

A Regression Approach to the Analysis of Serial Peak Flow among Fuel Oil Ash Exposed Workers

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We investigated the association between exposure to fuel oil ash and acute airway obstruction in 31 boilermakers and 31 utility workers during the overhaul of a large oil-fired boiler. Air flow was assessed with self-recorded serial peak expiratory flow rate measurements (PEFR) using a mini-Wright meter. Exposure to thoracic particulates with an aerodynamic diameter of 10 μm or smaller (PM_{10}) was assessed using personal sampling devices and detailed work diaries. All subjects were male, with an average age of 43 yr, and an average of 18 yr at their current trade. Average PM_{10} exposure on work days was 2.75 mg/m^3 for boilermakers and 0.57 mg/m^3 for utility workers. Three daily PEFR measurements (start-of-shift, end-of-shift, and bed-time) were analyzed simultaneously, using Huber linear regression. After adjustment for job title, welder status, age, height, smoking, and weld-years, for each mg/m^3 increase in PM_{10} , the estimated decline in PEFR was 13.2 L/min ($p = 0.008$) for end-of-shift, 9.9 L/min ($p = 0.045$) for bed-time, and 6.6 L/min ($p = 0.26$) for start-of-shift of the following day. This decline of the exposure effect over the 24-h period that follows was statistically significant ($p = 0.004$). No other factors were found to significantly modify the effect of exposure. Our results suggest that occupational exposure to fuel oil ash is associated with significant acute decrements in peak flow. **Hauser R, Daskalakis C, Christiani DC. A regression approach to the analysis of serial peak flow among fuel oil ash exposed workers.**

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As part of an ongoing investigation, we studied boilermakers and utility workers exposed to fuel oil ash during the overhaul of a large oil-fired boiler at an electricity generating power plant. In an earlier report, we found that short-term occupational exposure to fuel oil ash was associated with a significant decline in spirometric indices; there was a significant dose-response relationship between the exposure level to inhalable particulates with an aerodynamic diameter of 10 μm or smaller (PM_{10}) and the adjusted change in FEV₁ (1). To further investigate the exposure-response relationship between fuel oil ash and airway obstruction, we had the boilermakers and utility workers perform self-recorded serial peak expiratory flow rate (PEFR) measurements in the current study. Our primary objectives were to assess the effect of PM_{10} on PEFR, as well as the potential modification of that effect by other factors, such as job and welder status and sequential days worked.

Serial PEFR measurements are frequently used to assess the relationship between airborne occupational exposures and air

flow (2, 3). The across-shift change in PEFR has traditionally served as an indicator of the airways response to airborne occupational exposures. Although the across-shift change in PEFR is widely used, there are difficulties in both its application and interpretation. Therefore, in this study, we adopted a different approach to analyze the PEFR measurements. We analyzed the multiple (serial) daily peak flow measurements taken over time, as well as the across-shift changes of peak flow over time, using Huber regression.

METHODS

Subjects

The study subjects were boilermakers and utility workers at an electricity generating plant in Massachusetts, all involved in the overhaul of a large oil-fired boiler and turbine with an output capacity of 175 megawatts. The study was approved by the institutional review board of the Harvard School of Public Health. The study was first explained to the subjects and then written consent was obtained. Sixty-two of the 80 eligible workers agreed to participate; reasons subjects did not participate included: refusals ($n = 11$); reassignments to another boiler job at a distant site ($n = 2$); and working night shift ($n = 5$). All subjects studied worked the day shift.

Peak Expiratory Flow Rate Measurements

After being instructed by a trained technician, the subjects performed PEFR measurements with a mini-Wright peak flow meter (4) and recorded them in a diary. The identification number of the PEFR meter was recorded in the field log book to ensure that each subject used the same peak flow meter throughout the study period. The subjects were asked

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to perform PEFR measurements five times per day: upon arising, at start of shift, at lunch time, at end of shift, and at bed-time. At each of these five times, the subjects performed three peak flow maneuvers and recorded all three values in the diary; in the analysis, the maximum of these three values was used as the PEFR measurement for that time. Measurements were taken both on work days and on days off work, for up to 13 consecutive days during the boiler overhaul. On days off work the subjects were instructed to perform the measurements as close as possible to the times they would perform them on a work day. If they were unable to perform a measurement at any time, they were told to skip it and continue on with the next measurement time.

Exposure Assessment

The overhaul of the boiler and turbine included the removal of sections of the boiler firebox (water wall tubes), ash pit, and air-heater (air heat-exchange section), as well as the repair of the condenser and mudrum which recirculates the condensed steam to the boiler. The work involved metal cutting with oxygen-acetylene torches and the carbon arc process. After the removal of the old and damaged sections, the boiler ash pit and sections of the air-heater and boiler firebox were replaced and welded in place using shielded metal arc and gas metal arc welding. Welding was also performed in the mud drum and condenser. The study was designed so that exposure and peak flow measurements were performed during the initial phase (first four weeks) of the overhaul, the removal of the old and damaged sections of the boiler. This design was implemented so as to avoid potential time trends in exposure levels, as exposure levels fall during the placing of the new sections.

Occupational exposure to PM₁₀ was estimated in this study. Work history diaries were used along with personal air samples to estimate exposure because the number of personal sampling devices was limited. The personal sampling devices, consisting of a pump and an impactor (5, 6), were placed on workers at the start of shift and collected upon the end of shift. Sampling times varied from 1 to 10 h (1- to 10-h time-weighted average, TWA) and were independent of task or location. Shortened sampling times were due to the unwillingness of some workers to continue to wear the pump or due to the performance of the pump (e.g., pump failure). The number of work days each subject wore the personal sampling device varied from zero to five; personal daily exposure measurements (TWAs) were available for 15% of the total number of study days. Throughout the study period, each subject also completed a detailed self-administered work diary which listed the tasks performed (e.g., welding, cutting, and grinding) and the specific location at which they were performed (e.g., boiler, air-heater, condenser). The mean of all available personal air samples, weighted by duration of sampling, for each task-location combination was then used as the exposure value for all subjects with that combination. On days off work, no personal exposure measurements were taken; occupational exposure was assumed to be zero on days off work.

Questionnaires

Data on smoking history were obtained by a modified American Thoracic Society DLD-78 self-administered questionnaire (7). Workers were classified as current cigarette smokers, ex-smokers, or nonsmokers. A subject was classified as current smoker if he smoked at least one cigarette a day for at least the past year, or more than 20 packs in his lifetime and still smoked within the month prior to initiation of the study. The subjects also completed an occupational history addendum containing questions specific to their current and past occupations, including questions on whether they currently welded, the number of years they had spent in their present trade, and the number of years they had worked as a welder.

Statistical Methods

We used a modeling approach (linear regression) to assess the effect of exposure to inhalable particulates (PM₁₀) on PEFR. In our multiple measurements (MM) analysis, we regressed 3 of the 5 individual serial PEFR measurements, start-of-shift, end-of-shift, and bed-time, on PM₁₀ exposure and a number of other variables. Arising PEFR was not used because it was close in time (within 1 or 2 h) to start-of-shift PEFR. Lunch-time PEFR was not used because of the difficulty in modeling the effect of a time-weighted-average exposure on an outcome measurement that occurs before the end of the exposure period. Daily exposure

was estimated as a TWA during the sampling period and lunch-time PEFR was performed midway through this period. Therefore, it is unclear what the appropriate amount of exposure is for the lunch-time PEFR measurement. The core of the MM regression model is shown below:

$$\text{PEFR} = \beta_0 + \sum_{j=1}^2 \beta_{\text{TIME}_j} \cdot T_j + \beta_{\text{JOB}} \cdot \text{JOB} + \beta_{\text{WELD}} \cdot \text{WELD} + \sum \beta_k^* \cdot Z_k + \beta_{\text{ONOFF}} \cdot \text{ONOFF} + \beta_{\text{EXP}} \cdot \text{EXP} \quad (1)$$

Table 1 gives a detailed description of the covariates and the way we modeled them. In summary, we included terms for time of day for the PEFR measurement (T1 and T2), job and welder status (JOB and WELD), other covariates (age, height, smoking, job-years, and weld-years: the Z's), work pattern (ONOFF), and the day's PM₁₀ exposure (EXP). The effect of age and height appeared curvilinear and therefore we included quadratic terms for these variables. The effect of job-years and weld-years initially appeared even more complex and we decided to treat them as categorical. With respect to work pattern (or sequential days worked), we considered two different classifications. The simplest one was to use a single dichotomous variable (ONOFF), indicating whether the day was a work day or a day off. As an alternative, we investigated a more detailed classification into eight mutually exclusive work patterns (WORK terms, Table 1).

The main question of interest concerned the acute effect of PM₁₀ exposure on peak flow, given by β_{EXP} , the slope for the exposure. We refer to all other terms in Equation 1 (i.e., those not involving exposure) as affecting the intercept of the regression line of peak flow on particulate exposure. In the MM analysis, we paired the start-of-shift PEFR with the exposure of the previous calendar day. Therefore, each daily cycle included the day's PM₁₀ exposure, and its end-of-shift and bed-time PEFRs, as well as the start-of-shift PEFR of the next calendar day. This definition allowed us to associate all PEFR measurements with the PM₁₀ exposure during the preceding 24-h period. If we had employed the usual definition of calendar day to define a daily cycle, we would have linked the start-of-shift PEFR to the exposure that follows it, a nonsensical way to model the effect of particulate exposure on peak flow. A utility worker's exposure and peak flow measurements are shown in Figure 1 to simply illustrate the data layout over time. On Monday, October 12, for example, this worker returned to work after having Sunday off. His Monday cycle on-work, as defined in our analyses, consists of his Monday end-of-shift and bed-time PEFRs along with his Tuesday start-of-shift PEFR, all three linked to Monday's PM₁₀ exposure.

In addition to the main terms discussed above, we also looked at a number of interactions, primarily those involving the exposure term. We looked at the interaction between time of day (T1 and T2) and PM₁₀ exposure (EXP) to determine how the acute effect of exposure on peak flow varies over the 24-h period that follows. We also looked at interactions of JOB, WELD, and WORK1 to WORK5 by exposure to assess whether the effect of exposure is different among various subgroups of workers (i.e., whether the exposure slope differs across covariate strata).

In a separate analysis of across-shift change (ASC), we regressed the across-shift change in PEFR (XSHIFT, defined as the difference between the day's end-of-shift and start-of-shift PEFRs) on PM₁₀ exposure and the other covariates. The core of the ASC regression model is given below:

$$\text{XSHIFT} = \beta_0 + \beta_{\text{JOB}} \cdot \text{JOB} + \beta_{\text{WELD}} \cdot \text{WELD} + \sum \beta_k^* \cdot Z_k + \beta_{\text{ONOFF}} \cdot \text{ONOFF} + \beta_{\text{EXP}} \cdot \text{EXP} \quad (2)$$

The ASC approach differs from the MM analysis in that there is only a single outcome per day (the across-shift change, XSHIFT) and, therefore, no terms for time of day are included. Also note that, in the ASC analysis, both the start-of-shift and end-of-shift PEFR measurements (on which the across-shift change is based) are implicitly linked to the PM₁₀ exposure of the same calendar day.

In our study, peak flow measurements for each worker were strongly correlated over time, both within each day and from one day to the next (correlation coefficients exceeded 0.85). Across-shift changes in peak flow were also correlated over time, although weakly (average correlation coefficients of 0.2). When observations are not independent, ordinary linear regression yields valid coefficient estimates but incorrect (too small) standard errors. To account for the correlation of observations

TABLE 1
DESCRIPTION OF THE COVARIATES CONSIDERED IN THE
ANALYSIS OF PEAK EXPIRATORY FLOW RATE

Variable	Modeled As
TIME OF DAY 0 = end-of-shift 1 = bed-time 2 = start-of-shift (next day)	2 dummy variables: T1 and T2 (end-of-shift is reference)
JOB: job status 0 = utility workers; 1 = boilermakers	
WELD: welder status 0 = nonwelders; 1 = welders	
ONOFF: daily cycle on- or off-work 0 = cycle on-work; = cycle off-work	
WORK: work patterns (sequential daily cycles on- or off-work) 0 = first on-work daily cycle (after 1+ off-work cycles) 1 = second on-work cycle 2 = third on-work cycle 3 = fourth on-work cycle 4 = 5+ on-work cycles 5 = first off-work cycle (after 1+ on-work cycles) 6 = 2-7 off-work cycles 7 = 8+ off-work cycles	7 dummy variables: WORK1-WORK7 (first on-work cycle is reference)
AGE, yr	Continuous: AGE and AGE ²
HEIGHT, inches	Continuous: HEIGHT and HEIGHT ²
SMOKING 0 = nonsmokers; 1 = ex-smokers; 2 = current smokers	2 dummy variables (nonsmokers is reference group)
JOB-YEARS: years in present trade 0 = 1-9; 1 = 10-19; 2 = 20-24; 3 = 25+	3 dummy variables: JYRS1-JYRS3 (1-9 yr is reference group)
WELD-YEARS: years welding 0 = 0; 1 = 1-9; 2 = 10-19; 3 = 20+	3 dummy variables: WYRS1-WYRS3 (0 yr is reference group)
Particulate (PM ₁₀) exposure (mg/m ³)	Continuous: EXP

(both between days or daily cycles within a subject, and between individual PEFR measurements within a single daily cycle), we used Huber linear regression which is based on ordinary least squares but uses a robust estimate of the variances (8). This is essentially equivalent to using generalized estimating equations (GEEs) with an independence working correlation matrix. All our analyses were performed with STATA (9).

RESULTS

These results are based on data from 62 male workers: 31 utility

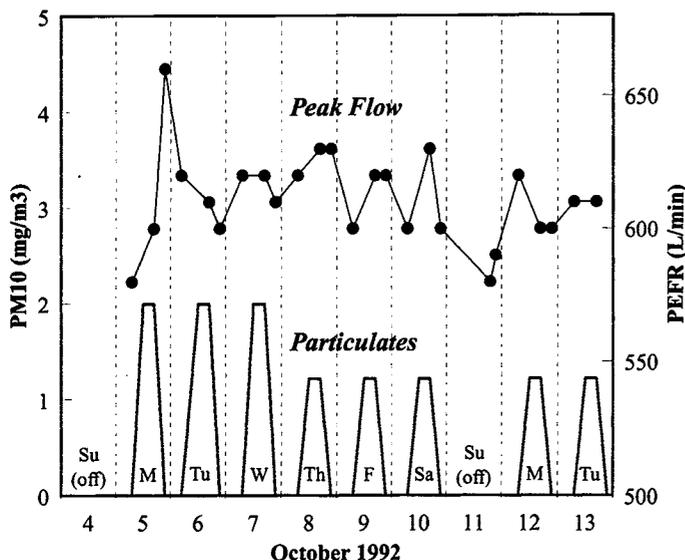


Figure 1. Inhalable particulate (PM₁₀) exposure number and PEFR data collected over time for study subject number 39 (utility worker, welder, 36 yr old, 69 inches tall, ex-smoker, with 8 yr in the trade, and 6 yr of welding).

workers and 31 boilermakers. Of these 62 workers, 26% were welders; these included nine utility workers and seven boilermakers. Table 2 summarizes the sociodemographic and work history characteristics of the subjects.

In the MM analysis we used the individual start-of-shift, end-of-shift, and bed-time PEFR measurements, whereas in the ASC analysis we used the across-shift PEFR difference as the outcome. The 62 workers contributed a total of 1,061 PEFR measurements (350 start-of-shift, 351 end-of-shift, and 360 bed-time) for which PM₁₀ exposure information was available, 660 of them on cycles on-work and 401 on cycles off-work. The data on particulate exposure and peak flow are summarized in Table 3. Note, however, that subjects contribute an unequal number of measurements and no covariates are controlled for in this crude summary. In particular, job status may confound these crude data because cycles on-work with low exposure (< 1.5 mg/m³) are largely based on the experience of utility workers, while cycles on-work with higher exposure are based on boilermakers. The average PM₁₀ exposure on work-days was 2.75 mg/m³ for boilermakers and 0.57 mg/m³ for utility workers.

Table 4 shows the regression coefficients and 95% confidence intervals from both the MM and ASC multivariable Huber linear regressions. In addition to the variables shown in Table 4, both approaches controlled for age and height (with linear and quadratic terms), as well as for work pattern (with a dichotomous variable indicating whether the daily cycle was on- or off-work).

In our MM analysis, we estimated that each additional mg/m³ of PM₁₀ depresses the end-of-shift PEFR by 13.2 L/min ($p = 0.008$), the bed-time PEFR by 9.9 L/min ($p = 0.045$), and the next day's start-of-shift PEFR by 6.6 L/min ($p = 0.26$). The decline of the effect of PM₁₀ on PEFR over the 24-h period following exposure is highly significant ($p = 0.004$ for the interaction of time of day and exposure). Our analysis is consistent with the known effects of other risk factors. In the final multivaria-

TABLE 2
DESCRIPTION OF THE CHARACTERISTICS
OF THE 62 STUDY SUBJECTS

Variable	n (%)	Range	Mean \pm SD
JOB			
Utility worker	31 (50)		
Boilermaker	31 (50)		
WELD			
Nonwelder	46 (74)		
Welder	16 (26)		
AGE, yr		26-60	43.1 \pm 8.7
HEIGHT, inches*		63-77	69.7 \pm 2.5
SMOKING			
Nonsmoker	23 (37)		
Ex-smoker	28 (45)		
Current smoker	11 (18)		
JOB-YEARS			
1-9	14 (23)	1-38	18.1 \pm 9.0
10-19	19 (31)		
20-24	14 (23)		
25+	15 (24)		
WELD-YEARS			
0	26 (42)	0-32	8.0 \pm 9.0
1-9	11 (18)		
10-19	18 (29)		
20+	7 (11)		
Days contributed per worker, n		1-13	7.2 \pm 3.2
PEFRs contributed per worker, n			
Total		1-31	17.1 \pm 8.8
Start-of-shift		0-11	5.6 \pm 3.1
End-of-shift		0-11	5.7 \pm 3.1
Bed-time		0-11	5.8 \pm 3.0

* Height missing for one subject.

ble model shown in Table 4 (when simultaneously adjusting for all variables, including PM_{10} exposure), PEFR was on the average lower for smokers compared with nonsmokers (by 10 L/min), boilermakers compared with utility workers (by 29 L/min), and welders compared with nonwelders (by 14 L/min). In contrast, the longer a worker had worked as a welder, the higher his PEFR (by up to 72 L/min, for having welded for more than 20 yr compared with having done no welding at all).

Using the more detailed classification for work pattern (sequential days worked: WORK, in Table 1), we found no significant interaction with exposure. Interactions between job or welder status and exposure were not significant either, suggesting that the exposure-response association is similar across subgroups of workers. We also found no evidence for nonlinearity of the effect of PM_{10} exposure on PEFR.

Figure 2 displays the MM results for a cycle on-work of a typical (30-year-old, 70-inch tall, nonsmoker, nonwelder) utility worker and boilermaker separately. Illustrating the attenuation of the acute effect of PM_{10} exposure over time, the line for bed-time is flatter than the one for end-of-shift, and that for next day's start-of-shift is flatter than that for bed-time. Note that the three lines for the boilermaker are shifted downward by 29 L/min compared with the respective lines for the utility worker but the slopes are the same. For any other set of covariate values, the lines shown in Figure 2 will have to be adjusted upward or downward using the appropriate coefficients shown in Table 4 but their slopes will remain unchanged.

In our ASC analysis, we found a less dramatic effect of exposure. The average across-shift PEFR change in our study group was 5.7 L/min (with a standard deviation of 29 L/min). In the final multivariable model, we estimated that each mg/m^3 of PM_{10} was associated with a decrease of 0.78 L/min ($p = 0.64$) in the across-shift PEFR change. We also found that most covariates were not associated with the across-shift change in PEFR, possibly because they affect both the start-of-shift and end-of-shift PEFR similarly.

DISCUSSION

In this cohort of boilermakers and utility workers, occupational exposure to inhalable particulates comprised of fuel oil ash, as well as other constituents such as welding fume, was associated with acute decrements in peak flow; there was a significant exposure-response relationship between inhalable particulates exposure and end-of-shift and bed-time PEFR. The results of the serial peak flow measurements are consistent with our earlier report of an association between short-term (over 4 wk) occupational exposure to fuel oil ash inhalable particulates and a significant decline in spirometric indices (3). The spirometry and serial peak flow studies were performed simultaneously on the same cohort of boilermakers; the utility workers participated in serial peak flow measurements but did not perform pre- and post-exposure spirometry.

In this study, we adopted an uncommon approach to analyze the serial peak flow measurements. If we had followed the traditional approach, we would have had to calculate average exposure and average peak flow (or average across-shift change) over time for each subject, and then analyze the 62 averages using ordinary linear regression. However, this can lead to invalid inferences since it does not account for the fact that the averages may be based on unequal numbers of measurements for each subject, it may introduce measurement error by averaging exposure and response values over time, and it ignores the potentially differ-

TABLE 3
SUMMARY OF INHALABLE PARTICULATE (PM_{10}) EXPOSURE AND PEFR,
BY WORK PATTERN (DAILY CYCLE ON- OR OFF-WORK)

Daily Cycle*	PM_{10} (mg/m^3)		N [†]	PEFR (L/min)		
	level	mean \pm SD		End-of-shift mean \pm SD	Bed-time mean \pm SD	Start-of-shift mean \pm SD
Off-work		0	401	606 \pm 68	594 \pm 71	606 \pm 73
On-work	(0.0-0.5)	0.11 \pm 0.09	317	624 \pm 60	608 \pm 66	608 \pm 67
	(0.5-1.5)	1.23 \pm 0.23	92	632 \pm 53	618 \pm 64	629 \pm 48
	(1.5-2.5)	1.87 \pm 0.32	103	598 \pm 68	581 \pm 68	588 \pm 72
	(2.5+)	3.66 \pm 0.86	148	581 \pm 69	575 \pm 63	590 \pm 70
	(all on- levels)	1.34 \pm 1.47	660	611 \pm 65	598 \pm 65	604 \pm 67
Total (on- and off-work cycles)		0.83 \pm 1.33	1,061	610 \pm 66	596 \pm 67	605 \pm 70

* Each daily (24 h) cycle includes the day's PM_{10} exposure, end-of-shift, and bed-time PEFRs, as well as the start-of-shift PEFR of the following calendar day.

[†] N indicates total number of observations (total number of PEFR measurements).

TABLE 4
MULTIVARIABLE* HUBER LINEAR REGRESSION COEFFICIENTS
(95% CONFIDENCE INTERVALS) FOR THE PEFR ANALYSES

	MM Analysis [†]	ASC Analysis [‡]
PM ₁₀ exposure, mg/m ³		
For end-of-shift PEFR [§]	-13.21 (-22.97 to -3.45)	
For bed-time PEFR	-9.86 (-19.47 to -0.25)	
For start-of-shift (next day) PEFR	-6.62 (-18.19 to 4.94)	
For across-shift change in PEFR		-0.78 (-4.00 to 2.44)
JOB, boilermaker	-28.81 (-71.11 to 13.49)	-2.83 (-16.90 to 11.24)
WELD, welder	-13.74 (-93.97 to 66.50)	-1.72 (-10.99 to 7.55)
SMOKING, smoker	-9.93 (-60.27 to 40.41)	-10.66 (-20.40 to -0.92)
WELD-YEARS		
1-9	29.36 (-52.75 to 111.5)	6.89 (-3.72 to 17.50)
10-19	61.91 (-12.98 to 136.8)	-2.75 (-16.66 to 11.16)
20+	71.70 (-22.75 to 166.1)	0.26 (-19.78 to 20.29)

* Controlling for age, height, and work pattern (daily cycle on- or off-work).

[†] Multiple measurements regression for the individual serial PEFR measurements (start-of-shift, end-of-shift, and bed-time).

[‡] Across-shift change regression for the across-shift change in PEFR (end-of-shift minus start-of-shift).

[§] PEFR regression coefficients are in units of L/min.

ent variability of individual measurements across subjects. Therefore, we decided to analyze the individual serial peak flow measurements, using Huber linear regression to account for their correlation. Huber linear regression analysis is a very useful competitor to more complex longitudinal analyses, such as multivariate analysis of variance and mixed-effects models. It is easily performed, even when subjects have contributed unequal numbers of observations, when there are occasional missing data, or when the more advanced techniques lead to unstable results. In our approach, we used the more appropriate definition of daily cycle (as opposed to the usual use of calendar day defining a daily cycle), where we linked each day's exposure to the day's end-of-shift and bed-time peak flow, as well as to the next day's start-of-shift peak flow. This definition had the added advantage of allowing us to investigate the interaction between time and exposure over the 24-h period that follows exposure.

In the analysis of the serial peak flow measurements, we found that each mg/m³ of inhalable fuel oil ash particulates was associated with statistically significant drops in end-of-shift and bed-time peak flow, by 13.2 L/min (a 2.2% decrement) and 9.9 L/min (a 1.7% decrement), respectively. The next day's start-of-shift peak flow was also depressed, though by a lesser amount

which was not statistically significant. In comparison, the earlier spirometry results showed an average decline of 140 ml in FEV₁ over a 4-wk work period (3). Higher average exposure over the study period was associated with a larger decline in adjusted change in FEV₁ (post- minus pre-exposure FEV₁, divided by the average of pre- and post-values); for each additional mg/m³ in average exposure, adjusted change in FEV₁ declined 0.91% (3).

The peak flow results indicate that occupational exposure to inhalable particulates (comprised of fuel oil ash, as well as other constituents such as welding fume) is associated with an immediate airway obstructive response, but that the effect diminishes significantly over the 24 h following exposure. The spirometry results, on the other hand, suggest that there is a cumulative response to repeated fuel oil ash exposure over weeks. In other words, even though the acute response to exposure declines over time (hours), repeated exposure over a period of weeks results in a cumulative response as evidenced by the short-term decrements in spirometric indices. The peak flow results demonstrate an association between fuel oil ash exposure and acute (hours) airway obstruction, while the spirometry results show an association between fuel oil ash exposure and short-term (weeks) airway obstruction.

We also investigated the hypothesis that the exposure-response relationship may vary by the number of sequential days worked, i.e., that the response to exposure may be more pronounced in the beginning of the work week and decline as the worker spends more days at work. Previous studies with subjects experimentally exposed to ozone, another respiratory irritant, have reported a similar adaptation in response (10-12). However, we found no evidence for this hypothesis in our data. Neither did we find any evidence of modification of the exposure effect by job trade or welder status.

The workers studied represent a survivor cohort, individuals who were able to gain employment as boilermakers and utility workers and work in the trade for an average of 18 yr. Because this selection of workers, defined as the healthy worker effect, would tend to bias the results toward the null (13), our results may actually underestimate the true magnitude of the effect of fuel oil ash exposure on lung function. The existence of a healthy worker effect in this cohort is indeed supported by our finding that peak flow tended to increase with the number of years spent in welding tasks.

Our results show that boilermakers tend to have lower peak flow than utility workers: a boilermaker's peak flow was estimated to be 29 L/min lower than that of a utility worker, every-

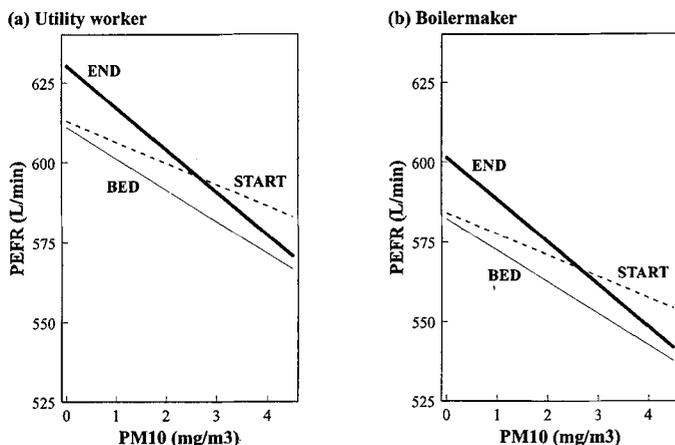


Figure 2. Multiple measurements analysis results: multivariable linear regression of PEFR on inhalable particulate (PM₁₀) exposure during a cycle on-work for a typical study subject (30 yr old, 70 inches tall, nonsmoker, nonwelder). (a) Utility worker. (b) Boilermaker.

thing else being equal (including the level of particulate exposure). Boilermakers tend to experience higher levels of exposure to fuel oil ash than utility workers (averages of 2.75 versus 0.57 mg/m³ PM₁₀ in our study). Chronic (years) exposure to higher levels of fuel oil ash may then account for the lower peak flow measurements seen in boilermakers compared with utility workers, although other factors may also be involved. Welders were also found to have lower peak flow measurements than nonwelders, by an estimated average of 14 L/min. Welding generates respirable particulates, as well as ozone and oxides of nitrogen, which may contribute to such a decrement in lung function (14, 15).

The analysis of across-shift change in peak flow suggests a much weaker effect of fuel oil ash exposure than our analysis of the serial peak flow measurements. However, the across-shift change results seriously underestimate the true exposure effect for two reasons. First, consider the simplified assumption of constant fuel oil ash exposure over time for each worker. In this case, the across-shift change analysis essentially estimates a difference of effects of exposure: the effect on end-of-shift minus that on start-of-shift peak flow. Naturally, if the exposure effect does not dissipate substantially over a 24-h period, both peak flow values will be similarly depressed and the across-shift change analysis may find no association between exposure and across-shift change in peak flow. In our study, the MM results show that this difference of the exposure effects is equal to -6.6 L/min (the difference of -13.2 minus -6.6), i.e., a predicted decline of the across-shift change by 6.6 L/min for each additional mg/m³ of PM₁₀. The corresponding ASC estimate, -0.8 L/min, is substantially smaller in magnitude. This further attenuation of the estimate of the exposure effect in the across-shift analysis is due to how response is paired with exposure. When across-shift change in peak flow is analyzed, both start-of-shift and end-of-shift peak flow measurements are implicitly linked to the same day's exposure. However, the start-of-shift peak flow is subject to the effect of the previous day's exposure. In practice, exposure is not constant from one day to the next, and the true relevant exposure for start-of-shift peak flow will often be different (either higher or lower) from the one assigned. It is this nondifferential misclassification of exposure that leads to further bias of the exposure effect toward the null in the analysis of across-shift change.

Limitations

Exposure assessment has some weaknesses in our study, including: (1) personal exposure measurements were available for only a fraction of subjects and days on-work; (2) the accuracy of the work history diaries is unknown; (3) information on use of personal respiratory protective equipment was not available; (4) exposure misclassification may have resulted from grouping subject work days by task/location work combinations; and (5) the exposure categories are based on relatively small numbers of exposure measurements. Furthermore, the assumption of zero exposure on days off-work may not be correct because environmental PM₁₀ levels are not zero. However, compared with the occupational exposure levels measured in the study, this misclassification of days off-work is minimal; in any case such misclassification may lead to a slight underestimation of the exposure effect on start-of-shift. Because we are estimating an average intercept for PEFR off-work, this assumption of zero exposure has essentially no effect on the estimated average PEFR on cycles off-work.

Additional limitations include some that are not uncommon in occupational studies. The small number of workers studied may have limited our power to detect adaptation effects (i.e., sequential daily cycles on- or off-work) or possible nonlinearity of effect of exposure. The statistical approach that we used (Huber

regression) is not the most efficient method, especially for factors that differ between workers (e.g., job status). The estimated coefficients are valid, but the associated confidence intervals may be too wide (see Table 4). Huber linear regression is equivalent to a GEE approach, with an independence working correlation matrix. A more accurate working correlation matrix could probably improve the efficiency of the method, resulting in narrower confidence intervals. Finally, up to 20% of individual PEFR measurements are missing (see Table 2); therefore, the possibility of some bias (either away or toward the null) in our estimates of the exposure effect cannot be discounted.

In summary, we found occupational exposure to fuel oil ash to be associated with acute decrements in PEFR. There was a strong and statistically significant dose-response (linear) relationship between exposure to inhalable particulates and peak flow. This acute airway response to fuel oil ash was found to gradually diminish over the 24-h period following exposure, although it did not disappear entirely. These results, combined with spirometry results from a previous report on the same cohort of workers (3), suggest that fuel oil ash exposure is associated with significant acute (hours) and short-term (weeks) decrements in lung function. Further study is needed to determine if such decrements contribute to chronic and irreversible loss of lung function.

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