conducted for specific machine-coolant combinations at 13 different shops (n = 80 samples). The shops represented a good cross-section of machine shop types (large and small production shops, automotive machine shops, remanufacturing shops, and jobbers). The shops chosen were selected systematically from lists of potential shops which hire apprentices and from the actual workplaces of the apprentices enrolled in the study. Only 3 shops refused to participate. Straight cutting oil was never used exclusively in any of the shops tested, although it was used in combination with synthetic and soluble fluids. Exposure concentrations ranged from non-detectable to 3.65 mg/m<sup>3</sup>, with a mean value of 0.46 mg/m<sup>3</sup>. Worksites and jobs with mixed coolant exposures tended to have higher aerosol concentrations (mean 0.72 mg/m<sup>3</sup>) than either soluble fluid alone (mean 0.25 mg/m<sup>3</sup>) or synthetic fluid alone (mean 0.44 mg/m<sup>3</sup>).

It is not possible to discuss all results at this Symposium; therefore, this report concentrates on changes in bronchial responsiveness over the two year follow-up period, in relation to type of machining task and fluids used. Data are presented only for those subjects with complete data on both

testing occasions. Characteristics of the participants at baseline and at follow-up are shown in tables 1 and 2.

	Machinists	Others	p
n	82	159	
Age	24.3	24.2	ns
Non-white	6%	4%	ns
FEV <sub>1</sub> (% predicted)	100.2	102.3	ns
Non - smokers	59%	43%	
Ex - smokers	14%	17%	.07
Current smokers	28%	40%	
Positive skin test	48%	40%	ns
Methacholine slope <sup>1</sup>	-19.3	-19.6	ns

**Table 1 - Baseline Characteristics of Participants**

	Machinists	Others	p
n	82	159	
Years between tests	2.07	2.05	ns
Quit trade	16%	3%	.001
Hours of work with metalworking fluid exposure; mean (range)	199.0 (0,658)	0	
ΔFEV <sub>1</sub> (ml/yr)	-60.5	-63.5	ns
Quit smoking between tests	3%	3%	ns
Positive skin test	57%	45%	.07
Methacholine slope <sup>1</sup>	-35.7	-18.4	.08
Change in methacholine slope	-16.4	1.2	.05

<sup>1</sup> Least squares regression slope of the relationship between FEV<sub>1</sub> and methacholine concentration

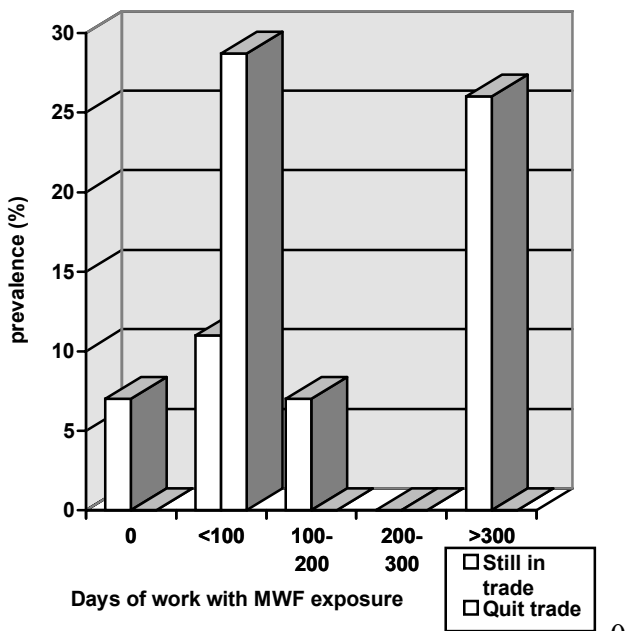
**Table 2 - Characteristics of participants at follow-up**

At baseline, the groups were well matched for age, level of pulmonary function, and atopic status (measured as a positive skin test response to common environmental allergens). Machinists were somewhat more likely to be non-smokers than the comparison population. At follow-up, there continued to be no differences between the groups for routine pulmonary function test results and the number who had quit smoking between tests. Machinists were slightly more likely to have developed a positive skin test response (but not significantly so). They were also more likely to have quit their trade between the two tests (p<0.001). Among machinists, duration of work involving metalworking fluid exposure ranged

from 0 to 658 hours; none of the control population reported work involving metalworking fluid exposures.

As shown in table 1, bronchial responsiveness (measured as methacholine slope) was not different between the groups at baseline. At follow-up, the mean level of bronchial responsiveness had increased (almost 2 fold) among the machinists but had not changed among the control population.

Methacholine challenge test data are most commonly described, clinically, according to PC<sub>20</sub> category (eg. PC<sub>20</sub> < 2, 2-8, 8-16, 16-32, 32-64). When an individual is shown to have an increase in bronchial responsiveness that results in a shift in PC<sub>20</sub> (to the low end) of more than one category, that increase is generally regarded as marked and of considerable clinical significance.

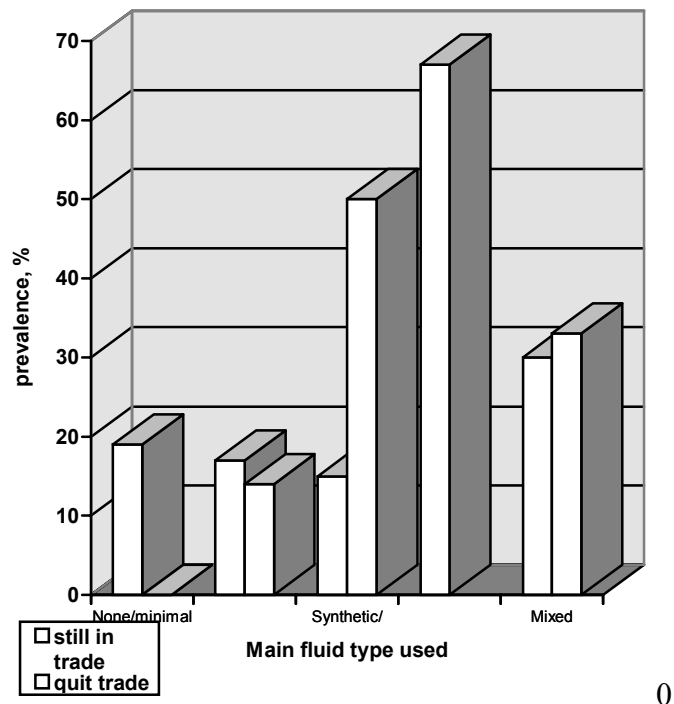


**Figure 1** - Prevalence of Marked Increase in Bronchial Responsiveness

Figure 1 shows the prevalence of a marked increase in bronchial responsiveness among subjects according to duration of work in jobs with metalworking exposure. Shown separately in the figure are those subjects who quit their respective trades between the two testing occasions. For those machinists still in the trade, the difference in

the prevalence rates for a marked increase in bronchial responsiveness according to days exposed was statistically significant ( $p < 0.05$ ). For the small group who had quit the trade, the difference according to days exposed was not statistically significant.

When the subjects were further stratified according to the type of machining fluid exposure and duration of exposure to various fluid types, no significant differences were observed with respect to a marked increase in bronchial responsiveness.



**Figure 2** - Prevalence of a moderate increase in bronchial responsiveness

However, as shown in figure 2, a moderate increase in bronchial responsiveness (defined as a shift in PC<sub>20</sub> of at least one category) was more frequent among machinists working with a mixture of fluid types and among the small number of machinists working mainly with computer controlled machines with synthetic fluids than among those exposed to any one fluid type alone, or those not exposed ( $p < 0.05$ , for differences among all groups).

Although a shift in bronchial responsiveness of this smaller magnitude is of uncertain clinical significance, in this population, the

increase in responsiveness was significantly associated with the development of work-related wheezing and chest tightness at follow-up, and was significantly less frequent among machinists who wore respiratory protection some of the time ( $p < 0.05$ ).

Finally, to evaluate other host and environment characteristics associated with both baseline responsiveness and the change in bronchial responsiveness after two years, multiple linear regression was performed with methacholine slope or change in methacholine slope (log transformed) as the dependent variable and demographic characteristics (smoking, sex, race, age), factors associated with asthma (family history, childhood symptoms), atopy (response to skin tests, hayfever), pulmonary function, as well as exposure to metalworking fluids, as potential predictor variables. Table 3 shows results from the best fitting models. When respirator use was included in the model for change in methacholine slope, it had a negative coefficient and the coefficient for metalworking fluid exposure increased to 0.21 ( $p=0.01$ ).

Factor	Baseline slope		Change in slope	
	co-efficient	p	co-efficient	p
+ve skin test at baseline	0.125	.05	0.127	.04
history of childhood asthma	0.406	<.01	-	ns
FEV <sub>1</sub> (% pred.) baseline	-0.0097	<.01	-	ns
Metalworking fluid exposure	not in model		0.112	.07
Methacholine slope, baseline	not in model		-0.379	<.001

**Table 3** - Linear regression analysis of factors associated with baseline methacholine slope and change in methacholine slope at follow-up (positive coefficient indicates an increase in responsiveness)

We are not aware of any subject in the study population who has developed specific occupational asthma. Therefore, to date, it appears that the increase in bronchial responsiveness associated with exposures in the metal working environment in this population may be a non-specific pulmonary response. However, further

analysis of the results from this study are still underway and these results should not be interpreted as the final conclusions to be derived from this study.

#### ACKNOWLEDGMENT

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## ACUTE RESPIRATORY EFFECTS OF MACHINING FLUID AEROSOLS: EVIDENCE FOR A ROLE OF BACTERIA

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### INTRODUCTION

Several previous studies have reported that machining fluids, or their individual components, can cause impairment of airways function (Hendy et al., 1985 Kennedy et al., 1989; Robertson et al., 1988). However, the mechanisms, magnitude, and the specific agent(s) responsible for airways dysfunction among workers exposed to different machining fluids are incompletely characterized. Our study was specifically designed to address the acute effect of machining fluid exposure on respiratory health. Cross-shift and cross-week changes in pulmonary function and respiratory symptoms were the primary outcome measures.

### METHODS

#### Subject Selection

This study was conducted at an automotive transmission plant in the Midwest This plant has two major machining departments, Case and Valve Body. Both use soluble oils supplied from one of three large sumps. Use of biocides in machining fluids was infrequent. Final Assembly, chosen as the department from which to draw comparison subjects, was physically isolated from, and under positive air pressure with respect to, machining areas and contained no identifiable respiratory hazards. All persons working in Case and Valve Body believed to have machining fluid exposure were individually recruited by University of Michigan study personnel as were a stratified random sample of workers in Final Assembly with a similar age and race distribution to those working in machining areas.

This study involved a preliminary

exposure evaluation (April 1992) and three rounds of full data collection: June 1992, January 1993, and June 1993. During each round of the study participants completed questionnaires and underwent pulmonary function testing (spirometry) on the first work day of the week (Monday) pre- and post-shift and on the fourth work day of the same week (Thursday) pre- and post-shift, and wore air sampling devices on these days.

#### Exposure Measures

Air samples were collected using a sampling device having a median cut diameter of 10 microns, resulting in collection of approximately the "thoracic" fraction particulate on the filter (Marple, 1989). All air samples represented at least 5 1/2 hours of sampling. All filters were analyzed for total thoracic particulate; a randomly selected subset of filters were analyzed for total thoracic bacteria (viable plus non-viable) as well. Personal exposures to thoracic particulate and thoracic bacteria were selected as the key exposure indices. Because measures of personal exposures to endotoxin were available only in Round 3, these were not used in most analyses. In addition, vapor phase nicotine was measured in order to adjust total thoracic particulate for the contribution of particulate derived from tobacco smoke. The findings using tobacco adjusted thoracic particulate were essentially identical to those using total thoracic particulate and are not presented here.

#### Pulmonary Function Testing

Spirometry testing was performed following all current ATS recommendations (ATS, 1987) using computerized water sealed volume displacement instruments (Warren E. Collins Eagle II with Survey, Warren E. Collins, Inc., Braintree, MA) calibrated three times daily with a 3 liter syringe.

### **Relationship Between Exposure to Machining Fluid and Lung Function**

Associations between thoracic particulate concentration or bacteria concentration and change in FVC and FEV<sub>1</sub> across the shift on Monday, across the shift on Thursday, and across the week, were investigated using multivariable linear models. Models which combined data from all rounds were fit using the generalized estimating equation (GEE) method to account for lack of independence of observations on the same individual (Zeger and Liang, 1986). A decision was reached early in the analysis to present separate regression models for current smokers versus ex and never smokers in the final regressions because of many highly significant interactions with current smoking status in preliminary models. The natural log of thoracic particulate was used in models, rather than simple thoracic particulate based on findings from prior animal and human studies (Schaper and Detwiler, 1991; Castellan *et al.* 1987). The natural log of bacterial concentration was also used for consistency.

## **RESULTS**

### **Participation**

Demographic characteristics for Round 1 participants (Table 1) show that there were

significant differences in age, seniority, and shift between assemblers and machinists: machinists tended to be older, had more seniority, and were more likely to be on the second shift. There were no significant differences with respect to height, race, smoking status, or history of asthma. In Rounds 2 and 3, machinists were again significantly older and had more seniority but differences in shift worked were no longer significant.

### **Exposure Results**

Mean concentration of thoracic particulate over the three rounds of the study were 0.13 mg/m<sup>3</sup> in Assembly, 0.32 mg/m<sup>3</sup> in Valve body, and 0.56 mg/m<sup>3</sup> in Case. Average personal exposures thoracic bacteria were 0.38 bacteria/cc in Assembly, and 0.87 bacteria/cc in Valve Body, and 2.66 bacteria/cc in Case. Average personal endotoxin levels, which were collected only in Round 3, were 16.4 endotoxin units/m<sup>3</sup> in Assembly, 34.7 EU/m<sup>3</sup> in Valve Body and 234 EU/m<sup>3</sup> in Case.

### **Cross-Shift and Cross-Week Changes in Lung Function**

Subjects were grouped into three exposures categories using approximately the 25th and 75th percentiles of thoracic particulate measures, and the percentages of workers having at least a 5% cross-shift decrement in FVC or FEV<sub>1</sub> in each exposure group were calculated. A consistent pattern of greater percentages of subjects with 5% decrements in FEV<sub>1</sub> and FVC were seen across all rounds on Monday. The pattern for Thursday did not show such consistency. (Figure 1)

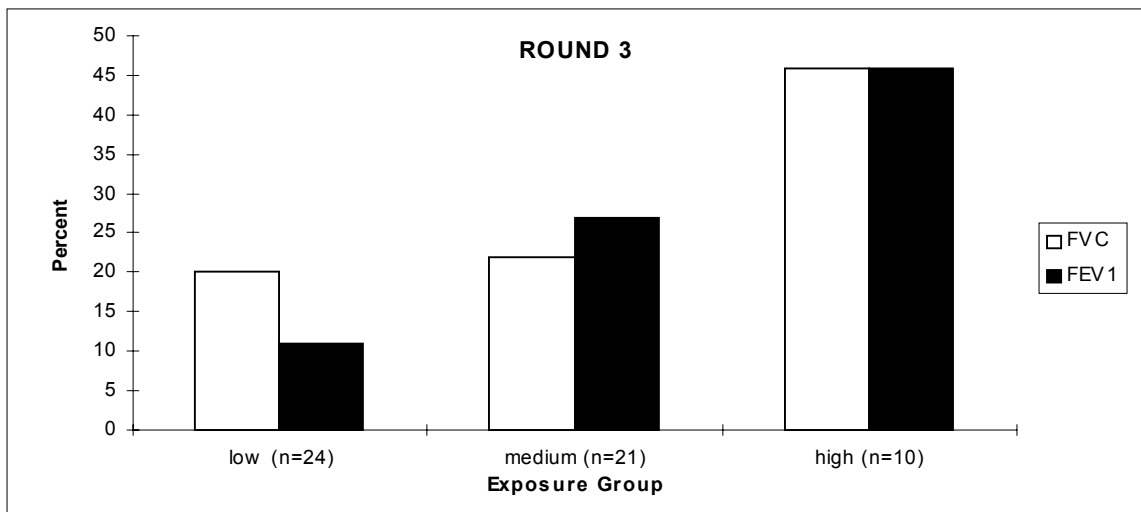
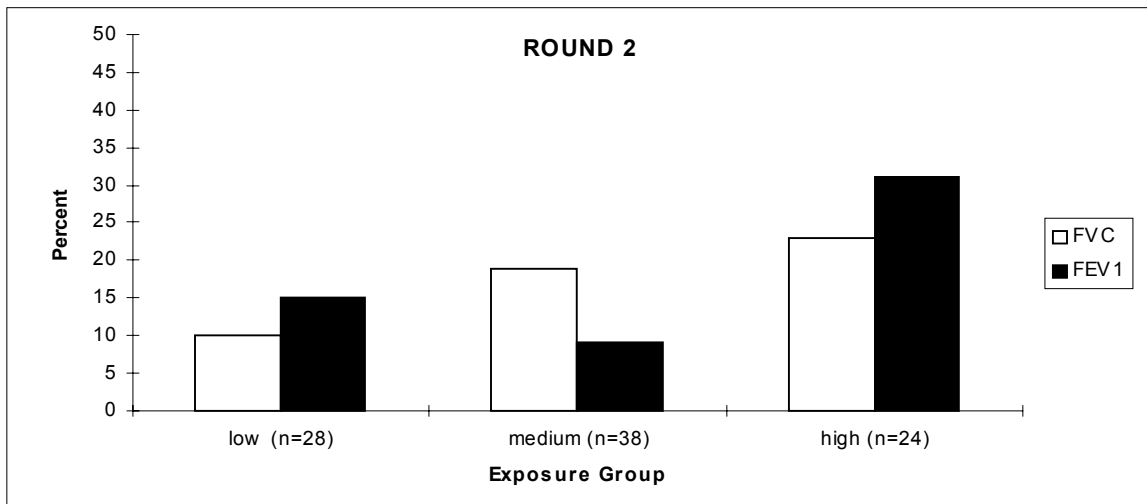
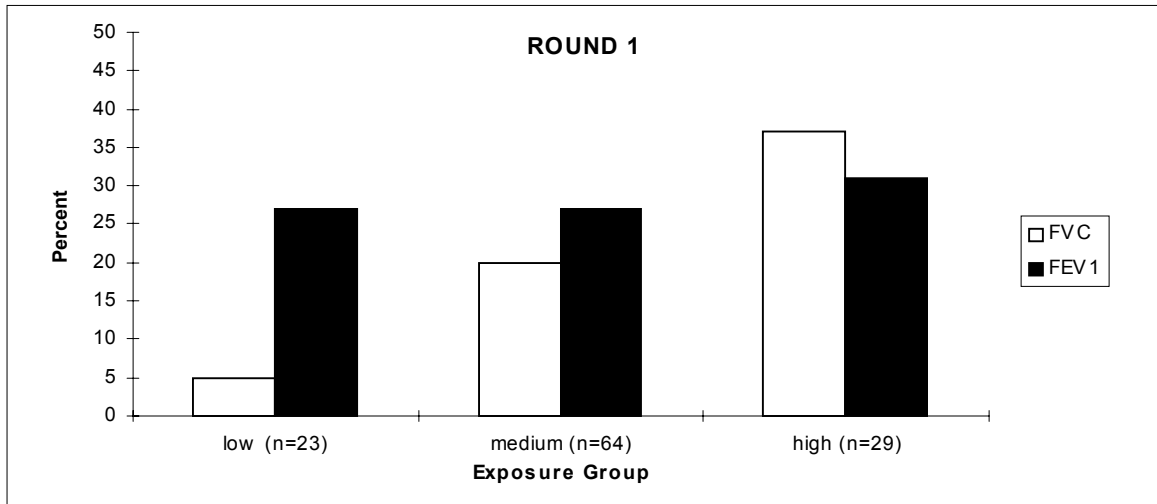
**TABLE I**  
DEMOGRAPHICS OF PARTICIPANTS

	<b>Round 1</b>		<b>Round 2</b>	
	Assemblers	Machinists	Assemblers	Machinists
No.	34	83	34	52
Mean Age, yr.	40.3 ± 1.2	45.3 ± 1.0**	41.3 ± .9	47.6 ± 1.1***
Mean Seniority, yr.	12.1 ± .9	18.6 ± .8***	13.5 ± 1.0	19.9 ± .9***
Mean Height, in.	69.0 ± .5	69.6 ± .3	69.8 ± .5	69.3 ± .4
Race, % black	35.3	50.6	35.3	42.3
Shift, % 1st shift	70.6	44.6**	64.7	55.8
Smoking Status (%)				
Never Smokers	26.5	19.3	29.4	11.5
Ex Smokers	38.2	43.4	35.3	48.1
Current Smokers	35.3	37.4	35.3	40.4
History of asthma predating GM employment, %	8.8	4.8	8.8	7.7
	<b>Round 3</b>			
	Assemblers	Machinists		
No.	22	35		
Mean Age, yr.	41.6 ± 1.4	46.8 ± 1.40**		
Mean Seniority, yr.	13.4 ± 1.1	19.4 ± 1.1***		
Mean Height, in.	70.3 ± .5	69.6 ± .6		
Race, % black	27.3	48.6		
Shift, % 1st shift	77.3	54.3		
Smoking Status (%)				
Never Smokers	36.4	20.0		
Ex Smokers	45.4	34.3		
Current Smokers	18.2	45.7		
History of asthma predating GM employment, %	9.1	8.6		

\*\* differs significantly from assemblers (.001 < p-value < .05)

\*\*\* differs significantly from assemblers ( p-value < .001)

**Figure 1**  
 Percentage of Subjects (All Departments) With At Least a 5% Cross-Shift Decrement  
 On Monday in FVC and FEV1 by Exposure Group



see text for definition of exposure categories

## Regression Models

Multivariable GEE models of cross-shift or cross-week change in FEV<sub>1</sub> which combined data from all three rounds for current smokers and using thoracic bacteria as the exposure measure are presented in Table 2. The baseline-ratio x bacteria term is highly significant ( $p \leq 0.0002$ ) and positive for all three models (i.e., change in FEV<sub>1</sub> on Monday, Thursday, and cross-week). For the Monday and cross-week FEV<sub>1</sub> models the baseline ratio term is also significant and positive. For all three of the analogous changes in FVC models (not shown), the baseline-ratio x bacteria term is again significant and positive. Thus all six models predict that current smokers with low baseline FEV<sub>1</sub> /FVC ratios and high bacteria exposures will have particularly large cross-shift decrements in FEV<sub>1</sub> and FVC. Graphical representations of the models for cross-shift change in FEV<sub>1</sub> on Monday as an example (Figure 2) corroborate this expectation. Associations for the analogous models for thoracic particulate related exposure measures, though generally in the same direction, were not as consistent. In contrast to the models for current smokers, the GEE models combining data from all three rounds for never and ex-smokers demonstrated few significant associations with either type of exposure parameters (not shown).

Table 3 presents tabular results for Monday changes in FEV<sub>1</sub> for those reporting current asthma plus those with a 12% or greater cross-shift change in Monday FEV<sub>1</sub> in at least one round. Among the nine subjects in machining areas and 2 subjects in Assembly who demonstrated 12% or greater decrements in Monday FEV<sub>1</sub> only one from each working environment reported asthma prior to working at this facility (a total of 2 out of 11). Of particular note, 6 of 85 (7%) subjects working in machining areas, but none of the 46 subjects working assembly, demonstrated cross-day decrements in at least one round (Monday or Thursday, FEV<sub>1</sub> or FVC) of unequivocal clinical significance (i.e., greater than 19%) (Fisher's exact test, one tailed:  $p = 0.07$ ).

## Discussion

Bivariate analyses demonstrated positive associations of working in machining areas and higher exposures to thoracic particulate (Figure 1) with decrements in PFTs (especially Monday FEV<sub>1</sub>). These findings closely parallel those of Kennedy et al.

The results of the multivariable analysis are indicative of a three way interaction between higher end bacterial exposures, relatively low baseline FEV<sub>1</sub> / FVC ratios (i.e., pre-shift on Monday), and current cigarette smoking to produce larger cross-day and cross-week decrements in FEV<sub>1</sub> and FVC. It is uncertain whether the total bacterial concentrations themselves or some other parameter correlated with bacterial concentrations (e.g., the correlation coefficient with endotoxin measures is 0.9) is responsible for the observed effect.

The findings that 6 of 85 subjects working in machining areas, but none of 46 subjects working in assembly, had greater than 19% cross-shift decrements in FEV<sub>1</sub> or FVC, strongly suggests that exposures in machining areas using soluble oils are associated with clinically significant adverse acute pulmonary effects in some individuals. The associations between exposures in machining areas and the development of lower respiratory and mucous membrane symptoms during the shift (not shown), lends further support to the hypothesis that these exposures are related to clinically relevant adverse respiratory effects.

In considering the overall findings, certain limitations must be borne in mind. Firstly, there is at least some potential for selection bias as there are some differences between participants and eligible non-participants in Round 1 and between participants in Round 1 versus those in subsequent rounds. However, it appears unlikely that systematic selection differences occurred. Most of the differences seen were in age, race, and shift. Age and race generally were not associated with outcomes of interest and shift was adjusted for in all regression models. Secondly, the study was conducted on a "survivor" population. The mean seniority among machinists was nineteen years.

If, in fact, exposure to machining fluids aerosols is associated with symptomatic respiratory effects, a study of this cohort is likely to underestimate such effects.

**TABLE II**

GEE MODELS COMBINING DATA FROM ALL THREE ROUNDS FOR FRACTIONAL CHANGE\* IN FEV<sub>1</sub> IN CURRENT SMOKERS USING BACTERIA (bacteria/m<sup>3</sup>)

	% Change across shift on Monday	% Change across shift on Thursday	% Change across week
Total # of observations	76	74	75
Number of Subjects	42	42	41
Mean Squared Error	0.0017	0.0032	0.0020
Constant	0.0126** 0.010 (0.2225)	0.0187 0.017 (0.2670)	0.0539 0.015 (0.0005)
Machining area (0=no, 1=yes)	-0.0017 0.009 (0.8493)	0.0169 0.015 (0.2670)	-0.0131 0.014 (0.3371)
Bacterial Level ***	-0.0016 0.005 (0.7566)	-0.0001 0.007 (0.9840)	0.0061 0.004 (0.1362)
Shift (0=1st, 1=2nd)	-0.0510 0.012 (0.0000)	-0.0559 0.014 (0.0001)	-0.0404 0.012 (0.0012)
Number of cigarettes before shift	0.0030 0.001 (0.0285)		
Baseline FEV1/FVC ratio	0.0124 0.007 (0.0910)	0.0085 0.010 (0.4179)	0.0189 0.008 (0.0193)
Baseline FEV1/FVC ratio/ Bacteria Interaction	0.0219 0.006 (0.0001)	0.0232 0.006 (0.0002)	0.0238 0.002 (0.0000)
Pack years	-0.0016 0.000 (0.0000)	-0.0015 0.000 (0.0009)	-0.0029 0.000 (0.0000)

\* fractional change = (final reading - initial reading) / initial reading. For example, cross week change is (Thursday post-shift - Monday pre-shift) / Monday pre-shift.

\*\* estimated effect with robust standard error underneath (robust p-value is parantheses)

\*\*\* calculated as the natural log of the bacterial concentration (average of Monday and Thursday for cross-week)

**FIGURE 2**

Relationship Predicted by GEE Model Combining Data From All Three Rounds Between THORACIC BACTERIA CONCENTRATION and Fractional Change in MONDAY FEV<sub>1</sub> for Monday pre-shift FEV<sub>1</sub>/FVC Ratio X 100 Values of 60, 70, and 80 in the Summer for a White, Male, CURRENT SMOKER on 2nd Shift with a 20 Pack-Year History, Who Smoked 3 Cigarettes Before Shift and Worked 6 Hours During the Shift

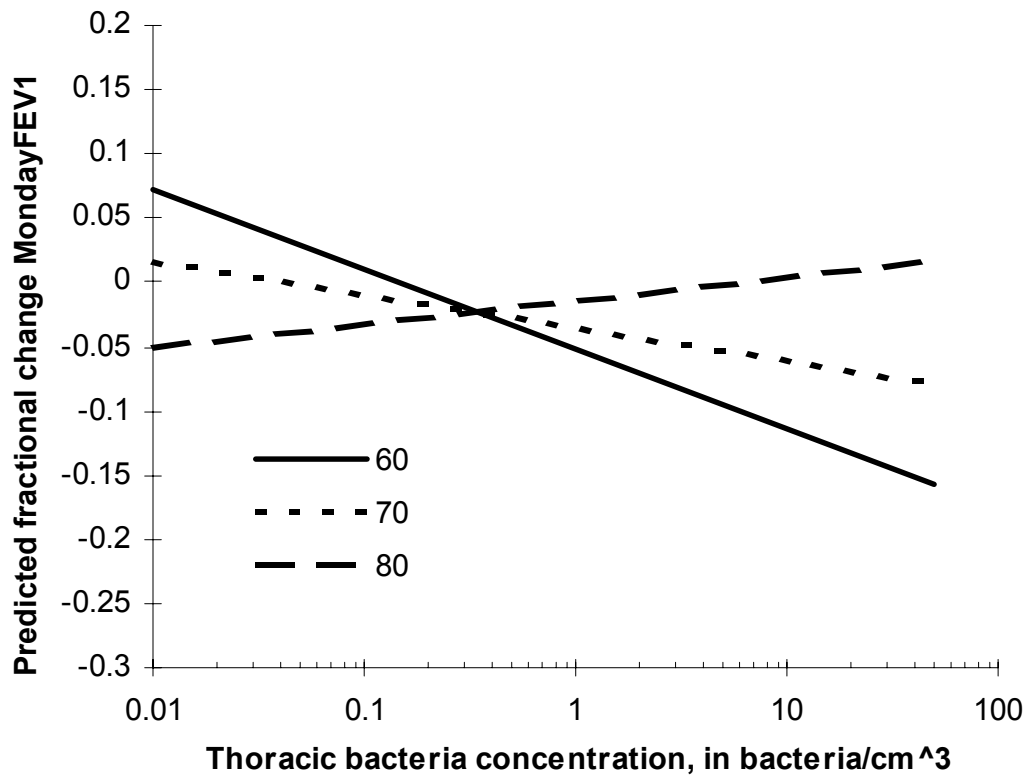


TABLE III

SUBJECTS REPORTING CURRENT ASTHMA AND/OR A 12% OR GREATER  
CHANGE IN MONDAY FEV<sub>1</sub> IN AT LEAST ONE ROUND

Sub- ject	Reports current asthma	Dept	Reports asthma prior to GM	Smoking status	ROUND 1				ROUND 2				ROUND 3			
					BR~	TP** mg/m <sup>3</sup>	Bacteria per cm <sup>3</sup>	Fractional change in FEV <sub>1</sub>	BR~	TP** mg/m <sup>3</sup>	Bacteria per cm <sup>3</sup>	Fractional change in FEV <sub>1</sub>	BR~**	TP** mg/m <sup>3</sup>	Bacteria per cm <sup>3</sup>	Fractional change in FEV <sub>1</sub>
1	yes	case	yes	yes	43	0.46	2.88	-0.253	*36	0.56	0.49	*0.156	*41	1.36	39.56	*+-0.106
2	yes	case	no	yes	59	0.51	0.74	-0.193	65	0.82	5.23	-0.189	-	-	-	-
3	yes	case	no	yes	79	0.42	2.63	0.004	-	-	-	-	-	-	-	-
4	yes	case	yes	no	84	0.56	1.50	0.073	84	0.70	3.40	-0.031	83	0.36	4.25	-0.050
5	yes	case	no	yes	82	0.34	1.47	-0.005	-	-	-	-	-	-	-	-
6	yes	assy	yes	yes	69	.0.20	0.19	0.202	-	-	-	-	-	-	-	-
7	yes	assy	no	yes	83	0.17	0.49	0.052	81	0.15	0.014	0.104	83	0.09	1.35	-0.071
8	yes	assy	yes	no	-	0.14	0.14	-0.003	52	0.16	0.16	++0.355	59	0.07	0.41	0.113
9	no	case	no	yes	48	0.61	2.58	-0.408	42	0.74	1.40	-0.317	43	0.54	10.47	-0.394
10	no	case	no	yes	72	0.56	1.36	-0.136	69	0.66	3.19	-0.184	-	-	-	-
11	no	case	no	no	89	0.38	0.18	-0.124	-	-	-	-	84	0.36	3.08	-0.113
12	no	case	no	yes	81	0.77	1.93	-0.041	86	0.80	0.96	-0.168	78	0.56	17.19	-0.069
13	no	valve	no	yes	72	0.31	3.43	-0.113	79	0.17	0.007	-0.248	77	0.17	0.31	-0.120
14	no	valve	no	no	81	0.23	0.26	-0.196	-	-	-	-	-	-	-	-
15	no	valve	no	ex	79	0.26	0.22	-0.008	69	0.26	0.030	0.127	-	-	-	-
16	no	valve	no	no	87	0.18	0.44	-0.130	-	-	-	-	-	-	-	-
17	no	assy	no	no	-	-	-	-	-	0.11	0.37	-0.161	-	-	-	-
18	no	assy	no	no	-	-	-	-	82	0.15	0.16	-0.180	-	-	-	-

~ Baseline ratio = 100 ( FEV<sub>1</sub>/FVC ) preshift Monday

\*\* Thoracic Particulate

\* Smoking status changed to ex

+ Used inhaler during shift

++ Used "sinus medication" during shift

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## Field Investigation of the Acute Respiratory Effects of Machining Fluids

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### ABSTRACT

The purpose of the study was to investigate the hypothesis that exposure to machining fluids (MF) increases the incidence of short-term (over the work day) decrements in pulmonary function and symptoms of respiratory irritation. A secondary objective was to attempt to identify likely causal agents of such effects from among the various components of machining fluids.

MFs are used for their lubrication and cooling properties and are of 3 main types: straight, soluble and synthetic.

The study was conducted in a large automotive vehicle parts manufacturing facility in a Midwestern state. The plant has been in existence since before the Second World War, and employed approximately 3200 hourly employees running production on three shifts in addition to 1700 salaried employees. Participants were drawn from among the day-shift hourly employees of the facility. The plant performs all types of machining operations, using all three coolant types, although straight and soluble coolants predominate. Exposure to synthetic fluids was not studied in this investigation. Unlike many large automotive machining operations, the machines at this plant were for the most part provided with their own individual coolant systems, rather than being hooked to centralized coolant sumps.

The non-machining populations were recruited from assembly areas and gauge rooms ("assembly") as well as from the training center ("classrooms"). Assembly areas were physically separated from machining areas, although

common air circulation and conditioning systems served both machining and assembly areas. The classrooms in contrast were in a separate building.

Each participant reported to the study office before beginning work on a pre-scheduled day. He/she performed pulmonary function tests and answered a questionnaire on respiratory symptoms and general health status. A personal sampling pump was hung on the participant's belt, and a sample cassette attached to the collar. A filter collected a full shift sample of aerosol in the breathing zone of the participant. A high-volume sampler with Andersen impactor was used to measure viable bacterial concentrations at each participant's work station. Additional industrial hygiene measurements were also made at the participant's work station during the day. For a subset of the participants, a skin prick test was performed to determine whether the participant was atopic (sensitive to common allergens like grass and dust). At the end of the day the pulmonary function tests were repeated.

Each participant's aerosol exposure concentration, the exposure to bacteria in the air at the work station, and the concentrations of a series of components of the bulk MF in the sump on the machine used by each machining participant were calculated. For a subset, the airborne concentration of endotoxin was also estimated.

A total of 216 machining workers participated, which represented approximately 87% of the day shift workers with consistent exposure to either straight or soluble MF, without exposure to synthetic MF. In addition 170 non-

machining workers were recruited into the study, and these comprised approximately 70% of the eligible non-machining day shift workforce.

In general the MF exposure levels that were measured at Allison were lower than in other automotive machining facilities studied. For example, the geometric mean level of inhalable aerosol was  $0.18 \text{ mg/m}^3$  in the machining areas studied at Allison, while it was  $0.17 \text{ mg/m}^3$  in the assembly areas of the two plants studied by Kennedy *et al.* In contrast the machining areas of the Kennedy *et al.* plants had levels about four times higher than in this facility. Airborne bacterial concentrations and endotoxin levels were also lower than in previously studied MF environments.

While the emphasis of the study was short term (acute) respiratory effects, respiratory symptoms that may reflect longer term lung health were also studied. Several of these symptoms did appear to be more common in machining participants than in non-machining participants. These associations held even after the possible confounding effects of age, race, and gender were accounted for in logistic regression models. Especially notable were symptoms of sinus problems which were reported by 47% of machinists and 38% of non-machinists. Machinists exposed to straight MF were more likely to report chronic cough than non-machinists or machinists with soluble MF exposure. There was a nearly three fold increase in the risk of reporting cough in those with straight MF exposure, compared to non-machinists. Machinists with soluble MF exposure were somewhat more likely to report asthma than non-machinists.

Each participant was asked at the beginning and the end of the day to rate the intensity of various acute respiratory symptoms. The change in these ratings was calculated for different groups of participants. Machinists with soluble MF exposure were more likely than nonmachinists or straight MF exposed machinists to report increases in symptom intensity over the workday. In particular, the soluble MF exposed machinists reported increases in eye, nose and

throat irritation.

The average pulmonary function of the participants at baseline (before the start of the shift) was compared to the level of function predicted for individuals with the same age, height, race, and gender as the participants. For most measures of pulmonary function, the participants were quite close to normal. However machinists with soluble MF exposure had approximately 115 ml lower FEV<sub>1</sub> on average than non-machinists, after controlling for the other predictors of lung function mentioned above. This is about 3% of the average value of this lung function parameter in this population.

The principal measure of lung function that we studied was the change in the FEV<sub>1</sub> from the beginning until the end of the workday. A drop or decrement in the FEV<sub>1</sub> over the day is interpreted as an indicator of acute (short term) response of the airways to an irritating or inflammatory agent in the air. We calculated the percent of the population who experienced a drop in FEV<sub>1</sub> over the day that was at least 5% of the morning value rather than study the average change in FEV<sub>1</sub> over the day. Because this method is essentially a count of those responsive individuals in the "tail" of the distribution of outcomes, it tends to be a more sensitive measure of early effects on pulmonary function. The FEV<sub>1</sub> response was higher in non-machinists than in machinists. However, there was evidence that within each of these two groups the FEV<sub>1</sub> response increased with increasing exposure to aerosol. These data suggest that there was approximately a three-fold increase in the incidence of 5% FEV<sub>1</sub> response in those with exposures above  $0.15 \text{ mg/m}^3$  compared to those with exposures below  $0.08 \text{ mg/m}^3$ .

It is possible that the higher incidence of FEV<sub>1</sub> response in non-machinists compared to machinists was due to selection pressures through which more sensitive individuals move from the more highly exposed machining environment into non-machining. Indeed, most non-machinists had at one time worked in machining. We observed only a weak association between endotoxin exposure and cross-shift change in FEV<sub>1</sub>.

However, the levels of exposure were much lower than those for which such effects have been previously reported. We observed no association between lung function and viable bacterial concentration.

For a subset of the Phase I participants, analyses of the concentrations of a series of elements were conducted on the air samples. With these data it was possible to investigate hypotheses about particular elements and their compounds and the associations of these with pulmonary function. From these investigations we identified an association between sulfur and its compounds and cross shift change in FEV<sub>1</sub>. Specifically, those participants in a nested case control study who had sulfur exposures above the median (3.2 mg/m<sup>3</sup>) were about three times as likely to experience decrements in FEV<sub>1</sub> over the work shift of 5% or greater than those with exposures below the median.

Using a statistical model, we estimated the sulfur exposure concentrations for those Phase I machinists whose elemental sulfur concentration was not actually measured. Using these sulfur concentration data, the association with cross-shift drop in FEV<sub>1</sub> could be studied among all the machinists in the full Phase I cohort. The incidence of 5% or greater drop in FEV<sub>1</sub> over the

day rose with sulfur exposure, in a linear trend ( $p=0.05$ ). When the group was divided into thirds, the relative risk of 5% or greater drop in FEV<sub>1</sub> over the day for those in the highest third ( $> 1.5$  mg/m<sup>3</sup>) was approximately 3.7 times that for the lowest third ( $< 0.9$  mg/m<sup>3</sup>). In conclusion, this study provides evidence consistent with both chronic and acute respiratory responses associated with MF exposure. The chronic effects include increased prevalence of sinus problems, cough, and possibly asthma in MF exposed participants, as well as a decrease in the FEV<sub>1</sub> of soluble MF exposed machinists. The acute responses are consistent with the observation by Kennedy *et al.* of an association between aerosol exposure level and cross-shift FEV<sub>1</sub> decrement. In addition, an association between sulfur exposure and cross-shift FEV<sub>1</sub> decrement was observed. We hypothesize that sulfur is not the single MF constituent responsible for the irritant effects observed. Instead, we suspect that it represents a marker of the MF exposure conditions in this plant that were particularly irritating.

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## Occupational Asthma and Respiratory Symptoms Among Workers Exposed to Machining Fluids

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### ABSTRACT

From 1988-1994, the Michigan Department of Public Health has received 86 occupational disease reports of occupational asthma secondary to exposure to machining coolants. Machining coolants are the second most common cause of occupational asthma reported in the state. Most of the reports are from the auto industry.

Followup inspections have been conducted at 37 facilities where the individuals with occupational asthma worked. Seven hundred and fifty-five workers at these facilities were interviewed. Only one facility was above the allowable oil mist standard. Despite the exposure levels being within the legal limits, approximately 20% of the fellow workers of the reported cases had daily or weekly respiratory symptoms suggestive of occupational asthma. Workers exposed to emulsified, semi-synthetic or synthetic machining coolants had an increased prevalence of respiratory symptoms consistent with occupational asthma as compared to workers exposed to mineral oil machining coolants.

### INTRODUCTION

Exposure to machining coolants and ethanalamines found in machining coolants have been associated with occupational asthma. We have reviewed the data from a state-wide surveillance system for occupational asthma to identify individuals with occupational asthma from exposure to machining coolants. Additionally, we have reviewed respiratory symptoms among workers at facilities where the individuals with occupational asthma worked.

### METHODS

In 1988, the Michigan Department of Public Health (MDPH), with financial assistance from the National Institute for Occupational Safety and Health (NIOSH), instituted a surveillance program for occupational asthma. There are three sources used to identify persons with occupational asthma: (1) reports from physicians; (2) workers' compensation claims filed with the Michigan Department of Labor; and since 1989, (3) reports from hospitals. Both physicians in private practice and those working for industry send reports to the State Department of Public Health. Reports from hospitals are requested once each year. Hospital discharge summaries for individuals with a primary or secondary diagnosis of a respiratory condition due to chemical fumes or vapors (ICD 506.0-9) are obtained and the work-relatedness of the condition is determined.

A person is considered to have occupational asthma from sensitization to a workplace exposure if: (1) they have a physician diagnosis of asthma, and (2) onset of respiratory symptoms associated with a particular job that then improve or are relieved when the patient is not working, and (3) they work with a substance previously associated with asthma, or have evidence of an association between work exposures and a decrease in pulmonary function testing.

If only criteria (1) and (2) above are met the person is considered to have work-related asthma from a substance not previously associated with asthma. If a person had physician diagnosed asthma before beginning work and their asthma became worse at a particular job the person is considered to have aggravated asthma. However, individuals with childhood asthma whose asthma became asymptomatic for a year or more and who

then had symptoms at work were not considered to have aggravated asthma. Occupational asthma from exposure to an allergen at work typically develops after a variable period of symptomless exposure to the sensitizing agent. However, if a person develops asthma for the first time immediately after an acute exposure to an irritating chemical at work the patient is considered to have Reactive Airway Dysfunction Syndrome (RADS).

Only individuals who met all three criteria for occupational asthma from sensitization to a machining coolant are included in this analysis. After the patient has been interviewed and the work-relatedness of their condition evaluated, an industrial hygiene investigation may be conducted at the patient's work place. At this follow-up investigation, co-workers who work in the same area as the index case and are present at work during the industrial hygiene inspection are asked to complete a confidential medical questionnaire concerning respiratory symptoms. OSHA logs for the previous five years are reviewed to identify workers with occupational asthma. An industrial hygienist conducts air monitoring for any suspected allergens and reviews the company's health and safety program. At the conclusion of the investigation, a report is compiled. The report includes when appropriate: air sampling results; citations; and recommendations.

## RESULTS

From 1988-1994, the MDPH received 86 occupational disease reports of work related asthma from exposure to oil mist at 45 different facilities. Oil mist is the second most common cause after isocyanates of work-related asthma in Michigan. These individuals were exposed to oil mists from a machining operation in the types of facilities listed in Table I. The type of machining coolant is shown in Table III.

Among the 45 facilities identified, 37 were inspected. Among the 37 facilities inspected, air sampling for oil mist was performed in 22. Among the 22 facilities where air sampling was performed only one facility was identified with exposure levels above the OSHA (MIOSHA)

standard of  $5 \text{ mg/m}^3$ . Both interviews and air sampling were conducted at 19 of the companies inspected. Interviews of 429 workers were conducted at the 18 facilities where exposure levels were below  $5 \text{ mg/m}^3$ , and showed that 79 had either developed asthma since beginning work at the facilities or had daily or weekly shortness of breath, wheezing or chest tightness associated with work.

**TABLE I:** Types of industries where exposure to oil mist was reported to cause occupational asthma.

Manufacturing Industry (SIC)	#	%
Electroplating (3471)	1	1.2
Fabricated metal products (3499)	1	1.2
Internal combustion engines (3519)	1	1.2
Industrial trucks (3537)	1	1.2
Machine tools (3541)	1	1.2
Special dies and tools (3544)	2	2.3
Machines and cutting tools (3545)	3	3.5
Ball and roller bearings (3562)	1	1.2
Air conditioner equipment (3585)	1	1.2
Motor vehicle & car bodies (3711)	1	1.2
Auto parts (3714)	71	82.6
Aircraft parts, NEC (3728)	1	1.2
Transportation equipment (3799)	1	1.2
Total	86	100.4*

\* Percent does not total 100 due to rounding

These later symptoms are typical of those seen with work-related asthma. Oil mist exposures to employees in these 18 facilities ranged from nondetected ( $< 0.1 \text{ mg/m}^3$ ) to  $3.57 \text{ mg/m}^3$ . Of the 67 air samples analyzed, only 11 were greater than  $1.0 \text{ mg/m}^3$ . In 13 facilities interviews were conducted but no sampling was done because in the industrial hygienist's opinion the oil mist levels would not have exceeded the State of Michigan OSHA standard.

**TABLE II: Results of Industrial Hygiene Inspections of 37 Facilities using Machining Coolants**

Air Sampling Status	Number of Facilities	Number of Interviews	Workers with symptoms suggestive of Occupational Asthma	
			Number	Percent
No Air Sampling*	15 <sup>†</sup>	318	76	23.9
Air Sampling <0.1-3.57 mg/m <sup>3</sup>	21 <sup>††</sup>	429	79	18.4
Air Sampling >5.0 mg/m <sup>3</sup>	1	8	0	---
Total	37 <sup>‡</sup>	755	155	20.5

\* Air sampling was not performed because in the industrial hygienist's opinion, the oil mist standard would not have been exceeded.

† Interviews were conducted in 13 facilities.

†† Interviews were conducted in 18 facilities.

‡ Interviews were conducted in 31 facilities.

**TABLE III: Percentage of Individuals with New Onset Asthma or Symptoms Suggestive of Work-Related Asthma by Type of Machining Coolant**

Coolant Type	Number of Occupational Asthma Reports Received	Number of Facilities	Range & Avg. % of Symptomatic Individuals, by Facility		Number of Individuals Interviewed	Number & Percent of Symptomatic Individuals	
			% Range	Average %		#	%
Mineral Oil	17	12*	0.0-23.8	8.7	183	18	9.8
Emulsified	13	9 <sup>†</sup>	0.0-44.4	25.7	115	27	23.5
Semi-synthetic	2	2	0.0-50.0	25.0	14	4	28.6
Synthetic	44	13 <sup>††</sup>	0.0-49.5	20.3	420	106	25.2
Total	76	36 <sup>‡</sup>	0.0-50.0	18.5	732	155	21.2

\* Interviews were conducted in 10 facilities.

† Interviews were conducted in 7 facilities.

†† Interviews were conducted in 12 facilities.

‡ Interviews were conducted in 31 facilities.

Interviews of 318 workers at these 13 facilities indicated that 76 had either developed

asthma since beginning work at the facility or had the respiratory symptoms listed above at work which are consistent with work-related asthma (Table II). In five facilities inspected, no interviews of workers were obtained.

In 36 facilities the type of machining fluid was characterized: 12 used only mineral oil; nine used an emulsified oil (two also used a mineral oil); two used a semi-synthetic (one also used emulsified oil, one also used a mineral and emulsified oil); and 13 used a synthetic (four also used an emulsified oil, one also used a mineral oil, one also used a semi-synthetic oil, one also used semisynthetic and emulsified oils; and two also used mineral, emulsified and semi-synthetic oils). The average percentage of symptomatic individuals by coolant type is shown in Table III. The results remain the same when controlling for cigarette smoking. Ten other workers were identified by the company on the OSHA log as having work related asthma: four workers from two facilities using mineral oil; and six from four facilities using synthetic oils.

## CONCLUSIONS

Machining coolants are the second most common cause of occupational asthma reported by physicians in the State of Michigan. Followup investigations at the workplaces where the reported cases became ill show high percentages of symptomatic individuals even though exposures in the workplaces are within the legal air standards for oil mist. Work with emulsified, semi-synthetic or synthetic coolants was associated with a higher percentage of symptomatic individuals than work with mineral oil coolants (Table III).

Limitations of our data include: 1) physicians who report occupational asthma rarely confirm their diagnosis with pulmonary measurements performed in relationship to exposures at work; 2) no confirmation of occupational asthma is performed on fellow workers who are identified by questionnaires at the workplace; and 3) individuals with workplace asthma who leave the workplace will not be included during the followup interviews.

Additional work is needed to determine what particular chemical components and/or microbial contaminants are the cause of the respiratory symptoms and work related asthma associated with exposure to machining coolants.

## ACKNOWLEDGEMENTS

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## Review of Acute Respiratory Health Effects

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### ABSTRACT

This extended abstract is designed to provide some background to some of the issues that will be discussed at the Symposium when data from some of the recently completed and ongoing epidemiological investigations examining the acute health effects of exposures to metal working fluid (MWFs) aerosols will be presented. Some of the confounding factors are presented that make identification of the causes of adverse health effects from the measurements of acute pathophysiological responses to inhaled substances complex. Definitions and examples of what constitutes an adverse health effect are discussed in terms of impairment in functions of daily living. The airway reflexes associated with acute exposures to non-allergic stimuli that include high pH, hypotonic saline, and irritants are outlined. The mechanism and requirement for establishing sensitization in defining occupational asthma is presented together with a short discussion of some of the predisposing factors that can account for a diversity of airway reactivity to non-specific exposures that are observed in a typical study group. These factors include airway inflammation associated with asthmatic airways, viral infection, and chronic bronchitis. A short discussion concerning the beneficial and detrimental effects of exposure to bacterial endotoxins is included.

### INTRODUCTION

It is generally recognized that working with metal working fluids (MWF) is associated with an increased prevalence of acute respiratory responses that include cough, increased upper and lower airway secretions, and airway constriction that can potentially result in wheezing and a shortness of breath. These effects have been

linked to the usage of all types of fluid that include straight oils, soluble oil emulsions, semi-synthetic, and synthetic fluids. Additional problems appear to be associated with the use of those fluids with relatively high water content (> 60%), that often have been attributed to microbial contaminations.<sup>(1)</sup> Although there have been a range of both experimental animal and human exposure studies conducted to identify the potential health hazard associated with specific MWF components, there have been few studies conducted at work-sites to establish dose-response relationships to ascertain whether observed biological responses are manifestations of normal host defense mechanisms or truly indicative of adverse health effects under conditions of repeated exposure. There is also a need for identifying populations at risk, although there is an indication that individuals with moderate and severe asthma associated with increased hyperreactive airways most likely do not stay in jobs with constant exposure to aerosols that potentially contain both non-allergic and allergic stimuli. However, mild asthmatics and individuals with airway inflammatory conditions might be expected to have elevated responses.

Unlike other occupational exposures, epidemiological studies directed towards the investigation of the health effects of metal working fluid exposures is complicated by a considerable diversity in formulation and application, and in a wide range of management procedures used to control microbial contamination. However, one particular published study is noteworthy for its demonstration of an association between MWF exposures and a substantial proportion of workers (23.6%) demonstrating a Monday cross-shift decrease in airway caliber measured by > 5%

decrements in forced expiratory volume measured in 1 sec ( $FEV_1$ ).<sup>(2)</sup> This value is compared with a prevalence of 9.5% in a control group of assembly workers. Although in this investigation, a substantial percentage of both machinists and assembly workers demonstrated improved cross-shift pulmonary function, the presence of a sub-population of affected machinists has raised the major issue that such observed responses might be predictive of chronic MWF exposure-induced occupational asthma, in a similar fashion to that identified in industries where individuals have been exposed to chemical and biological sensitizers.<sup>(3,4)</sup>

Although the more recent studies extending this previous MWF investigation have yet to appear in the peer-reviewed literature, data and the associated synthesis and conclusions are to be presented for discussion at this Symposium.

Rather than predicting the results and conclusions of these presentations, it would appear more appropriate in this preview to outline in general terms some of the issues that could be raised by the participants and discussants at the Symposium.

## **BACKGROUND FOR DISCUSSION**

### **Adverse Health Effects:**

In 1964, as part of a report of the Advisory Committee to the Surgeon General, members of the American Thoracic Society established guidelines to assist in the interpretation of epidemiological data for establishing what pathophysiological responses constitute "adverse respiratory health effects."<sup>(5)</sup> They list a series of health effects that result from exposures to airborne substances ranging in increasing severity from eye, nose, and throat irritation, to reversible reductions in  $FEV_1$ , to enhanced rates in the predictive age-related decline in baseline  $FEV_1$  associated with the development of irreversible chronic obstructive lung diseases (COPD), and to other diseased states that result in impairment of activities of daily living and premature death.<sup>(5)</sup> These latter effects include increased frequency of symptomatic asthmatic attacks, lower respiratory tract infections, and the development of cancers.

The authors note that although a finding might be statistically significant, it could require a medical judgement to assess its medical or biological significance. Such judgements might vary considerably between, physicians, patients, and investigators. Physiological or pathological changes that either interfere with normal activity, or result in episodic illness, or are disabling, or result in irreversible and/or progressive dysfunction, can clearly be identified as being adverse. For example an asthmatic attack would be considered to be adverse since it clearly affects normal activities. However, eye, nose and cough irritation could be considered to be a nuisance but not necessarily an adverse health effect. However, if such an irritant exposure results in a repeated response or triggers a more severe condition such as an asthmatic attack, one might expect a profound effect on the productivity and the quality of life of the exposed individual. Such an exposure could therefore be considered adverse. In contrast, relatively small reversible changes in airway obstruction, indicated by declination of  $FEV_1$  and often associated with airway infection or exposures to irritant air pollutants, might not necessarily be considered to be representative of an adverse health effect even under conditions of repeated incidence, especially if there is no evidence of long-term irreversible effects on pulmonary function.

### **Reflexes:**

The sneeze, the cough, airway constriction, and enhanced production of nasal and conductive airway secretions all represent important lung defense mechanisms that protect the more sensitive lower airway and alveolar structures from the damaging effects of inhaled, corrosive agents, irritant gases and particulates, and other inhaled foreign substances. These reflex responses result from nasal and conductive airway neural receptor interactions with the inhalant that result in a range of physiological responses that include decreases in the frequency and pattern of breathing (Kratschmer reflex), and chemical irritant receptor-mediated airway constriction.<sup>(6)</sup> The Kratschmer or diving reflex

has been extensively used in mouse experiments to predict the potential of airborne irritants including metal working fluids and their constituents to cause sensory irritation.<sup>(7)</sup> In the case of MWF exposures in the work-site environment, odors resulting from microbial contamination, irritant additives, and the alkaline additives added to sustain a relatively high pH to retard microbial growth, all have the potential to trigger these reflex responses. It should be noted that the development of droplet nuclei resulting from water evaporation in dry atmospheres, could concentrate MWF components into smaller less visible respirable particles that would more readily reach the lower airways on inhalation. Such a process might also raise water-containing MWF pHs to even higher levels than the recommended value of 8.5, enhancing irritation, mucus membrane disruption and cell death. Since in some cases metal working fluids are diluted with deionized water, it should be noted that inhalation of hypo- and hyper-osmolar aerosols can potentially trigger both cough and bronchomotor reflexes, especially in mild asthmatics with increased non-specific airway reactivity to non-allergen challenges.<sup>(8,9)</sup>

### **Cell-Mediated Bronchospasm:**

Inhalation of both non-allergen and such specific antigens as pollens, animal dander, dust-mite feces, and chemical sensitizers such as heavy metal salts (eg. cobalt and nickel) and isocyanates, can trigger airway mast cell release of such spasmogens as histamine and leukotrienes that directly act on airway smooth muscle to cause immediate airway constriction.<sup>(4)</sup> Prior low level exposures can lead to the development of allergic asthma associated with the stimulation of the immune system to increase specific immunoglobulin (Ig)E antibody receptors on bronchial mast cells and basophils, enhancing sensitivity so that the bronchospasm is triggered at lower inhaled concentrations. Understanding the inherent, cellular, and physiological determinants that explain why some individuals identified as asthmatics, demonstrate intense reversible airway bronchospasms, continues to be a major area of

investigation. Some asthmatic individuals will also demonstrate an inflammatory cell-mediated late phase reaction that is often observed several hours after the initial reaction has subsided as increased mucus secretion and a bronchospasm. In some cases, only the late phase response is expressed. It is the complexity and range of asthmatic responses that has resulted in difficulties in diagnosis and the reliance on working definitions, since wheezing, cough and breathlessness that are characteristic of asthma, are also associated with non-specific airway reactivity and chronic bronchitis. Occupational asthma has been defined clinically as "wheezing breathlessness occurring after exposure to a sensitizer at work."<sup>(4)</sup> Therefore, even though observed acute respiratory effects elicited by MWF exposure might be considered to be indicative of the early signs of a developing occupational asthma, increased sensitivity to exposures over a period as short as 4 or 5 days and as long as several years, would be considered to be a prerequisite by many investigators. The identification and removal of components from MWFs that are known sensitizers would represent a major component of risk management programs.<sup>(10)</sup>

Although bronchial asthma is considered to be determined by both genetic and exogenous factors, there has been a dramatic worldwide increase in allergic- and exercise-induced asthmas during the last ten years. This increase has been attributed to a wide range of factors that include changes in diet, increased indoor and outdoor air pollution, and the accumulation of allergens as a result of enhanced recycling of air within buildings to conserve energy.

### **Airway Reactivity:**

The lung parasympathetic vagal nerves mediate both bronchial constriction and mucus secretion. Alterations in the local environments of the afferent nerve endings associated with chemoreception and the cholinergic efferent nerve synapses with the airway smooth muscle also represent major determinants of response to non-specific stimuli.<sup>(11-13)</sup> Airway epithelial cell

damage as a result of mechanical disruption, irritant exposures, or the presence of a viral infection can increase access of inhalants to the afferent nerve endings that trigger reflex bronchoconstriction. The associated increased secretion of airway mucus and tissue swelling has the potential to cause increased airway obstruction that would be observed as a decreased FEV<sub>1</sub> measurement. Low level exposures to irritants such as those found in cigarette smoke can result in the infiltration of inflammatory cells. These cells include macrophages, eosinophils, neutrophils, and neutrophils that by their ability to release lipid and protein mediators, have been associated with altered smooth muscle activity and vagal nerve signal processing. Enhanced bronchial reactivity to non-specific challenges that include distilled water, methacholine, histamine, strong smells, cold air, irritants, and deep breathes have been shown to be enhanced in asthmatics who in most cases have underlying airway inflammation.<sup>(11)</sup> Certain groups of individuals that have either transient or chronic inflammation of the airways would also be affected, and although there is a wide range of reactivity to non-specific airway challenges observed in the general population, it is reasonable to expect that individuals with predisposed airway diseases such as a viral infection or chronic bronchitis who may or may not have detectable decreased predicted FEV<sub>1</sub>'s, would demonstrate enhanced bronchoconstrictive responses to non-specific inhaled aerosols.<sup>(14)</sup>

It should be noted that individuals who have experienced either a single or repeated acute exposures to a toxic substance that has caused major airway mucosal damage and airway inflammation, have acquired airways that are hyperreactive to non-specific stimuli. This reactive airways dysfunction syndrome (RADS) is not associated with any sensitization and although in most cases pulmonary function returns to normal, a relatively long period of disability with symptoms similar to an asthmatic are experienced.<sup>(4)</sup>

### **Bacterial and Fungal Contamination:**

The health risks associated with exposure to MWF contaminated with Gram negative bacteria are well recognized.<sup>(1)</sup> Although exposure to high levels of the endotoxins cell wall product of Gram-negative bacterial death can result in fever,<sup>(15)</sup> it is the exposure to low levels of MWF containing endotoxins that has become of recent interest, especially since some biocides may remove bacteria and fungi, but not necessarily inactivate endotoxins. Endotoxins are found in a variety of domestic outdoor and occupational dusts and have the potential to stimulate alveolar macrophage release of cytokine mediators that cause bronchoconstriction and the initiation of an airway inflammatory response.<sup>(16,17,18)</sup> In the case of endotoxin-contaminated cotton dust, there appears to be a relatively consistent dose-response relationship between exposure and observed cross shift decrements in FEV<sub>1</sub>.<sup>(19,20,21)</sup> However, low level exposures to airborne and ingested endotoxins are a part of every day living which are dealt with by lung and gut defense mechanisms that can tolerate moderate levels of exposure. Low level inhalation exposure is considered to be beneficial because of endotoxin-stimulation of macrophages to produce tumor necrosis factor- $\alpha$ , enhancing lung defences against tumors, as discussed by Rylander.<sup>(22)</sup> There is also a suggestion that this level of inflammatory stimulation could also depress IgE-mediated allergic reactions. However, if defense mechanisms are overwhelmed, it is clear that endotoxin can cause major airway irritation, permeability damage, bronchoconstriction, and inflammation.<sup>(15,18,22,23)</sup>

Since bacteria are more susceptible to biocide action than the fungal molds and yeasts, failure to provide sufficient biocide to deal with both these MWF contaminants could result in differential growth of fungi. Hypersensitivity pneumonitis which in some cases progresses to pulmonary fibrosis, has been associated with aerosol exposure to molds and Gram-positive bacteria. It is interesting to note that there is experimental evidence in guinea pigs that endotoxin and mold wall  $\beta$ -glucan act

synergistically in the development of a histology resembling hypersensitivity pneumonitis with early formation of granulomas.<sup>(22,24)</sup>

### CONCLUSIONS:

Based on this very short review, the determination of whether or not MWF aerosol-induced cough, increased nasal secretions, and/or incidences of reflex bronchoconstriction are truly acute adverse health effects are most likely a matter for local judgement, where the application of exposure management protocols might be readily linked to quantifiable measures of improved performance and qualitative indices of improved quality of working conditions. Careful use of biocides and regular changes of the MWF represent methods of intervention that can be readily tested for their effectiveness in decreasing the consequences of microbial contaminations. Interpretation of decreased cross-shift FEV<sub>1</sub> measurements in subpopulations of sensitive machinists as indicative of an adverse health effect is obviously complex. It could be difficult to clearly separate effects that can be directly attributed to MWF exposures from the many interrelated factors that determine individual airway tone, reactivity, and reversible airway obstruction on exposures to dusts and irritants found in both domestic and workplace settings. Longitudinal studies with more detailed clinical evaluations to determine possible baseline changes in pulmonary function tests, bronchodilator reversibility of cross-shift decrements in FEV<sub>1</sub>, measurements of specific and non-specific airway reactivity in controlled exposure settings could be considered a prerequisite to establishing any association between MWF aerosol exposures, acute health effects, and the development of irreversible diseased states such as occupational asthma. The ability to conduct such studies could continue to be confounded by the diversity of different MWF compositions and their changing composition and contamination during use. However, measurements of acute respiratory symptomatic responses and changes in airway reactivity should be considered for use in evaluating the implementation of cost-effective site-specific interventions and management

procedures.

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**Dr. JAMES D'ARCY, General Motors:**

Thank you very much Dr. Bassett. At this point we've heard five presentations in this important area for health in the industrial metalworking environment. This is an area that has only been systematically studied now for about ten years or so, and it is certainly going to be an important area as we move forward and make changes in the workplace. It is likely to be one of the major concerns, so I'm looking forward to the discussion of this subject, but at this point we want to adjourn for some refreshments, and we'll reconvene in 15 minutes.

## DISCUSSANT'S COMMENTS and OPEN DISCUSSION

**Dr. JAMES D'ARCY, General Motors:**

Well, we would like to continue this session looking at respiratory health effects and the epidemiologic study of those and so I would like to introduce now our first Discussant who is Charles Bradford, Director of Health and Safety for the International Association of Machinists and Aerospace Workers and he's essentially going to give us the workers' perspective on this particular important area of health.

**Mr. CHARLES BRADFORD, IAMAW:**

Thank you very much. I appreciate being here because I think this is an important Symposium. I think when we can bring all the folks together like we have here, that who is going to come out ahead is going to be our workers.

I guess I would like to say that our workers sort of, in spite of some of the things I have heard today, that without research and without the data that we have here, they think that there's still a problem because some of the tumors in their bodies and the infections on their skin and the problems with breathing are there and they just can't explain why.

There are those who work with metalworking fluids who have respiratory problems that other workers in the plants don't have and without scientific evidence, they have come to the conclusion that machinists who work with metalworking fluids get sicker or sick more often than other workers in the plant who don't work with these metalworking fluids. They think that they have unsolved health problems and unsolved health problems can mean not only the loss of their health, but the loss of their livelihood as well. Machinists know that the metalworking fluid problem is complex.

It's not just the manufactured product and what's in it, but how it gets contaminated on the shop floor, improper engineering controls, the effects of other chemicals and substances on the product and how we inform and educate our workers who have to work with and in the product

every day. We know this is not a simple problem with a single solution.

Let me give you an example of a shop floor situation where one of our members working with these fluids not only has his health jeopardized, but his economic future is jeopardized as well. In a machine shop in an aerospace manufacturing plant, the machinist had approached the safety committeeman and complained of the rash and respiratory problems that he had been experiencing and asked the committeeman what could be done about it.

The committeeman checked all monitoring data which revealed that the permissible exposure level had not been exceeded. The committeeman also checked to make sure that the member was wearing all the necessary proper protective equipment. The member was wearing what was required for the job. The committeeman approached the employer and asked what can we do for this worker?

The company's response was that the coolant was probably not causing the rashes or the respiratory problems that the member was experiencing. The employer sent the machinist to the plant hospital and the physician gave him some cream for the rash and told him that he may be asthmatic and if the problem does not change, that he should go see his physician.

After a number of months, his condition did not change. So he went to his personal physician and his physician recommended that he no longer work in that coolant, but to work on another machining operation. So the member went back to the plant's medical physician and showed them the letter from his doctor, stating that his doctor highly recommended that the machinist no longer work with this coolant for health reasons. So the company medical staff assigned a physical code to this member, saying that he could no longer operate the machine that was using this coolant.

Now the member returned to the machine shop and gave his supervisor a slip of paper

showing that he had been assigned a code for medical. The supervisor and his upper management told the machinist "you were hired to operate that machine. If you can't operate it, we can't use you." So what do the members do? They keep quiet, and we not only have a worker whose health continues to degenerate, but you have an under-reporting problem of these physical health conditions which can obviously lead to more serious health problems. So if we have under-reporting and these things go on all the time, do we really have a handle on how serious the problem is on the shop floor?

The problem is more than just the chemical composition in the machine working fluids, it's also the engineering controls of cutting operations.

The control of cutting fluids is a concern. If an operation is not properly controlled, such as the mist sprays too much or not enough fluid, the metal cutting fluids and their by-products become airborne and health problems occur. Engineering controls must be put into place to address these concerns, such as the enclosure of the operation or adequate ventilation at the cutting source, among many other considerations.

The proper monitoring of these operations must be accomplished on a continuous basis. Even with general or local exhaust ventilation, our members continue to experience health related problems. Remember, there are thousands of small machine shops that don't have the resources of the auto and the aerospace industries. In one plant, machinists who worked on CNCs complained of chronic skin rashes and migraine headaches during peak production when a mandatory overtime schedule was in place. Ventilation complaints were never fully addressed by the company and whenever one walked through the machine shop, there was a visible haze of cutting oils in the air. The odor of airborne contaminants forced approximately 40 workers to go home because the contaminants were so heavily concentrated. The workers got sick because of the lack of proper ventilation.

The company's reply was that they had a good exhaust ventilation system in place. The fact that approximately 40 workers had inhaled so

much of these metalworking fluids that they became sick because of the lack of proper engineering, sort of makes that a little bit of an argument.

Our machinists think that another part of the problem is contamination of the metalworking fluids. There are many different ways of contaminating metalworking fluids. Our members work with these contaminated fluids on a daily basis and continue to experience exposures to who knows what. In small machine shops that have about ten machinists in one of those shops, workers complained that their fluid was smelling, that it had a really bad odor. The foreman of the company said that he would take care of it. A few days later, the same workers complained again. Then workers were complaining of the odors on a daily basis.

Workers got sick because the metalworking fluid they were working with had been contaminated with other machine oils and fluids that are vital to the machine's operating functions. There were also solids and solvents and other chemicals present in the metalworking fluid with which they were working. A simple change of the fluid and several leaks being repaired on the machines that they were using was all that was needed. Because the majority of machinists in this machine shop became sick, procedures were finally put in place so this problem would not occur in the future. Such as the cycle time was changed for the fluids and the proper down time was scheduled so that the maintenance crew could do proper maintenance on the machines to prevent leaking and contamination of these metalworking fluids.

We are also concerned about the proper balance of chemical mixtures in the fluids. The improper balance of biocides, among many other chemicals, are common in some of our shops. Our concerns, as well as that of our members, continue to be on the health effects to of our members who are subjected to the improper balance of these chemicals. For example, it's quite common to add the biocides to metalworking fluids if one senses that bacteria has formed. What continues to happen on the shop floor is that those responsible for maintaining the metalworking fluids simply

add too much biocide for whatever reason, and our members become sick. They break out in rashes, they have breathing problems and some experience eye, nose and throat irritations.

For example in a machine shop that has one large retrieval system where metalworking fluids are circulated and filtered, there is a designated area designed to add concentrated mixtures of chemicals, the biocides, which is located in a pit and some of our members started having respiratory problems and just couldn't handle staying at their machines while they were in operation.

After some 15 members went to the first aid station over a period of four days, it was discovered that concentrated chemicals were being added downstream instead of in the mixing area. This caused a concentrated buildup of these chemicals and did not allow the proper dilution of the chemical. The machinists were breathing these chemicals in the most concentrated form for over a week. Some members are still experiencing respiratory problems from this incident.

The thing our members ask for most is for specific chemical information and proper education. Many concerns of machinists throughout the labor community are ones which should be covered by the Hazard Communication Standard 1910.1200. Our members have many questions and concerns about the chemical hazards that they work with when using these metalworking fluids. They simply don't have or are not provided with proper information.

For example, machinists ask what kind of gloves they should be using when handling this particular fluid. The MSDS sheet says impervious gloves. Now we want to know, really, what are impervious gloves.

This is a prime example of the lack of adequate information on MSDS sheets. The majority of our members believe that manufacturers who produce chemicals, as well as metalworking fluids, in many cases have inadequate and misleading information on these MSDS sheets. MSDS's should have a better breakdown for workers to understand in plain English.

Employers must also comply with the hazard communication laws. I see my little red light flashing, and I have some other examples, but I'll just try to summarize for you.

There are all kinds of examples of what goes on every day in these shops that are not quite like some of the examples we give here. Unfortunately, we do our sampling in the big shops in the aerospace industry and in the auto industry, but we have hundreds and perhaps thousands of small machine shops where machinists and tool and die makers are working in conditions that you just really wouldn't believe. I think a Symposium like this is going to help make that condition better because I think the facts that are being brought out can do nothing but help our members, and so I thank you very much for inviting me to be with you.

**Dr. JAMES D'ARCY, General Motors:**

Thank you, Mr. Bradford. I don't need my cheat sheet to introduce our next Discussant. He is one of my colleagues. I'd like to introduce Dr. Kenneth Gross, Senior Staff Research Scientist with the Department of Automotive Safety and Health Research at the R & D Center. Ken.

**Dr. KENNETH GROSS, General Motors:** Thank you, Jim. I guess you are in your seventh or eighth hour now of listening to people up here talk. Hang in there and I will be brief.

I'm going to present my perspective as a physiologist on the field studies that were presented that examined the correlations between metalworking fluid exposures and pulmonary effects. First of all, I have to commend all these people for having completed these studies. Jim and I did a field study several years ago with Ian Higgins and we're quite aware of the enormous complexities in recruiting people, the confounding factors that occur, the difficulties in collecting the data and then finally working with it once you have got the data. I know that for some of the Presenters, this has been a two-year evolution examining their data, and they are to be commended for that.

What can we say about the end points that have been measured? Most studies use the forced expiratory maneuver and the most often used parameters from this test are the forced expiratory volume in one second which you see represented as the FEV<sub>1</sub> and the forced vital capacity, which is abbreviated by FVC. This test is a popular one, due largely to the fact that the equipment is fairly portable and can be brought into the field, and does usually give us meaningful data. However, it may not always be the right test to perform. It is an effort-dependent test and, therefore, subject to some variability.

Some studies I have performed in which asthmatics were purposely broncho-constricted, indicated that there is not always a clear correlation between the FEV<sub>1</sub> decreases and the measurement of something like specific airway resistance, which is performed in a whole body plethysmograph, however this whole body plethysmograph is quite a cumbersome, non-portable piece of equipment. Nevertheless, I'm not always sure that the FEV<sub>1</sub>'s and the FVCs are always the right ones to use.

Bronchial provocation tests, such as the methacholine challenge, is another test that can be employed and Dr. Kennedy, I guess you knew this was coming, but there are some problems with this test. For instance, we found that when a certain percentage drop in FEV<sub>1</sub> is used as the end point, and asthmatics are being tested, the forced maneuver itself can set up a reflex bronchial constriction which will lower the next FEV<sub>1</sub> measurement without any constrictor agent administered. So the result may not truly be a pure response to the pharmacological agent given.

Furthermore, increased bronchial sensitivity itself is a difficult measure to interpret. Does it mean that asthma is on the way? Not necessarily. In the Textbook of Respiratory Medicine by Murray and Nadel, they state that the presence of an increased airway response to histamine or methacholine does not mean the experimental animal or the human has acquired the hyper-responsiveness that is characteristic of asthma. Does it by itself mean the person has chronic obstructive pulmonary disease? No. Does it mean the person is not normal? Again, not

necessarily.

What about symptom scoring? Well, the subjective sense of well-being and perceived quality of life is certainly important, however, we and others have found that there may be little correlation on a subject-to-subject basis between symptom scores and more objective measures of respiratory function. Some people have clear evidence of acute and significant decrements of lung performance, many have no symptoms and others who show very small measurable changes in lung function report very significant symptoms.

Another issue is how the data should be analyzed and this is something that itself could take up an entire symposium. It's a complex issue because of the many ways data can be analyzed and the uniqueness of each study design. There is no one way to analyze data, but rarely does it neatly fit into a positive or a negative resultant interpretation and I'll give an example of that in a minute.

Now, another question which I think Dr. Bassett very exquisitely touched on was how do we determine what's a significant or adverse health effect as opposed to a normal, biological response. In other words, what constitutes pathophysiology versus physiology. Several years ago the American Thoracic Society, which is the medical and scientific branch of the American Lung Association, had a go at it and published a panel opinion which was entitled: "What Constitutes an Adverse Respiratory Health Effect, with special reference to epidemiological studies of air pollution." This report caused a lot of controversy. Some people embraced it; many people totally rejected it. But the report did point one's attention to the fact that statistical significance does not necessarily mean clinical or health significance, and I think that's an important point.

Also the opinion was presented that reversible decrements in lung function do not, of themselves, indicate adverse effects unless they produce episodic respiratory illness, incapacitating illness, permanent respiratory injury or progressive respiratory dysfunction. They also, I think, correctly point out that the pollutant might induce symptoms that affect the welfare of the

individual and now we're talking about symptoms like wheezing, pain in the chest, hoarse coughing, sore throat, and that by itself could certainly be enough to merit its control.

So what can be said about the very complex studies that were presented to you in this session? I'm really only going to make a few points and apologize in this short time allotted for recognizing each study. I think Dr. Robins' study is very interesting and at the same time very complex and difficult. I think that one important conclusion to look at from his study is that it seems like a lot does not happen to the exposed workers in the course of the week in terms of lung function unless they are smokers and already have evidence of obstructive lung disease.

I think this is a new finding and very interesting. However, those same regression models tend to show that with good baseline lung function, the lung function improves still further across the week with continued exposure to metalworking fluids and I'm not sure how to look at that. We need to consider that this result of the model does not seem plausible and therefore should we accept other outcomes of the model as well.

In the past presentations of Dr. Robins, I have had some difficulty in buying into his suggestion that his data shows a no threshold effect. However, I'm glad to hear that there are some new analyses done on it and I really look forward to seeing some of this data.

Dr. Kennedy's work is important. I do look forward to her follow-up reports as more rounds of this study are completed. I previously pointed out the uncertainties regarding the measuring of increase in bronchial responsiveness, but coupled with reported symptoms of wheezing and tightness which she presented in the abstract but didn't talk about in her presentation, is making a very interesting picture, although occupational asthma has not yet been found.

So what's my end conclusion? Do we have a clear picture of what's going on in the lungs with metalworking fluids? No. Do we need more studies? Absolutely. Particularly the ones that more closely look at the physiology of the lungs in

these exposed workers. Does this mean nothing should be done? Absolutely not. In my opinion and maybe the best way to put it is in the term that's always used by that famous American Judge Wopner, there's a great enough preponderance of the evidence I think in all the studies being presented, even though no one study by itself really is definitive, that when you take all this data in total, there is indication that decreasing the exposure of the workers to metalworking fluids is a wise choice, but I'm glad I don't have to decide what the new standard should be. I think there is too little data available to be able to judge with any certainty how much better health any given change in the standard will produce.

Lastly, I want to make the point that we need research to tell us what in the metalworking fluid is causing the problem. By understanding what specifically induces any observed effects, how to control the problem will become more obvious and more obtainable. Thank you.

**Dr. JAMES D'ARCY, General Motors:** Thank you, Dr. Gross. The next Discussant is Dr. William Lucke, Manager of Regulatory Affairs for Cincinnati Milacron, but he's actually here today representing the Independent Lubricant Manufacturers Association.

**Dr. WILLIAM LUCKE, Cincinnati Milacron:** Thank you, Jim. Twenty years ago, I was given the assignment to develop an analytical method to test for levels of water-based metalworking fluids in the air. The methods that were used at that time consisted of taking in a sense a vacuum cleaner motor, putting a filter in front of it, running it for a specific period of time, collecting the filter, drying it, weighing it and determining how much weight had been picked up generally that was mineral oil and was reported as a milligrams per cubic meter figure.

When you're dealing with water-based fluid, when you dry the fluids, you purged your sample and you're left with nothing to measure, so some different methods were needed. Once I had developed these methods, then the temptation was

there to send me out in the field to use methods to generate data for areas where there were complaints about breathing the mists. I found that I could walk into a plant and pick up a pattern. You would go into the plant, into the area where the machines were, you would look at the ceiling and you'd see a cloud of oil, a haze hanging up there. You would get not so much an odor from the plant, as a taste. And you can develop your taste buds to the point where you can say this is a soluble oil or this is a semisynthetic and that's spindle oil. It ruins you as a wine connoisseur.

But what you would see is that the more oil there was, basically depended on how much soluble oil was being used in the plant. But if you had a synthetic which is theoretically free of oil, you still had that oil haze because you were putting oil into the fluid on a continuing basis from the machine; spindle oils, way oils, hydraulic oils, that sort of thing that gets in the fluid and it's not uncommon to have five to ten percent oil in a synthetic fluid system, and that oil would be carried up with the rest of the fluid and float around. The drops are small enough that they don't really fall to the ground to that degree. Instead, they'll collect on the beams up on the ceiling and kind of coalesce together and form a larger drop and eventually they will fall off when there is a white shirt underneath them.

You would get plants where a show area was being developed and they wanted to bring people in to see the process and this is the best part of our plant and the oil would continually drop down off the ceiling and management would say, we want a synthetic fluid in here and studies would be run to show the benefits of changing to the synthetic fluid.

After several years I noticed a pattern was forming. Every January, February and March, I was packing up my gear and going to New York State, Pennsylvania, Northern Ohio, Michigan, Northern Illinois and investigating complaints from operators that the fluid was irritating them. They would say they were getting a sore nose, a sore throat, dry, itchy, scratchy, a bloody discharge when they would blow their nose, a tight-ness in the chest, a cough. Over and over you would get

this complaint. You would have this in plants where one section of the plant would say I have a problem the next section using the same fluid, on the same system, did not have a problem.

So you would start looking for common elements. And what it came down to was in an area that was doing grinding, generating a lot of mist, you'd have the machines close together. You could spread your arms and touch two grinders, turn 90 degrees and touch two more grinders. The operator would be maintaining all four machines throughout the day and he'd be getting the concentrated mist from all those machines. You would have a low ceiling so the fluid cannot get away.

In the other areas, you would have the high ceiling, you would have a wider dispersion of the machines and not complaints. It was easy to see what was going on. In the course of this, you would come across some extreme examples. I went to one plant in Massachusetts where business was very good, and they were putting things in any space that they could. They had two centerless grinders installed in a two-car garage, and ran them full bore. The operators had breathing troubles. It's not that hard to figure out.

At the other extreme, there was another plant with an 80,000 gallon central system. I visited there in March. There were a lot of people with breathing problems. The records showed that no cutting fluid concentrate had been added to that system since January. All the maintenance had been done by adding 50 percent sodium hydroxide and biocide through that period of time. There was no metalworking fluid left in that system and they were still having the problems. This caused me some problems later on because I developed, in my own mind, the theory that the cause of the irritation was the alkalinity in the fluid and it turns out that's not right.

But you get all of this and you can see the patterns developing. The pattern changed in recent years, though. Suddenly we were getting complaints from the South, we were getting complaints in the Summer. Plants that used to have problems in the Winter now they have them in the Summer. Management was outraged. "We

spent all this money to air condition this plant and now we recirculate all the air so we don't bring in any bad air from the outside and now they're complaining." In the old days when the Summer came, they would open the doors and the windows and the complaints went away. Now they didn't go away.

This is basically where we stand right now. Plants are air conditioned, self-contained, with very little fresh air makeup and the problems are getting worse and more numerous. I think you are seeing the effects of that at this Symposium.

Why am I telling you all this? Basically because at this point we don't need all of these epidemiological studies to say there is a problem. There is a problem. The operators are telling you this. There are breathing problems associated with being exposed to too much fluid for too long. There are changes that are needed to some degree within the metalworking fluids. Ann Ball's paper this morning indicated that we had found things that fluid manufacturers could do that will relieve the problem. We are learning which raw materials to avoid, which ones to eliminate, and which ones we can add to make things better. But to the extent that we have a biological vector [endotoxins] to worry about, reformulation is not going to help. In that case, controls won't be the final answer either, but controls can help.

We need to use some common sense in the way we apply fluids. I can think of one plant that I went to in the aerospace industry, a large spar mill that was as long as this platform [48 feet]. The operator sat in a little cage that went up and down the part while it was clamped onto the machine. They were cutting with an eight-inch cutter running at 4,500 r.p.m. The cutter is running like this. They were spraying the coolant into the side of the cutter at a high rate so they could get some down in the cut zone. The result was a large amount of spray, that came out of the machine and was affecting everybody. If you would move the nozzle over to direct the fluid into the cutting zone at a low rate, you will get better cutting, you will have much less mist. You can do things like this. You can put up a rubber baffle. You can put a fan in the right place to blow the mist away from the

operator.

The limits that are in place right now, five milligrams per cubic meter for oil mist, 15 milligrams per cubic meter for total particulate, really are much too high. They are not real world. I indicated this morning that at three milligrams per cubic meter, the operator is angry. And that doesn't matter if the fluid is a synthetic, a soluble oil, a semisynthetic, or a straight oil. You tend to get fewer complaints with a straight oil because straight oils are used at low surface cutting feet operations where you don't generate the mist, so that by and large, a given gallon of straight oil will not generate as many complaints. If you get that mist level up to three milligrams per cubic meter, the operator doesn't care about all the other data. He's uncomfortable, he's angry.

Our data indicate that something less than three milligrams per cubic meter will be an improvement. Based on the RD<sub>50</sub> data we saw this morning, the most irritating fluids have RD<sub>50</sub>s between 100 and 200 milligrams per cubic meter, divide that by 100, you get one to two milligrams per cubic meter. A safety factor of 100, not 60, seems more reasonable.

Professor Alarie of the University of Pittsburgh this spring at SOT presented some work that indicated that the mice in the RD<sub>50</sub> study began to show threshold effects at levels between two and three milligrams per cubic meter. This is within the range that we're talking about here, where the operators are happy, where we have our 100 fold safety factor from the RD<sub>50</sub> so somewhere in that one to two milligram per cubic meter range seems like a good place to start.

Studies that are out now surveying the mist levels in plants find the average to be pretty close to one milligram per cubic meter, so controlling exposure at that level is attainable without putting in a whole lot of expense. As I indicated last year in Cincinnati, there's a real question whether the data indicate that there are long-term irreversible health effects like cancer that result from exposure to the metalworking fluids, but there's no question that these short-term health effects are there. This question should be reversed. But in the meantime, if we could take some simple steps to even

eliminate a nonadverse health effect, then we've made progress.

If you make the worker stand at his machine all day long with a rock in his shoe, he's not going to die, he's not going to lose the use of his leg, but the most important thing in his universe is going to be that rock. If you can take it out, simply, take it out.

Another area where we can use some improvement is in the measurement techniques. We will get into that tomorrow. There are some sessions in the poster session that will get into some improvements. I know Dennis O'Brien at NIOSH has some new toys to play with that he's just getting started with. I think the industrial hygiene area in this is going to be much changed in the future. We will be able to look at individual compounds. We can look at dynamic levels, instead of getting only a number that represents eight hours of exposure. If an operator is exposed at two milligrams per cubic meter on the average all day long, but he's getting spikes up to six, he can still show those adverse health effects.

Basically I think we're overdue to get a more realistic limit and it ought to be accomplished whether it's through legislation and regulation or just through voluntary actions in individual plants. Thank you.

**Dr. JAMES D'ARCY, General Motors:**

Thank you, Dr. Lucke. Our fourth Discussant for this afternoon is Dr. Gregory Wagner from the Division of Respiratory Disease Studies at NIOSH. Dr. Wagner.

**DR. GREGORY WAGNER, NIOSH:**

Thank you. It's really a pleasure to be here to be able to comment on these excellent studies and also on Dr. Bassett's initial commentary on the murkiness in the field.

I'm impressed as I was listening to the studies that epidemiology is really difficult. You really have difficulty characterizing the exposures.

You have enormous difficulty characterizing the correct human health response, and drawing the relationship between them in order to make some

assessment as to the determinants of the disease in human populations. It's no wonder that a friend of mine once characterized an ecological disaster as being one of such severity that even an epidemiologist can recognize it.

There are enormous factors working against the recognition of any health problem through the tools of epidemiology, which is an observational science, instead of the experimental science that you saw this morning. And so I think that it really is important as we listen to these studies that we ask the questions: "What does it mean? Are we talking about something serious? Is it important? What should we do? We also need to realize that when we do find something, it really is worth paying some attention to.

Let me tell you briefly some of the things that I heard, maybe not the specific things that the presenter wanted to tell us, but some of the things that were embedded within their presentations that I think do begin to help point us in some useful directions.

Susan Kennedy's study of previously naive workers to metalworking fluid exposures tells us that in the initial rounds of her longitudinal study, that those folks who were markedly responsive quit with 100 days or fewer of exposure, and the fact that many of them quit, I think, is a really important finding, and one that can only be done by setting up the cohort and looking longitudinally; it feeds in to understanding some other studies that have been previously reported.

This quitting is obviously nonrandom. That the people who are responsive, are the quitters; the people who were nonresponsive, are less likely to quit and even with that, she reports that at least in this stage of the game that you have increased bronchial hyper-responsiveness in those who do remain, but have greater exposures than those who remain with less responsiveness. The more exposure, the more responsiveness. This will lead to the question that I'll try and look at shortly as to what does bronchial hyper-responsiveness mean.

Tom Robins' interesting analyses of a fairly small data set say that some people, when you get away from all the math, he has a half dozen people

out of fewer than 100 who had a very significant drop in their FEV<sub>1</sub> after exposure to metalworking fluids cross-shift. And he's working hard to try to understand who it is and why, and points out that it is the obstructed current smokers who appear to have the dose response relationship to thoracic exposure with his small numbers.

The Kriebel, *et al* study, I think points out the difficulty in actually setting up an epidemiologic study well in order to be able to compare an exposed and a non-exposed group. He actually gives us information about two exposed groups, but they are exposed under different exposure settings. One is currently exposed, one is past exposed, one is greater exposed currently, one is lesser exposed currently. He tries to look at some of the same health end points in both. In comparing these two exposed groups, he finds that lower levels of exposure give less human health response, at least the response that he's looking at, than people in either group exposed to higher levels. Less exposure brings less response, more exposure brings more response.

At the end of his conversation, he also brings up something that I'm concerned about, which is actually looking at human beings as, well in the mining field, you might remember the miners back at the turn of the century and thereafter would bring canaries in cages into the mines as a biological assay to determine whether the mines were gassy and whether unhealthy conditions existed that could result in explosion and loss of life. If the canary keeled over as a sensitive species, they'd evacuate the mines. I think that we need to pay careful attention to these sensitive subgroups and see what they are trying to tell us about the potential adverse health effects here.

Ken Rosenman, in looking at surveillance data, not setting up an epidemiologic study, but the most general of broad observational studies that a physician reports in are things that physicians are seeing in the communities, unhealthy workers, sick workers, finds a not trivial number of work-associated asthma reports associated with exposure to metalworking fluids, particularly the synthetics in the field.

I think that this begins to bridge the questions that Dr. Bassett asked about whether or not this is consequential and it does tie together a number of the other studies where we have, in fact, seen in other occupational groups, that cross-shift decrements in lung function, that some of these physiologic changes that are being tested for in some populations, I think particularly of the populations of workers exposed to cotton dust, some of the same information in grain dust, that we're finding that in many, but not all populations, short-term, well-defined, adverse pulmonary effects that are significantly different between an exposed and unexposed population, can well predict longer term adverse health effects, including in this instance, potentially asthma.

Now is asthma a problem? Is it just the reversible constriction of airways? I would say that it is. Work-associated asthma, when you study the effects on human beings, first of all, you have the 'Kennedy effect' I'll call it. People quit work. People with acute asthmatic responses to things found in the workplace are leavers. They disappear from that specific work environment. Now depending upon how you look at it, this either is or isn't a problem. I would suggest that for workers, particularly in communities where there are limited numbers of choices, the exclusion of workers from the workplace because of the presence of a health hazard in the workplace makes a problem for those workers.

Second, the question of asthma followed longitudinally. People who do get work-associated asthma when followed long-term, have more of a tendency to end up on the Social Security Disability rolls, or are otherwise unemployed.

The question raised by Dr. Bassett as to what a non-adverse health effect is, I think was very important. The National Academy of Sciences Committee had a lot of difficulty defining what was an adverse health effect and so I'd suggest that we not follow the logical fallacy of reasoning from a non-adverse to an adverse, but take what they said at face value as defining a non-adverse health effect and then as Dr. Gross suggests, let's take a look at the continuum of health effects that the ATS [American Thoracic

Society] suggested as to what might be indicative of problems.

What's my bottom line on this? One is that I think that we have a growing, fairly coherent set of data consistent with the toxicology information that suggests that real adverse health effects are occurring. As Dr. Bassett points out, if there are dirty work places, you're likely to find problems resulting from them. And I'd say on the basis of those two observations, that there's a consistency, at least from the commentators that I'm hearing, first of all, if it's dirty, clean it up. I think it's real easy to talk about, not necessarily so easy to do.

The second is that as we do make interventions in the work places in order to clean them up, again as Dr. Bassett suggests, let's have ongoing surveillance, ongoing carefully constructed observations to ensure that the interventions are actually effective in reducing the problems that we want to prevent. Thank you very much.

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**Dr. JAMES D'ARCY, General Motors:**

At this point we would like to open this up to general questions from the floor. We do ask that you come to one of the three microphones and again please identify yourself and your affiliation before you state your question. Thank you. And we only have one microphone occupied, so we'll start over here.

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**Dr. Donald Milton:** Don Milton from Harvard School of Public Health. My question is: Given that asthma previously was defined mostly in terms of the variable airflow obstruction, but in recent years I think the pulmonary community would generally agree that asthma should be defined in terms of the airway's inflammation that one finds in asthmatics, for example, a person who had childhood asthma, even if they have not had exacerbations in recent years, will have abnormal inflammatory cells present in their airways and that virtually all persons who have active asthma will have sensitivity to methacholine, that is they'll

have nonspecific bronchial responsiveness.

Given those factors and given that metalworking fluid contains a lot of inflammatory agents that may act together and that we have seen from Dr. Kennedy's data that there is an increasing nonspecific bronchial hyperresponsiveness among machinists, what role is the nonspecific irritant action of metalworking fluids playing in the development of clinical occupational asthma and people who are getting diagnosed, and how much of that is likely to be due to specific sensitization to these agents? Perhaps Dr. Rosenman would like to address that question.

**Dr. KENNETH ROSENMAN:** The surveillance data does not allow one to separate out those two mechanisms so I guess I have no data to address it. I will say that there are known allergens in some machining fluids, so it suggests that sensitization could be a role, plus people could be sensitized to microbial agents, but you'd need a lot more specific testing of the actual people developing asthma to answer your question.

**Dr. JAMES D'ARCY:** We'll go to the microphone on the right side.

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**Dr. Roger Jenkins:** I'm Roger Jenkins from Oakridge National Laboratory. I have sort of a two-part question related to tobacco smoke and the interpretation of some of the data. The first part of it is sort of to the general number of people that presented papers this afternoon. The second part is specific to Dr. Robins' study.

There have been a number of reports in the literature regarding the self-misreporting of smoking status. That is, an individual will report that they are either an ex-smoker, when in fact, they are an active smoker, or that they are a lifetime never-smoker when in fact, they're currently active in smoking cigarettes.

Many of the studies that were reported this afternoon had a relatively small number of individuals reporting specific symptomatology. In any of these studies, was there any effort made to

independently examine the rate of misclassification or mis-reporting of smoking status or in the absence of that, have you tested any of your data sets, say for the sensitivity to something between a four to ten percent rate of misclassification, and how that might impact on the data. So that's my first question. Does anybody have an answer to that?

**Dr. THOMAS ROBINS:** I could answer that second question part with respect to my study. We didn't have urinary creatinine levels. We had a much more expensive measure, which was vapor-phase nicotine and we had personal samples for vaporphase nicotine. We also asked detailed questions about smoking history and specifically asked the person about the number of cigarettes they had smoked that day, both before work and during work among people that said they were current smokers.

The separation in terms of what the measure of vaporphase nicotine levels between the people that reported themselves to be smokers versus nonsmokers was rather clean, meaning that we're talking, I'd have to go look at the data, but it was substantially higher, several times higher among the people that reported they were current smokers as compared to people that said they were not current smokers and I don't think we had any substantial out liers. So to that extent, I suspect that the reports we were getting in our study were probably quite accurate.

With respect to your second part, we didn't try to do any sensitivity analysis of well what if there was misclassification of current smoking status, so that wasn't addressed.

**Dr. Jenkins:** Do you recall what the vaporphase nicotine levels were for the nonsmoker individuals? That was my second question.

**Dr. ROBINS:** I don't recall the numbers offhand, but I might be able to find them in some of the documents I brought. Bear with me while I pass the microphone to my colleague to my left.

**Dr. DAVID KRIEBEL:** Just very quickly, all I can say is that we don't have any sensitivity analyses, any independent measure of cigarette smoking other than the self-report and so it's fair enough to wonder about the problems in misclassification there. All I could say, though, is that there are fairly predictable standard expectations about the relationship between smoking and base line measures of pulmonary function. We understand what a healthy blue collar population ought to look like in terms of their relationship between their reported smoking levels and the lung function that they have at base line.

Our study is entirely consistent with that. That is to say, we see the expected effects of cigarette smoking which to my mind is sort of a confirmation that this is a valid measure of smoking. I don't doubt that there is some misclassification, no question, but I don't think it's a serious problem because we saw the sorts of effects one would expect to see from smoking at base line.

**Dr. Jenkins:** Maybe in the interest of time if I could just talk to Dr. Robins later individually, because I would like to have the information.

**Dr. JAMES D'ARCY:** That would probably be the best thing, if you could just talk to him afterwards about that.

**Dr. Jenkins:** Thank you very much.

**Dr. JAMES D'ARCY:** I think we're back over to the left side. Then we'll get to the center, Frank.

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**Dr. Jane Teta:** Jane Teta, Union Carbide. I'd like to ask a question of Dr. Kriebel again and it might respond to Dr. Wagner's comments about the difficulties of conducting epidemiology studies.

One of the things we typically do is a feasibility assessment and so I ask whether such an effort was made where you had a location where both your controls and your exposed were both

exposed, the nonmachinist had ten years average exposure, you had a common ventilation system and you had a very little variation exposure. We don't need to make more difficulties for ourselves, so I guess I'd ask whether you did a feasibility assessment and if so, why you went forward with that type of a design.

And secondly, to explain away not finding what you were looking for by saying we had exposed controls for acute effects, but then to say you did see differences in the reported chronic symptoms and not have the same explanation for that. You know, you can't have it both ways.

**Dr. DAVID KRIEBEL:** Thank you. Those are both very good points. I appreciate you bringing them up. It's a good opportunity to talk more about the interesting issue of how one goes about selecting a study like this.

We did this study, as I said, funded jointly by UAW and GM National Joint Committee on Safety and Health and as such, we had available to us a set of plants from which to choose. However, the process of choosing a plant for this study was not entirely under our control and I think appropriately so. We had to identify a plant that met our criteria for this study, but also that had a local management and a local union that were interested in cooperating and we spent more than a year looking for a plant and this was the plant that we found that most closely met our criteria. And I believe that it was worth doing. I do think we learned some useful things, but I absolutely agree with you that in an ideal world we would have chosen a different plant.

On the second point, I think that first of all you have to remember that because our main focus is on acute effects, our primary exposure response relationship analyses focused on current exposure, those milligram per cubic meter levels of gravimetric aerosol that I spoke about and those, as I said, do, in fact, differ markedly between the machining and nonmachining areas and so we think that we did still have some ability and succeeded in identifying exposure response relationships there.

The fact that one sees on top of that some

differences in chronic health affects, I think is probably attributable to the fact that the chronic health effects, things like chronic cough, sinus problems, result from some complex combination of current and past exposure, so I think that it's not entirely inconsistent. I agree with you that it is not the ideal situation in which to look at chronic health effects, but I don't think it's entirely inconsistent to observe some chronic health effects between those two groups which have, on average, different levels of exposure. Despite the fact that we think there were, in fact, some selection of things going on.

**Dr. JAMES D'ARCY:** Okay. We're to the center microphone.

**Dr. Franklin Mirer:** Frank Mirer again. As we move tomorrow to talk about feasibility in the next day, I think we ought to keep in mind the exposure levels observed in these population studies as we're trying to determine what's feasible in terms of levels of control because it certainly influences my thinking that we have populations with these particular exposure levels.

My questions are really some to Dr. Rosenman and then the clinical investigations. For Dr. Rosenman, the question is: If you could repeat how many extra cases typically are found once you go back to the workplace where the index case came from. How many additional cases do you harvest of people at work with the asthma condition when you go back and then what I took from his summary is that if you go back and survey with the questionnaire the department where the victim worked, you find in some of these plants 25 percent on the average of people reporting the same condition as the index case and so the question would be, you know, is this rule of thumb for us to take forward or do some people fill out questionnaires or not? How difficult is it to get the questionnaires done? Is this like reliable estimate or worst case 25 percent?

And the question for everybody is: Are these the rates of symptoms and the lung function

effects being observed in the control groups, are these plausible for nonexposed population or are, in fact, is it simply a low exposed group that's obscuring associations which would be clearer if we were getting the controls from another environment, not from the same plant.

**Dr. KENNETH ROSENMAN:** There seemed to be a lot of questions there, Frank.

We've gone back to facilities where 50 percent, and I'm talking about of the workers having daily or weekly symptoms. Is it doable? I think it's very doable. We rarely have individuals refuse. We're coming in as a third party and we're promising them confidentiality and we don't share the results with management, with labor. But certainly it's very doable. The questionnaire takes five to ten minutes and it doesn't appear to be very disruptive on the shop floor. I guess I'm not sure I answered all parts.

**Dr. Mirer:** What's the ratio of cases found to the index case?

**Dr. ROSENMAN:** If you're talking about cases found meaning physician diagnosed asthma, you know, there were ten reported on the OSHA log and there were five or six with physician diagnosed asthma. Most of the people there had these daily or weekly symptoms, but I think we heard about people leaving work. When you go back and do this, you're interviewing a survivor population there, so I think you always have to keep that in mind.

**Dr. Mirer:** What's the reasonable background of these symptoms for the group? I mean for an unexposed group. What would we be expecting in symptoms and asthma?

**Dr. ROSENMAN:** Well, there are a whole host of facilities that it's zero. Again talking about frequent symptoms. If you use seldom or monthly, you're going to have them more frequently. But certainly less than ten percent in my experience.

**Dr. SUSAN KENNEDY:** I would just like to point out that our control populations were not people in the same facilities. These were people who worked in similar blue collar jobs who would be exposed to any number of other irritants, so the issue of just simply saying that this is just an irritating environment. Construction workers are exposed to sort of the general kind of milieu of potentially unpleasant air, although an important difference is for the most part the construction workers are outdoor workers compared to the machinists being indoor, but I think it is fair to say that the rates of certainly of increased bronchial responsiveness that we saw in the control population would be about what I would expect. That is, it's not very high. There is a low prevalence of that. Whereas in the machinists group, it was considerably higher.

**Dr. THOMAS ROBINS:** In our study, I think it's a little difficult to answer for the assembly workers, our comparison group, the question "did they have a reasonable background rate of various complaints," without reading you a lot of numbers. What is perhaps more relevant to the question of whether they had a very different exposure than the machinists was, we did ask people about whether they did have symptoms at the beginning of the shift before they worked and the same symptoms at the end and just give you a couple of very quick numbers. We asked people about what we call lower respiratory symptoms, including cough, wheezing, chest tightness and dyspnea and 36 percent of the people working in machining said they developed that during the shift versus 12 percent of the people working in assembly, which is very significant.

Similarly, we asked people about what we called mucous membrane irritant symptoms, irritation of the nose, throat irritation, sinus trouble, eye irritation developing during the shift and we had 18 percent of the machinists saying that they developed that during the shift, versus six percent of the people in assembly.

Again, I can't claim that the assembly workers have absolutely no exposures, but clearly

there is something very different with respect to their exposure.

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**Ms. Cathy Walker:** Thank you. Cathy Walker, Canadian Auto Workers, Toronto. I think the area of respiratory disease is a particularly important one. Our experience has been the same as Brother Bradford's. We have a lot of our members complain about respiratory disease caused by exposure to metalworking fluids in all sorts of different workplaces and not at all surprisingly, we find that people who are exposed to more airborne metalworking fluids experience more problems of respiratory disease.

We have a whole variety of suspicions about what the exact diagnosis may be. I'd like to describe one particular workplace that's a Big Three plant and unfortunately nothing has been done about reducing exposures until we have recently got a commitment several weeks ago to finally tackling this problem. This particular plant I've described as being basically an oil mist factory that coincidentally happens to produce components almost as a by-product.

Fortunately something will be done, but in the meantime, unfortunately, one of our members has contracted a very serious problem. We have a lot of people who are on ventilators, puffers, their family doctors have been diagnosing asthma. It may or may not be asthma. The ventilators may or may not be doing them much good, but there's no question in my mind that they have a serious lung problem and it's as a result of the metalworking fluids.

This one particular individual, however, had a problem which was life-threatening and he was diagnosed as having extrinsic allergic alveolitis by the occupational health specialist who examined him. I suspect were he examined by some of the panel members, they may have diagnosed hypersensitivity pneumonitis and this particular individual, it was determined that the cause of his problem was a particular fungal organism called *fusarium salani* and fortunately he's been removed from the exposure and is fine

now, but certainly had he not been, he might not be around to still remain at work in that particular plant in another area.

My question is in the area of fungal organisms and in the area of pneumonitis, I'm wondering which of the panel members might have encountered this problem and how prevalent it may be and maybe I could just preface this by saying: It's my understanding that as we're adding biocides and getting rid of the bacteria, we may be increasing the amount of the fungal organisms and certainly in this particular plant you can almost see them visibly growing. So I just wonder what panel members might be able to comment on that.

**Dr. JAMES D'ARCY:** I'm not sure if there's anyone who wants to. If they want to, feel free. But we do have some people tomorrow who are specifically going to be talking about biological aerosols and that contamination of the workplace and they might be able to also address that question. I don't know if there's anybody right now.

**Dr. KENNETH ROSENMAN:** I'll make one comment. I think, at least the two physicians on the panel would have come up with the same diagnosis because the allergic alveolitis and hypersensitivity pneumonitis are the same disease, so there's no difference in that diagnosis.

I mentioned four such outbreaks in Michigan and in one of them I similarly have found fungus growing in the coolant and antibodies in the patient's blood to that material. I don't know about cause-effect there, but I don't know, it's possible.

**Dr. THOMAS ROBINS:** At University of Michigan we have an occupational medicine clinic that meets a half day a week. People are referred by a variety of paths. In my own personal experience, there's at this point a total of five patients that I have seen which, without going into a lot of details I personally had a high degree of suspicion that 1) these people were diagnosable as having hypersensitivity pneumonitis and 2) that

there was a work-related component where they were working in machining operations, so I certainly think it's an issue that clearly needs to be addressed, just based on my clinical experience.

That's not studies, of course, and I do not have the advantage of having any clear documentation of a relationship between a particular antigen present in the workplace and demonstrating antibodies in the blood of these workers, but some, as I say, clinical suspicions.

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**Mr. Gregory Foltz:** Greg Foltz with Cincinnati Milacron. I have several questions. My first two are for Dr. Kriebel.

At the beginning and the end of your presentation you showed some pictures or slides of some machinists and their machines, and the machines quite obviously were manual loading and unloading and showed a lack of any type of guarding or very little guarding, if at all. The question is: Were those representative of the machines in the plant where all the exposed workers were working?

And the second question is: At the end of the presentation you mentioned some concern over sulfur and sulfur, is used in very many different forms of metalworking fluids. Do you have any definition of the type of sulfur that you are concerned with?

**Dr. DAVID KRIEBEL:** Thank you. The pictures, there hadn't been any pictures of the real operation in the whole couple of days, so I thought I ought to put some in, but they certainly were not scientifically chosen to be average in some way from our study, but yes, many of the machines in this plant were of that sort, limited amounts of controls.

Dr. Woskie tomorrow will spend a little bit more time on this actually and so you will get a little bit more detail about this, but in general, this plant uses machines that have limited amounts of controls on them, yes, that's true.

In terms of sulfur, what we did was to collect aerosol samples, personal aerosol samples

on each of our workers using a lapel carried filter and then those were analyzed by a Pixie analysis to measure the concentrations of a whole series of elements and so all we know is the concentration of elemental sulfur, and clearly this is a long way from what you would really like to know, which is the molecular structure, which molecules that have sulfur in them were those. Were they sulfonates, was this sulfur dioxide, what was it? And we don't know.

This is I think, an interesting little hint that perhaps along with the animal tox data, there's a suggestion that perhaps there's something to this, but unfortunately all we were measuring was elemental sulfur.

**Mr. Foltz:** I have one more question for Dr. Bassett. During your presentation you mentioned that high pH is a trigger for airway constriction. Metalworking fluids typically will operate with a pH of 8.5 to 9.2. What do you define as high pH?

**Dr. DAVID BASSETT:** That is it exactly. I was throwing that out as a concern based on animal studies with a high pH. I think also, more interestingly is the hyperosmolarity. Some physicians I hear actually use distilled water to test for airway reactivity in fact, so I'm not in a position to comment about the pH, but certainly that sort of pH that you mentioned would certainly be of interest to study.

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**Dr. Michael Silverstein:** Michael Silverstein with the Washington State Department of Labor and Industries. This is directed at anybody on the panel.

I would share the observation that Dr. Robins did not report that smokers are at uniquely high risk in the group that he studied. If I heard correctly, what he did report is that smokers who also have a pre-existing base line of obstructions to lung flow, are at especially high risk in this population.

Now, it seems to me likely that the issue of

smoking is going to attract the most attention in that particular study. And, in fact, several of the questions already this afternoon have been directed at the issue of smoking in this population. But what I'm most intrigued about is the possibility that it's the base line of obstructive changes themselves which may very well be related to prior workplace exposures that place workers in this environment at specially high risk. And I'm interested in knowing how the researchers might go about teasing those factors apart.

**Dr. THOMAS ROBINS:** First of all, I want to say that I think this is a very important and correct observation about our study. We're seeing the effects, the dose related effects in a particular group, which is as you say are people that are current cigarette smokers, but also have some evidence of base line obstruction and as I think you're clearly alluding to, that raises the question of well, if there is a causal relationship, is the base line obstruction on Monday pre-shift somehow leading to the cross-shift decrements or is it ten or 15 years of these cross-shift decrements and whatever they represent in terms of pulmonary pathophysiology leading now to some degree of irreversible obstruction, which is reflected in the base line level.

Unfortunately, to the extent I can figure out, I don't think we can answer that question with the data we collected. We collected data over one year, but for practical purposes, we've collected a cross-sectional study is what it represents and we, unfortunately, had people with an average seniority of 19 years. We didn't have naive subjects first being exposed to machining fluids, so any ideas if someone had of what could be done with our data, I'd be intrigued with because I'm not sure how to answer that question.

But perhaps, Dr. Kriebel or one of the other panel members may have some other ideas about this. I won't name names.

**Dr. DAVID KRIEBEL:** I just wanted to say one thing. This is an extremely important piece I think that Dr. Silverstein has raised. A really critical missing piece of the picture that you are getting here this afternoon that I need to say

something about. What you have heard, what we have laid out here, Dr. Kennedy, very early, apprentices, increasing bronchial reactivity. At the sort of end of the picture, Dr. Rosenman saying there are cases of asthma occurring.

Somewhere in the middle, Dr. Robins and I finding cross-shift is acute irritant effects, perhaps dismissible as not terribly important in and of their own right, I don't necessarily agree with that, but certainly you can debate that.

The missing piece then there is what about base line lung function. There is another study that was funded by General Motors-UAW, National Joint Committee. The Kennedy study, so-called, was a subset of this larger study, several thousand GM-UAW workers, whose base line pulmonary function was measured. Quantitative measurements of exposure, historically, going back all the way. Lifetime cumulative exposures were estimated and this study shows that particularly for straight and synthetic fluids, there are dose response relationships between cumulative lifetime exposure to machining fluids and base line FEV<sub>1</sub>. That is to say, workers with longer lifetime exposures have lower base line FEV<sub>1</sub>. This is after controlling for smoking, properly dealing with the problem of smoking and all the other predictors of base line lung function and so I very much agree, I think it's very unlikely that this is a problem of smokers.

I think that in Dr. Robins' situation for a variety of reasons that we'll not necessarily ever understand fully, that's where he sees the strongest effect, but I doubt very much, given these other studies in the picture, that this is a problem restricted to smokers. It seems very implausible to me.

**Dr. SUSAN KENNEDY:** In our young workers, we looked very specifically at the question of whether there were other factors, or which other factors may be predictive of the nonspecific bronchial responsiveness we measured at the onset, that is sort of at your zero, and end, then at the change and this has been found many times that when you look at bronchial hyper-responsiveness measured at any given point

in time and in this case in these apprentices at year zero when they had almost no exposure that like many other studies, we find that base line lung function does, that is if your base line lung function is low, we are more likely to measure bronchial hyper-responsiveness.

Now most of that is in a sense an artifact because if your airways are narrow to begin with, the flow rate decreases more quickly if they get a little bit narrower than if they're wide open to begin with. So, yes, base line lung function is a risk factor, if you like, or is associated with bronchial hyper-responsiveness.

Once you correct for base line airway caliber, the size of the airways to begin with, base line lung function, cigarette smoking is not a predictor of bronchial hyper-responsiveness. In our young workers, cigarette smoking, whether we look at it based on their current status, whether we look at it based on the cumulative amount of cigarettes that they have been exposed to over their relatively short cigarette smoking history, is not a predictor of a base line bronchial hyper-responsiveness and neither is it a predictor of change in bronchial hyper-responsiveness. That is, that cigarette smokers were no more likely to show increased bronchial responsiveness than the nonsmokers.

Base line airway responsiveness, however, is a predictor. So having hyper-responsive airways to begin with means you are more likely to get more hyper-responsive. That's a predictor regardless of whether you're exposed to metalworking fluids or not. Metalworking fluids was a significant predictor of increase in bronchial hyper-responsiveness above and beyond both those factors.

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**Mr. Robert Park:** Bob Park, UAW Health and Safety Department. I'd like to go back to the hypersensitivity pneumonitis issue. In the four episodes that have been mentioned, to my understanding, at least two of them involved coolant systems using Cincinnati Milacron coolants and, in fact, those systems were being

managed by Cincinnati Milacron. I have three questions related to that.

First, is Milacron aware of any other outbreaks such as these? These were fairly large outbreaks involving many workers and second, has Milacron attempted to survey their major buyers on this question and third, which is directed to the industry: Is the industry willing to share some of their health effects information with researchers on these issues? For example, compiling a case series on hypersensitivity pneumonitis, which is a relatively new finding in machining fluid exposures.

**Dr. WILLIAM LUCKE:** I guess it's my turn. I'm not sure what you mean by an outbreak. Can you be specific?

**Mr. Park:** At General Motors Romulus Engine Plant there were 80 people that had lost time and within that group, there were a number of individuals seen by occupational physicians and diagnosed with hypersensitivity pneumonitis.

**Dr. LUCKE:** This was an incident a number of years ago?

**Mr. Park:** In the past two years. You're not aware of it, I take it?

**Dr. LUCKE:** I don't think I am, no, but we for the last two years have not, in fact, been the manager in that plant. The primary contractor was Betz and we were replaced three or four years ago. I'm pleased to disappoint you.

**Mr. Park:** I'm chagrined that you don't know about it.

**Dr. LUCKE:** There are an increasing number of reports of hypersensitivity pneumonitis that Dr. Bernstein in Cincinnati has published a paper this year on the topic and I believe that was a system that used our fluid. I can't tell you what product or anything.

I don't know. It's something that's just

coming up, we're aware of it and we were frankly looking at this meeting to be the source of information on that topic and our impressions are being verified, I think, that our speakers are mentioning that as something that is showing up, but I don't think we have any information beyond what everybody else in this room has.

**Mr. Park:** My last question was: Are formulators willing to open their records, at least at the level of allowing case series to be compiled and things like that within some, you know.....

**Dr. LUCKE:** What records are you referring to?

**Mr. Park:** I assume you get product complaints concerning health effects.

**Dr. LUCKE:** Okay. We ask our marketing people and our field people to file health effect reports on an ongoing basis when they get these things. I know we would not give you individual instances because we have to protect the confidentiality of our customers. It's possible we would be willing to put out summary reports. I think they would be of limited utility for this.

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**Ms. Jean Melvin:** Jean Melvin of Chrysler Corporation. I was just wondering, has any of the panel studies addressed any adverse health effects in employees with unusual workshifts such as 12-hour days, seven days a week, or three or four days in a row at 12-hour days?

**Dr. THOMAS ROBINS:** Well, my answer is simple. The plant where we did the study, at the time we did the study, they were not working overtime, so they were working, the people doing machining were working a Monday to Friday schedule, so in my case, the answer is no. I'm sure it's much more complicated for other people that studied multiple plants.

**Dr. SUSAN KENNEDY:** Maybe I could turn the question around to you and ask what you were wondering we might have found?

**Ms. Melvin:** Well, what I was wondering is if you found more significant asthma conditions or bronchial conditions with people that worked 12 hours a day, seven days a week shifts, or as a lot of companies are going to these 12-hour days for three or four days in a row and if there's more recovery if you go to that kind of shift or is there any recovery for someone working 12-hour days, seven days a week at say an exposure setting of one milligram per cubic meter, total particulate up to three or four.

**Dr. KENNEDY:** I think those are all very good questions and I certainly can't answer it at the moment, although I might, it occurs to me that I have collected information on the kinds of shifts and the shift schedules that all the people that in my population worked and may be able to look at that, but I think that to get it to the level of precision of being able to know, I mean, we're having enough trouble now seeing what is a safe level to be able to say whether a certain level would be safe if you had it at a different shift schedule. I think we're a long way from that.

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**Mr. Howard Ayer:** Howard Ayer, retired from NIOSH and the University of Cincinnati. And since we have had this whole day of science, I'd like to contrast that a little bit for these younger people with the origin of the oil mist limit and the respirable particulate limit for not otherwise specified.

The oil mist limit came in the mid 1950's when Herb Stokinger was doing a study of mineral oil mists on rats. At 40 and 50 milligrams per cubic meter, he wasn't really finding any particular effect on his little animals, so based on Michigan's Department of Health representative on the TLV Committee, who said well, if you get it any higher, you're going to have it dripping off the pipes, they picked a number. That's the oil mist TLV based on

a nuisance, not on a health effect.

The respirable particulate, not otherwise specified, came about because there was a 15 milligram per cubic meter limit for a total particulate and we figured, well, probably about a third of that is respirable, so we chose five.

**Dr. JAMES D'ARCY:** Thank you very much for those observations. I had heard the one about the oil mist, but not the other one.

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**Ms. Angela Weber:** I just have a comment. There's been several questions about HP [hypersensitivity pneumonitis]. I'm Angela Weber with NIOSH and we're presently working on two health hazard evaluations that were submitted to us specifically to address HP in the workplace and we're at the initial stages of this evaluation right now. The two facilities both have different chemical management companies and between the two there's approximately 20 cases and that's what we have, there are suspected that some are more strongly linked and we're just at the initial stages, so that's all I can offer, but if anyone would like to talk about it, that would be great

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**Mr. Jiamping Cui:** Thanks. My name is Jiamping Cui from Occupational Health Clinic for Ontario Workers. My feeling from today's meeting, I found this an interesting issue of cutting fluids or machining fluids and these respiratory problems. But for the whole body of scientific evidence from animal studies and human studies present today, I feel there is a tendency to make a relationship between these two, and my question is that it looks like the eight-hour exposure or any index we use, we try to correlate it with respiratory problems, as the study shows. Are there any studies that show the relationship between the instantaneous exposure or short term exposure to cutting fluids and respiratory problems because the respiratory problems look like acute ones, so maybe you should also relate it to acute exposure. Maybe this can be a 'yes/no' question, because there is no time

for explanation. Thank you very much.

**Dr. SUSAN KENNEDY:** I assume that by short term exposure you mean short term within a day, peak exposures. Is that the kind of short term exposures you are referring to?

I don't know if the others have any evidence on this point, but the only thing that I can tell you which has intrigued me and it's the reason why we ask the question in the first place and I'm not sure that I really know the answer yet, but one of the points I made in my presentation was that the highest rate of bronchial responsiveness that we saw was in the small group of workers who were working with CNC machines and in our area, the way that a person works with these machines is that in every case these machines were enclosed and I was intrigued by the possibility that they may have peak exposures, because, in fact, what they do is that they set the machine up, they test it out without the shield down and the exposure because the speed of the machine is much faster than in a conventional machine, there's a much greater sort of very short peak exposure, that is, people literally get soaked and then that's the testing phase, and then once you know that it's doing what you expect it to be doing, then you close the cover and you can essentially walk away.

And so we were interested in this possibility of peak exposures and unfortunately at this point in time within those first two years, it isn't something that apprentices do a lot of, so we only had four people who were working predominantly in that, with that type of equipment, but three of those four people have developed moderate increases in bronchial hyper-responsiveness, so that is intriguing to me. I don't know whether that will turn out to be significant over the long term.

**Dr. WILLIAM LUCKE:** In addition, as part of the anecdotal epidemiological study I talked about, when I would go into these plants, I would stick my head into the spray zone and leave it there just to get an impression, and typically at the end of the day when I would leave these plants, I would have a sore throat and a scratchy nose, so you can

get a very quick reversible effect there.

**Dr. KENNEDY:** But you have to remember that we were studying people when they were back in school. This is not an acute effect.

**Dr. JAMES D'ARCY:** Okay. Well, thank you very much. I'd like to hopefully see everybody tomorrow morning when we're going to be talking about how you assess exposure. Thanks again.