

Spirometric Abnormalities Associated With Chronic Bronchitis, Asthma, and Airway Hyperresponsiveness Among Boilermaker Construction Workers*

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Study objectives: In a 2-year longitudinal study of boilermaker construction workers, we found a significant association between working at oil-fired, coal-fired, and gas-fired industries during the past year and reduced lung function. In the present study, we investigated whether chronic bronchitis, asthma, or baseline methacholine airway responsiveness can explain the heterogeneity in lung function response to boilermaker work.

Design: This study is part of an ongoing prospective cohort study of boilermakers. Exposure was assessed with a work history questionnaire. Spirometry was performed annually to assess lung function. A generalized estimating equation approach was used to account for the repeated-measures design.

Setting: Boilermaker union members.

Participants: One hundred eighteen boilermakers participated in the study.

Interventions: None.

Measurements and results: Self-reported history of chronic bronchitis and asthma were associated with a larger FEV₁ reduction in response to workplace exposure at coal-fired and gas-fired industries. Although we found a high prevalence (39%) of airway hyperresponsiveness (provocative concentration of methacholine causing a 20% fall in FEV₁ of < 8 mg/mL) among boilermakers, we did not find a consistent pattern of effect modification by airway responsiveness.

Conclusions: Although chronic bronchitis and asthma were associated with a greater loss in lung function in response to hours worked as a boilermaker, and therefore they acted as effect modifiers of the exposure-lung function relationship, airway hyperresponsiveness did not. However, the high prevalence of airway hyperresponsiveness found in the cohort may be a primary consequence of long-term workplace exposure among boilermakers.

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Key words: airway responsiveness; asthma; chronic bronchitis; lung function; occupational health; respiratory tract disease

Abbreviations: ATS = American Thoracic Society; CI = confidence interval; GEE = generalized estimating equation; PC₂₀ = provocative concentration of methacholine causing a 20% decrease in FEV₁

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Several epidemiologic studies^{1–6} have shown an association between occupational exposure to fossil fuel ash and respiratory health effects. The early studies^{1,2} reported clinical symptoms and signs, such as upper respiratory tract irritation, a cough with dyspnea, and rhonchi on physical examination resulting from occupational exposure to fuel oil ash. This suggests that fuel oil ash is a respiratory irritant capable of inducing respiratory symptoms, including those suggestive of asthma. However, these early studies^{1,2} had limited measures of exposure and effect, and the exposures were generally extremely high compared to current occupational exposure. More recently, a small study³ of

17 men cleaning bottom ash from an oil-fired boiler found marked reductions in lung function (FEV₁). In another study of respiratory symptoms, Levy and Hoffman⁴ investigated a large outbreak of "boilermakers' bronchitis," described as asthmatic bronchitis, after 100 boilermakers worked on the oil-to-coal conversion of a utility company power plant. Studies^{5,6} on acute (*ie*, across a work shift) and short-term (over several weeks) changes in FEV₁ demonstrated decrements in lung function among workers who overhauled an oil-fired boiler.

We recently examined the long-term effects of workplace exposures among boilermakers by studying exposure and lung function decline over a 2-year period.⁷ An association was found between FEV₁ and working at gas-fired, oil-fired, or coal-fired boilers during the follow-up interval. Although this study lacked ambient measurements of exposure, previous work^{5,6} demonstrated that combustion particulates are the likely exposure.

In the present study, we sought to determine the distribution of host characteristics, such as chronic bronchitis, asthma, and methacholine airway responsiveness, among the same cohort of boilermaker construction workers. Since in occupational health studies there is heterogeneity in an individual's response, we sought to determine whether host characteristics modify an individual's response to workplace exposures. Specifically, we investigated whether chronic bronchitis, asthma, or airway responsiveness was an effect-measure modifier of the relationship between hours worked and FEV₁. In addition, we investigated whether an allergic predisposition, as determined by skin-prick test, total and specific IgE concentration, and peripheral blood eosinophil counts, modified the association between hours worked and FEV₁.

MATERIALS AND METHODS

Cohort Description

Between December 1997 and March 1998, the researchers, with the help of the union staff, assembled a cohort of 118 boilermaker construction workers from Local 29 of the International Brotherhood of Boilermakers, Iron Shipbuilders, Blacksmiths, Forgers and Helpers. The criteria for entrance into the cohort included being an active member of the union. A detailed description of the cohort has been reported earlier.⁷

The study was explained to each of the subjects and all questions were answered prior to signing the consent form approved by the Harvard School of Public Health human subjects committee. On signing the consent form, each subject underwent baseline spirometry and completed a modified American Thoracic Society (ATS) questionnaire.⁸ The following question was used to define asthma: "Have you ever been diagnosed by a physician as having asthma?" Chronic bronchitis was defined as phlegm on most days for ≥ 3 consecutive months during the

year, and for ≥ 2 years. At the yearly follow-ups (year 1 and year 2), each subject underwent spirometry and completed a detailed work history questionnaire.

Exposure Measurement

The boilermakers' trade is such that throughout the course of a typical year, workers will service numerous boilers at multiple power plants burning a variety of fuels. Throughout this article, the term *plant* is used to refer to fossil fuel-combustion power plants (natural gas, oil, and coal), trash incinerators, paper mills, or nuclear power plants. The term *fuel* is used to refer to the type of fuel predominately burned at the plant. Fuels include oil, coal, natural gas, trash, tree bark/sap (black liquor), and nuclear. We collected data on the number of hours worked at each type of plant during the intervals between lung function tests.

Detailed work history information was collected using a self-administered questionnaire. The questionnaire was completed 6 months after entrance into the study, at the 1-year follow-up, and again at the 2-year follow-up. To assist the workers in recalling their yearly work history, the union provided printed records that contained information about the dates worked, the number of hours worked, and at which plant an individual worked during the previous year. Each questionnaire was reviewed immediately after the worker completed it, inconsistencies were clarified, and any missing information was solicited.

Although the questionnaire collects information on duration of exposure, it does not directly collect information on intensity of exposure. However, our earlier studies showed clear differences in exposure intensity based on work location within a plant. For instance, work within the firebox was associated with higher particulate exposure than work performed outside the firebox. Therefore, in future analyses information on work location can be used to quantify exposure intensity.

Spirometry

The majority of the spirometry was performed in the boilermakers union hall (Quincy, MA) or at an apprentice training site (Portland, ME). The yearly tests were performed between December and March to control for possible seasonal variations in lung function that may result from seasonal allergies.

In cooperation with the union, we attempted to schedule spirometry tests after the worker had had several days off work. Since this did not always occur due to the boilermakers' work schedule, we collected information on the number of days since they last worked. Testing was generally performed between 9 AM and 2 PM; the time of testing was recorded on the spirometry data sheet. To minimize technical variation, the same nurses and technicians used the same equipment and techniques each year. A detailed description of the spirometry protocol has been reported earlier.⁵

Host Characteristics

Methacholine Challenge Test: The methacholine challenge tests were performed in the boilermakers' union hall at baseline testing. The methacholine challenge protocol was a modified method adapted from that described by Cockcroft and coworkers.⁹ A detailed description of the challenge protocol has been reported earlier.⁵ In the present study, the doses of methacholine used were 0.5, 1.0, 2.0, 5.0, and 10 mg/mL.

Allergy Skin-Prick Tests and Blood Tests for IgE and Eosinophils: Skin-prick tests were conducted using six common inhalant allergens (*Dermatophagoides pteronyssinus*, mixed grasses, ragweed, birch tree, oak tree, and *Alternaria*) and positive and

negative control agents (histamine and saline solution, respectively). Skin-prick tests were read at 15 min, and a positive test result was recorded if the maximum wheal diameter was 3 mm larger than the saline solution control. Subjects were defined as atopic if one or more skintest results were positive.

Blood samples were collected before skin-prick tests were performed. Eosinophils were measured using an STKS Hematology Flow Cytometer and GenS System2 Hematology Workstation (Beckman Coulter; Miami, FL). Peripheral blood eosinophilia was defined as cell count $> 275/\mu\text{L}$.^{10,11} Sera were analyzed for total and specific IgE levels (CAP System FEIA; Pharmacia; Uppsala, Sweden) as per instructions of the manufacturer using reagents purchased from Pharmacia-UpJohn Corporation (Uppsala, Sweden). The assay is a solid-phase immunofluorometric assay in which IgE antibodies bound to sponge matrix (Immuno Cap; Pharmacia) coated with either anti-IgE or specific allergen are detected with β -galactosidase-labeled rabbit polyclonal antihuman IgE and 4-methylumbelliferyl-D galactosidase substrate. Total IgE values are reported in kilounits per liter. High serum IgE levels were defined as > 100 kilounits per liter. Specific IgE (atopic status positive or negative) was estimated by assaying each sera against six Immuno CAP allergen mixes: grass mix, house dust mix, mold mix, tree mix, weed mix, and epidermal mix. The mixes were chosen because they contained allergens typically found in the New England region. Reaction to each mix was scored as either positive or negative, and a positive reaction to one or more mixes was evidence of atopy.

Data Analysis

The prediction equations of Hankinson et al¹² were used to calculate percent predicted FEV₁ based on age, height, gender, and race. The detailed work history questionnaires were used to determine the number of hours worked at each particular type of plant, for each of the 2 years of the study period.

A detailed description of the analysis of the methacholine challenge protocol has been reported earlier.⁵ Measurements of host allergic characteristics were dichotomized, *ie*, presence or absence of chronic bronchitis or asthma, presence or absence of skin test positivity, a high serum total IgE level (> 100 kilounits per liter), and peripheral blood eosinophilia (> 275 cells/ μL).

For the analysis of FEV₁ regressed on exposure and host characteristics, we used a generalized estimating equation (GEE) approach to account for the correlation between repeated measures of FEV₁ for each person.¹³ Using software (PROC GENMOD, SAS 8.0; SAS Institute; Cary, NC),¹⁴ the maximum lung function at each annual survey was examined in relation to yearly exposure, host characteristics, and other potential confounders. Although we measured FEV₁ yearly on everyone, the data were evaluated as cross-sectional, repeated measures rather than longitudinal change to examine the effect of annual exposure on FEV₁. Effect modification was assessed by including an interaction term between host characteristic and exposure in the regression model. We also assessed effect modification by stratifying regression models by host characteristics.

RESULTS

Cohort Demographics

The study cohort included 118 boilermakers. Seventy-six subjects had complete data consisting of baseline, year-1 spirometry, and year-2 spirometry. Ninety-eight boilermakers completed year-1 spirometry, and 94 boilermakers completed year-2 spirometry.

The reasons cited for missing follow-up spirometry included working out of state, family matters preventing participation, and scheduling difficulties. A detailed description of the cohort has been reported earlier.⁷

The demographics and lung function of the study subjects are presented in Table 1. The study population was older than typical working cohorts: the mean age of the cohort was 42.6 years, and 25 boilermakers (21%) were > 50 years old. There were 14 apprentices (individuals with < 5 years of experience) in the cohort. All boilermakers were male, and 97% were white. Thirty-one percent were current smokers, and 32% were never-smokers. The mean (SD) history of smoking among current smokers and ex-smokers was 23.7 (20.9) pack-years. Six boilermakers had a physician diagnosis of asthma, and 18 boilermakers reported symptoms of chronic bronchitis on the modified ATS questionnaire. The average baseline FEV₁ was 90% of predicted. Twenty-two subjects (19%) had baseline percent predicted FEV₁ of $< 80\%$.

Relationships Among Host Characteristics

Peripheral Blood Eosinophils, Serum Total, and Specific IgE: One hundred seventeen boilermakers

Table 1—Demographics, Lung Function, and Host Characteristics for the Cohort of Boilermaker Construction Workers (n = 118)*

Characteristics	Data
Age, yr	42.6 (8.8)
Height, cm	176.9 (6.9)
Years worked	18.1 (9.3)
Lung function	
Baseline (n = 114) FEV ₁ , mL	3,700 (760)
% predicted (SD)	90.4 (15.9)
Follow-up year-1 (n = 98) FEV ₁ , mL	3,727 (707)
% predicted (SD)	91.0 (14.2)
Follow-up year-2 (n = 94) FEV ₁ , mL	3,599 (698)
% predicted (SD)	89.2 (14.2)
Smoking status, No. (%)	
Nonsmokers	38 (32.2)
Ex-smokers	43 (36.4)
Current smokers	37 (31.4)
Physician-diagnosed asthma, No. (%)	6 (5)
Chronic bronchitis, No. (%)	18 (15)
Markers of Allergy, No. (%)	
Total IgE (> 100 kilounits/L) [n = 117]	37 (32)
Eosinophilia (> 275 cells/ μL) [n = 117]	15 (13)
Skin-prick test positive (n = 115)†	65 (57)
Airway responsiveness (n = 98)	
Methacholine dose response slope‡	- 184.7 (314.4)
Geometric mean	- 53.8
PC ₂₀ < 8 mg/mL	38 (39)

*Data are presented as mean (SD) unless otherwise indicated.

†A positive skin-prick test result is a wheal > 3 mm.

‡Slopes are in units of change in FEV₁ in milliliters per milligram methacholine/milliliter.

provided blood samples for eosinophils and serum and specific IgE (Table 1). Thirty-two percent of subjects had a high total IgE, while 47% of subjects had at least one positive specific IgE response to grass mix, house dust mix, mold mix, weed mix, tree mix, or epidermal mix. Thirteen percent of the subjects had eosinophilia. Based on χ^2 tests, there was a strong positive significant association between total IgE and specific IgE. However, there were no associations among any of the other serum measures of host reactivity.

Skin-Prick Test: One hundred fifteen boilermakers underwent skin-prick tests to common aeroallergens. Sixty-five subjects (57%) were atopic, defined as having one or more positive skin-prick test responses (Table 1). As expected, there were significant associations between skin-prick test results and specific IgE ($p < 0.0001$) and total IgE ($p < 0.002$). However, there was no association between skin-prick test results and eosinophilia or methacholine airway hyperresponsiveness.

Chronic Bronchitis and Asthma: Cohort demographics, lung function measurements, and host characteristics are presented stratified by chronic bronchitis ($n = 18$), asthma ($n = 6$) or neither chronic bronchitis nor asthma ($n = 95$; Table 2). Sixty-one percent of those with chronic bronchitis were current smokers, as compared to 17% of those

with asthma and 26% of those without asthma or chronic bronchitis. The mean baseline percent predicted FEV₁ was lowest for those with asthma (82.7%), low for those with chronic bronchitis (85.4%), and somewhat low for those with neither disease (91.2%). Decrease in FEV₁ for subjects with asthma and chronic bronchitis, as compared to those with neither disease, was 102 mL/yr and 105 mL/yr, respectively.

Airway Responsiveness: Ninety-eight of 118 boilermakers (83%) completed the methacholine challenge test. Subjects with asthma, chronic bronchitis, or FEV₁ percent predicted $< 70\%$ were generally excluded from methacholine challenge tests for safety reasons. Of the 11 subjects with baseline FEV₁ $< 70\%$ predicted, only 2 subjects underwent methacholine challenge tests. Of the 6 asthmatic and 18 chronic bronchitic subjects in the cohort, only 2 subjects and 12 subjects, respectively, participated in the methacholine challenge test.

The methacholine challenge test results are presented as both provocative concentration of methacholine causing a 20% fall in FEV₁ (PC₂₀) and dose-response slope. There were 38 subjects (39%) with hyperresponsive airways, defined as a PC₂₀ of < 8 mg/mL (Table 1). Since the distribution of the dose-response slopes were skewed, we calculated geometric means. The geometric mean of the slope was -53.8 mL FEV₁/milligram methacholine per

Table 2—Cohort Demographics, Lung Function, Measurements, and Host Characteristics by Chronic Bronchitis and Asthma Status*

	Chronic Bronchitis	Asthma	Neither
Subjects, No.†	18	6	95
Age, yr	43.0 (9.9)	40.2 (10.7)	42.7 (8.5)
Years worked	17.4 (10.8)	13.8 (9.4)	18.5 (9.0)
Smoking status, No. (%)			
Nonsmokers	1 (6)	3 (50)	34 (36)
Ex-smokers	6 (33)	2 (33)	36 (38)
Current smokers	11 (61)	1 (17)	25 (26)
Lung function			
Baseline FEV ₁ , mL‡	3,489 (1,122)	3,492 (1,290)	3,726 (675)
Follow-up year-1 FEV ₁ , mL§	3,639 (1,057)	3,645 (1,278)	3,718 (634)
Follow-up year-2 FEV ₁ , mL	3,241 (1,050)	3,195 (1,636)	3,637 (622)
% predicted FEV ₁ at baseline	85.4 (23.4)	82.7 (31.4)	91.2 (13.8)
Markers of allergy, No./total (%)			
Total IgE (> 100 kilounits/L)	6/17 (35)	2/6 (33)	30/95 (32)
Eosinophilia (> 275 cells/ μ L)	3/18 (17)	1/6 (17)	11/94 (12)
Skin-prick test positive	7/18 (39)	2/4 (50)	56/94 (60)
Airway responsiveness, No. (%)			
PC ₂₀ < 8 mg/mL†	4/12 (33)	1/2 (50)	33/84 (39)

*Data are presented as mean (SD) unless otherwise indicated.

†One subject had both chronic bronchitis and asthma.

‡Baseline FEV₁: chronic bronchitis ($n = 17$), asthma ($n = 6$), neither ($n = 92$).

§Follow-up year-1 FEV₁: chronic bronchitis ($n = 14$), asthma ($n = 6$), neither ($n = 79$).

||Follow-up year-2 FEV₁: chronic bronchitis ($n = 11$), asthma ($n = 4$), neither ($n = 80$).

milliliter. The larger the negative value of the slope, the more responsive the airways to methacholine.

Cohort demographics, lung function measurements, and host characteristics are presented stratified by airway responsiveness, $PC_{20} < 8$ mg/mL or ≥ 8 mg/mL, and for the 20 subjects who did not participate in the methacholine challenge tests (Table 3). Boilermakers with hyperresponsive airways ($PC_{20} < 8$ mg/mL) had lower lung function at baseline, and at follow-up year 1 and year 2, than boilermakers with normoresponsive airways. Overall, boilermakers who did not participate in the methacholine challenge tests had lung function that was lower than boilermakers who participated. Smoking status was similar among boilermakers with hyperresponsive airways, as compared to those with normoresponsive airways. However, among those that did not participate, there were more smokers and ex-smokers.

There was a significant relationship between airway hyperresponsiveness and FEV₁ percent predicted $< 80\%$. Those subjects with FEV₁ $< 80\%$ predicted were at 5.9 times the risk of having hyperresponsive airways. When FEV₁ was treated as a continuous variable, there was an inverse, but not statistically significant, relationship between airway hyperresponsiveness and FEV₁. Boilermakers with hyperresponsive airways had, on average, FEV₁ that was 154.6 mL lower than nonresponsive boilermakers ($p > 0.1$). There was no relationship between current cigarette smoking (yes/no) and airway hyperresponsiveness, and no association between pack-years and airway hyperresponsiveness.

Interaction Between Host Characteristics and Decline in FEV₁ in Response to Boilermaker Work

Exposure Response Models: The primary exposure variable used was the number of hours worked at each specific type of plant during the interval between lung function tests. A detailed description of the exposure distribution and exposure-response relationships in this cohort has been reported earlier.⁷ Briefly, we found a robust association between FEV₁ and the number of hours worked at gas-fired plants. The association between FEV₁ and hours worked at a gas-fired plant was -9.8 mL/100 h worked (95% confidence interval [CI], -16.0 to -3.5) after adjustment for age, baseline FEV₁, and cigarette smoking status. There was also evidence of a negative association between hours worked at oil-fired and coal-fired plants and annual FEV₁.⁷

Effect Measure Modification of Exposure-FEV₁ Relationship by Host Factors: To explore whether there was effect modification by host factors of the

exposure-response relationships, we stratified the exposure-response analysis by the host factor of interest. For asthma and chronic bronchitis, we investigated stratum specific differences between individuals with asthma ($n = 6$) or chronic bronchitis ($n = 18$), as compared to individuals with neither asthma nor chronic bronchitis ($n = 95$; Table 4). One subject reported both asthma and chronic bronchitis and is counted in both the asthma and chronic bronchitis subgroups. For airway responsiveness, there were three strata: one strata consisted of the nonparticipants in the methacholine challenge test ($n = 20$), one strata consisted of hyperresponsive boilermakers ($n = 38$), and one strata consisted of normoresponsive boilermakers ($n = 60$). Within each stratum, we regressed FEV₁ on hours worked at each type of plant in separate models, adjusting for age, baseline FEV₁, and cigarette smoking status (yes/no; Table 5).

The relationship between yearly FEV₁ and gas hours worked differed significantly between individuals with and without chronic bronchitis and with and without asthma; there was significant effect modification of the yearly FEV₁ and gas hours relationship by asthma and chronic bronchitis. All analyses were adjusted for current smoking status and age. The regression coefficients for gas hours for subjects with chronic bronchitis and asthma were -26.4 mL/100 h worked and -25.7 mL/100 h worked, as compared to -7.0 mL/100 h worked among those with neither disease. We also found effect modification by chronic bronchitis and asthma of the relationship between FEV₁ and coal hours. For subjects with chronic bronchitis and asthma, the regression coefficients for coal hours were -37.3 mL/100 h worked and -80.8 mL/100 h worked as compared to -1.7 mL/100 h worked for those subjects with neither disease. Except for the unexpected and unexplained finding of a positive relationship between FEV₁ and oil-hours worked among asthmatics (287 mL/100 h worked), as compared to the neither asthmatic nor bronchitic strata (-14.0), effect modification by chronic bronchitis or asthma was not found for the other fuels (data not shown).

Overall, we did not find a consistent pattern of effect modification by airway responsiveness among the participants. The exposure-response relationships for FEV₁ were stronger for coal work hours among the hyperresponsive subjects, whereas they were weaker for gas-fired and oil-fired work hours among the hyperresponsive subjects. Although a stronger relationship between yearly FEV₁ and coal hours was found among hyperresponsive workers, the CIs for the three groups overlapped and the interaction term was nonsignificant. All analyses were adjusted for age, current smoking status, and

Table 3—Cohort Demographics, Lung Function Measurements, and Host Characteristics by Airway Responsiveness*

Variables	PC ₂₀ Values		
	< 8 mg/mL	≥ 8 mg/mL	Missing
Subjects, No.	38	60	20
Age, yr	40.5 (9.5)	42.6 (8.2)	46.4 (8.3)
Years worked	16.9 (9.7)	17.2 (9.2)	23.0 (7.4)
Smoking status, No. (%)			
Nonsmokers	12 (32)	22 (37)	4 (20)
Ex-smokers	15 (39)	20 (33)	8 (40)
Current smokers	11 (29)	18 (30)	8 (40)
Lung function			
Baseline FEV ₁ , mL†	3,734 (676)	3,917 (558)	2,806 (976)
Follow-up year-1 FEV ₁ , mL‡	3,814 (668)	3,853 (548)	3,159 (955)
Follow-up year-2 FEV ₁ , mL§	3,565 (648)	3,792 (544)	3,034 (963)
% predicted FEV ₁ at baseline	88.2 (12.6)	96.4 (11.3)	73.0 (23.0)
Physician-diagnosed asthma, No. (%)	1 (3)	1 (2)	4 (20)
Chronic bronchitis, No. (%)	4 (11)	8 (13)	6 (30)
Markers of allergy, No./total (%)			
Total IgE (> 100 kilounits/L)	15/38 (39)	17/59 (29)	5/20 (25)
Eosinophilia (> 275 cells/μL)	6/37 (16)	6/60 (10)	3/20 (15)
Skin-prick test positive	21/38 (55)	33/59 (56)	11/18 (61)

*Data are presented as mean (SD) unless otherwise indicated.

†Baseline FEV₁: PC₂₀ < 8 mg/mL (n = 38), PC₂₀ ≥ 8 mg/mL (n = 60), PC₂₀ missing (n = 16).

‡Follow-up year 1: PC₂₀ < 8 mg/mL (n = 32), PC₂₀ ≥ 8 mg/mL (n = 50), PC₂₀ missing (n = 16).

§Follow-up year 2: PC₂₀ < 8 mg/mL (n = 33), PC₂₀ ≥ 8 mg/mL (n = 47), PC₂₀ missing (n = 14).

baseline FEV₁. The relationship between yearly FEV₁ and trash-fired, paper-mill, and nuclear plant hours did not differ by airway hyperresponsiveness status (data not shown).

We additionally stratified by positive/negative serum-specific IgE test, total IgE (IgE > 100 kilounits per liter), eosinophils (> 275 cells/μL) or skin test, and regressed yearly FEV₁ on hours worked at each type of plant in separate models, adjusting for age, baseline FEV₁, and cigarette smoking. These analyses also did not show a consistent pattern (data not shown) and failed to show effect measure modification by any of these factors.

DISCUSSION

This study provides evidence that boilermakers with self-reported chronic bronchitis and asthma

experienced an accelerated decline in FEV₁ in response to boilermaker work. Chronic bronchitis and asthma magnified the workplace response by twofold to 10-fold, and significant interaction terms were seen despite small numbers of asthmatic and bronchitic subjects.

The study provided little support for interactions between airway hyperresponsiveness or other host characteristics and response to boilermaker work. The stratum specific data for airway responsiveness show little consistency across fossil fuels. In some instances, individuals with hyperresponsive airways had a stronger negative association between yearly FEV₁ and hours worked at a specific fuel type (*eg*, coal-fired), but in other instances they had weaker negative associations (*eg*, gas-fired, oil-fired). When these analyses were repeated after adjusting for pack-years smoked, rather than just current smoking

Table 4—Regression Coefficients (95% CIs) Based on GEE Models With FEV₁ Regressed on Hours Worked at Plants Burning Specific Types of Fuel Stratified by Chronic Bronchitis and Asthma*

Variables	Chronic Bronchitis	Asthma	Neither
Subjects, No.	18	6	95
Adjusted models†			
Gas-fired plant work hours	− 26.4 (− 37.7, − 15.2)	− 25.7 (− 35.4, − 16.0)	− 7.0 (− 12.9, − 1.0)
Coal-fired plant work hours	− 37.3 (− 70.0, − 4.6)	− 80.8 (− 163, 1.7)	− 1.7 (− 22.2, 18.8)
Oil-fired plant work hours	− 22.3 (− 72.7, 28.0)	287.3 (216, 359)	− 14.0 (− 25.8, − 2.1)

*Coefficients are milliliters per 100 h worked.

†Covariates adjusted for age and cigarette smoking status.

Table 5—Regression Coefficients (95% CIs) Based on GEE Models With Annual FEV₁ Regressed on Hours Worked at Each Type of Plant, Stratified by Airway Responsiveness*

Variables	PC ₂₀ Values		
	< 8 mg/mL	≥ 8 mg/mL	Missing
Subjects, No.	38	60	20†
Adjusted models‡			
Gas-fired plant work hours	- 6.9 (- 21.6, 7.9)	- 9.1 (- 15.3, - 2.8)	- 19.0 (- 39.2, 1.3)
Coal-fired plant work hours	- 16.9 (- 44.7, 10.9)	- 4.1 (- 29.6, 21.3)	- 8.4 (- 36.9, 20.2)
Oil-fired plant work hours	- 2.3 (- 19.2, 14.7)	- 17.8 (- 30.1, - 5.5)	- 37.0 (- 88.7, 14.7)

*Coefficients are milliliters per 100 h worked.

†Four subjects were missing baseline FEV₁.

‡Covariates adjusted for were age, baseline FEV₁, and cigarette smoking status.

status, the results did not change (data not shown). The generally stronger negative associations seen among the nonparticipants most likely resulted from the exclusion of individuals with diminished lung function and disease (asthma and chronic bronchitis) from methacholine testing. However, it is unclear why this differential response among nonparticipants was seen within the gas-fired and oil-fired plant analysis and not the coal-fired analysis.

Other investigators have also found associations between longitudinal lung function decline and respiratory disease and respiratory symptoms. Sherman and coworkers¹⁵ investigated the rate of FEV₁ decline in relation to respiratory symptoms in a random population sample of adults 25 to 74 years old in each of six cities in the eastern United States. Follow-up was for 12 years, and respiratory symptoms at the initial visit were determined from standardized questions of the ATS-DLD questionnaire. After adjustment for height, age, and smoking, chronic cough and chronic phlegm identified individuals at an increased risk for accelerated decline in lung function. However, neither persistent wheeze nor dyspnea were significant predictors. Vestbo and colleagues¹⁶ examined the association between chronic mucus hypersecretion and FEV₁ decline; using data from the Copenhagen City Heart Study, they found a significant association between chronic mucus hypersecretion and FEV₁ decline. However, Kauffmann et al¹⁷ did not find an association between respiratory disease/symptoms and accelerated FEV₁ decline. Differences between studies may result from differences in study populations, covariates considered, and analytical techniques.

Airway hyperresponsiveness was strongly associated with a larger decrease in adjusted FEV₁ in boilermakers. In boilermakers with hyperresponsive airways, FEV₁ was 154.6 mL lower than in normo-responsive boilermakers. In addition, airway hyperresponsiveness was strongly associated with baseline FEV₁ percent predicted < 80%. Those subjects with

a baseline FEV₁ of < 80% predicted were nearly six times more likely to have hyperresponsive airways. Other occupational studies^{18,19} also found that bronchial responsiveness is a predictor of annual loss in lung function. Tabona and coworkers¹⁸ studied host factors affecting longitudinal decline in lung function among grain elevator workers, while Frew and coworkers¹⁹ studied the rate of decline in men at various worksites.

Among other cohorts with other occupational exposures, investigators have found an association between bronchial hyperresponsiveness and decrements in FEV₁. Specifically, Hodgins and coworkers²⁰ investigated the relationship between longitudinal FEV₁ change over 5 years and nonspecific bronchial responsiveness in a cohort of underground coal miners and working nonminers. They found that increased bronchial responsiveness at the initial survey was associated with an accelerated decline in FEV₁ only among individuals who also had increased bronchial responsiveness at the final survey 5 years later. They concluded that the initial measure of bronchial responsiveness was a weak predictor of subsequent FEV₁ decline. Since in the present study we only measured bronchial responsiveness at baseline, we are unable to determine whether a similar relationship exists between longitudinal FEV₁ change and bronchial responsiveness.

Although we did not find evidence of modification of the association between yearly FEV₁ and hours worked at a specific type of fuel, we did find a high prevalence of airway hyperresponsiveness in this cohort. There were 38 subjects (39%) with hyperresponsive airways. Subjects with asthma, chronic bronchitis, or an FEV₁ percent predicted < 70% were generally excluded from methacholine challenge tests. Exclusion criteria were conservative since all tests were conducted in a nonclinical setting. These exclusions make the 39% prevalence of airway hyperresponsiveness even more surprising, since this was found among a generally healthy

cohort of journeymen. In an earlier study on boiler-makers, we showed that airway responsiveness did not change after 4 weeks of work.⁵ This makes the high prevalence of airway hyperresponsiveness observed in the present study unlikely to be a result of transient or short-term effects of work in the boiler-maker trade, but rather a long-term effect of work in the trade. However, this remains speculative, since we currently have only cross-sectional measures of airway responsiveness.

In comparison to other studies of occupational cohorts, the percentage of subjects in this cohort with hyperresponsive airways is extremely large. Kennedy and coworkers²¹ studied airway responsiveness among apprentices exposed to metalworking fluids. They found a prevalence of 5% of airway hyperresponsiveness ($PC_{20} < 8$ mg/mL) among both the machinists and control subjects. The low prevalence in their apprentices may reflect that they are naïve to exposure, whereas the boiler-makers, on average, had 18.1 years of exposure. Other explanations for the low prevalence of airway hyperresponsiveness in the apprentices are: (1) the younger age of the apprentices (the mean [SD] age of the boiler-makers was 42.6 [8.8] years while the mean age of the apprentices was 24.2 [3.9] years); and (2) the higher lung function among the apprentices (the mean [SD] of the percent predicted FEV₁ among the apprentices was 102.9% [10.8%] as compared to 90.4% [15.9%] among boiler-maker construction workers). Another study on bronchial responsiveness and occupation was conducted by Frew and coworkers¹⁹ on 1,203 subjects who were grain elevator workers, sawmill workers, or office workers. They found a prevalence of airway hyperresponsiveness ($PC_{20} < 8$ mg/mL) between 12% and 19%, lowest for the office workers and highest for the sawmill workers. These prevalences are also lower than those found in our cohort of boiler-makers.

Among subjects who did not participate in the methacholine challenge tests, as compared to normoresponsive participants, we found a stronger negative relationship between FEV₁ and work hours. The 20 nonparticipants included 9 subjects who were not tested because of low lung function, 4 subjects with a history of asthma, and 6 subjects with chronic bronchitis. Therefore, it is not unexpected that they would experience a greater decline in FEV₁ per hours worked.

This cohort of boiler-maker construction workers showed a higher-than-expected prevalence of atopy. Fifty-seven percent of boiler-makers had one or more positive skin-prick test results. In general population samples, as well as occupational cohorts, this prevalence generally ranges from 20 to 35%.^{19,22} Since the allergy data are cross-sectional data, we cannot determine whether boiler-maker work altered an indi-

vidual's tendency to allergy. However, in the future, we will measure these markers of allergy to determine whether they have changed and whether any change, if present, is related to boiler-maker work. As compared to other studies^{23,24} that have found interrelationships between markers of allergy, the present study generally did not find interrelationships. There were only significant associations between skin-prick test results and specific IgE and total IgE.

Potential limitations of this study include small sample size (98 boiler-makers with methacholine challenge tests), short follow-up interval, and a study population that was comprised of mostly journeymen with an average length of employment of 18 years. A further limitation is the lack of ambient measurements to workplace exposures. Boiler-maker construction workers are exposed to combustion particulates from multiple sources since they work at a variety of plants that burn different fuels. They build, maintain, and repair boilers and related structures at power plants burning oil, coal, and/or natural gas. In the present study, we used the number of hours worked per year at each type of plant as the exposure metric, since it was impossible to perform workplace sampling at even a small fraction of the plants. Based on the work history diaries, the study participants worked at well over 100 individual plants in > 20 states. This is typical for this trade.

The apparent increases in FEV₁ between baseline and year 1, and the decrease between year 1 and year 2 among the subjects with asthma and chronic bronchitis should be interpreted cautiously (Table 2). Among the subjects with chronic bronchitis, the increase in lung function from baseline to year 1 follow-up (3,489 to 3,639 mL) is a result of both a change in the number of participants from the baseline test (n = 17) to the year-1 follow-up (n = 14), as well as a result of a few participants having a large (> 200 mL) unexplained increase in FEV₁. The subsequent decrease in year 2 is largely a result of the change in the number of participants in year-2 follow-up (n = 11). Among the asthmatic subjects, the apparent increase in lung function from baseline to year 1 (3,492 to 3,645 mL) is the result of one subject's FEV₁ increasing nearly 1,000 mL. This subject's spirometry were hand read to check for accuracy and found to be correct. Possible explanations include lack of effort or unreported illness at baseline.

CONCLUSION

In the present study, boiler-makers with chronic bronchitis and asthma experienced an accelerated decline in FEV₁ in response to boiler-maker work.

However, the study provided little support for interactions between airway hyperresponsiveness and other host characteristics and boilermaker work. We also found a remarkably high prevalence of airway hyperresponsiveness among boilermakers. To determine whether the high prevalence of airway hyperresponsiveness is associated with occupational exposures among boilermakers, we plan to assemble a cohort of apprentices and prospectively evaluate them with serial airway responsiveness tests. This will allow us to evaluate whether the high prevalence of airway hyperresponsiveness in boilermakers is a result of long-term exposure and not bias due to selection or confounding. The bias introduced by selection out of the workforce is generally in the opposite direction seen here; workers with airway hyperresponsiveness would be expected to select out of the trade. However, without longitudinal data, we cannot address this selection process or the direction of bias.

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