DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

Date: May 17, 2001

From: Roy M. Fleming, Sc.D., Director, Research Grants Program RMF
Office of Extramural Programs, NIOSH, D30

Subject: Final Report Submitted for Entry into NTIS for Grant 5 K01 OH000152-03.

To: William D. Bennett
Data Systems Team, Information Resources Branch, EID, NIOSH, P03/C18

The attached final report has been received from the principal investigator on the subject NIOSH grant. If this document is forwarded to the National Technical Information Service, please let us know when a document number is known so that we can inform anyone who inquires about this final report.

Any publications that are included with this report are highlighted on the list below.

Attachment
cc: Sherri Diana, EID, P03/C13

List of Publications

Hauser R, Eisen EE, Pothier L, Christiani DC: A Prospective Study of Lung Function among Boilermaker Construction Workers Exposed to Combustion Particulates. Amer J Ind Med, in press, 2001

Title: Fuel-Oil Ash, Host Factors and Lung Function
Investigator: Russ B. Hauser, M.D.
Affiliation: Harvard University
City & State: Boston, MA
Telephone: (617) 432-3326
Award Number: 5 K01 OH000152-03
Start & End Date: 9/30/1996–9/29/2000
Total Project Cost: $161,949
Program Area: Not NORA
Key Words:

Abstract:
Boilermaker construction workers are exposed to combustion particulates from multiple sources. They construct, maintain and repair boilers at power plants which burn oil, coal or natural gas, as well as boilers at trash incinerators burning waste and at paper mills which burn tree bark and sap. Given the evidence of both acute cross-shift and short-term decrements in lung function in boilermakers following occupational exposure to combustion particulates, we sought to determine whether exposure is associated with an annual loss in lung function. As part of an ongoing investigation of the health effects of boilermakers, we conducted a longitudinal study of lung function among 118 boilermaker construction workers exposed to combustion particulates. Exposure during a two-year study was assessed with a detailed work history questionnaire. Spirometry measurements were performed annually to prospectively assess lung function decline. A generalized estimating equation (GEE) approach was used to account for the repeated measures design. We found a robust association between FEV1 and the number of hours worked at gas-fired plants during the previous year, as well as an association with having ever worked at a gas fired plant during the previous year. The association between FEV, and hours worked at a gas-fired plant was -9.8 mls/100 hours worked (95% Cl: -16.0, -3.5) after adjustment for age, baseline FEV1 and cigarette smoking status. The adjusted association between FEV1 and "ever worked" at a gas-fired plant was -99.7 mls (95%Cl: -154.8, -44.5). There was also evidence of a negative association between hours worked at oil and coal-fired plants and annual FEV1, as well as a significant negative association between "ever worked" at an oil or coal-fired plant and reduced FEV1. These data suggest an association between annual lung function and working at gas-fired, as well coal-fired and oil-fired plants. These results should be replicated with further followup of this cohort, as well as other cohorts of boilermaker construction workers.

We also investigated whether host characteristics, such as methacholine airway responsiveness and atopy can explain a portion of the heterogeneity in longitudinal lung function response to combustion particulate exposures in this cohort of boilermaker construction workers. Measured baseline host characteristics included methacholine airway responsiveness, skin prick test for atopy, peripheral blood eosinophil counts, and serum total and specific IgE. Airway responsiveness was measured as the provocative concentration of methacholine that caused a 20% fall in FEV1 (PC20-FEV1) and the least squares slope of the dose response plot of FEV1 against concentration of methacholine. Increased airway responsiveness was associated with a lower baseline

FEV1 and with a steeper rate of decline in FEV1 although the latter association was not statistically significant. Although we found a high prevalence of airway hyperresponsiveness, (39% had hyperresponsive airways, defined as a PC20FEV1 < 8 mg/mL), we did not find that hyperresponsiveness modified the association between annual FEV1 and hours worked at either gas-fired, coal-fired or oil-fired boilers. The high prevalence of boilermakers with hyperresponsive airways may suggest an association with chronic occupational exposure to combustion particulates. Although we found a significant inverse association between airway hyperresponsiveness and percent predicted FEV1, airway responsiveness did not increase the magnitude of the association between annual lung function and working at gas-fired, coal-fired or oil-fired plants. These results suggest that rather than acting as an effect modifier, airway hyperresponsiveness may be a primary consequence of long-term exposure to combustion particulates.

Publications

Hauser R, Eisen EE, Pothier L, Christiani DC: A Prospective Study of Lung Function among Boilermaker Construction Workers Exposed to Combustion Particulates. Amer J Ind Med, in press, 2001

Final Performance Report: 5 K01 0H00152-03

Grant Award Title: "Fuel oil ash, host factors and lung function"

Principal Investigator: Russ Hauser
Harvard School of Public Health
Boston, MA 02115

February 05, 2001

Specific Aim #1: Use a prospective longitudinal design to determine if workers with chronic intermittent exposure to fuel-oil ash experience an accelerated decline in lung function.

Abstract

Boilermaker construction workers are exposed to combustion particulates from multiple sources. They construct, maintain and repair boilers at power plants which burn oil, coal or natural gas, as well as boilers at trash incinerators burning waste and at paper mills which burn tree bark and sap. Given the evidence of both acute cross-shift and short-term decrements in lung function in boilermakers following occupational exposure to combustion particulates, we sought to determine whether exposure is associated with an annual loss in lung function. As part of an ongoing investigation of the health effects of boilermakers, we conducted a longitudinal study of lung function among 118 boilermaker construction workers exposed to combustion particulates. Exposure during a two-year study was assessed with a detailed work history questionnaire. Spirometry measurements were performed annually to prospectively assess lung function decline. A generalized estimating equation (GEE) approach was used to account for the repeated measures design. We found a robust association between FEV_1 and the number of hours worked at gas fired plants during the previous year, as well as an association with having ever worked at a gas fired plant during the previous year. The association between FEV_1 and hours worked at a gas-fired plant was –9.8 mls/100 hours worked (95% CI: -16.0, -3.5) after adjustment for age, baseline FEV_1 and cigarette smoking status. The adjusted association between FEV_1 and "ever worked" at a gas-fired plant was –99.7 mls (95%CI: -154.8, -44.5). There was also evidence of a negative association between hours worked at oil and coal-fired plants and annual FEV_1, as well as a significant negative association between "ever worked" at an oil or coal-fired plant and reduced FEV_1. These data suggest an association between annual lung function and working at gas-fired, as

well coal-fired and oil-fired plants. These results should be replicated with further follow-up of this cohort, as well as other cohorts of boilermaker construction workers.

<u>Significant findings</u>

We found an association between FEV_1 and both ever-working at a gas fired boiler and hours worked at gas fired plant during the follow-up interval. The crude association between yearly FEV_1 and hours worked at a gas-fired boiler was –11.0 mls/100 hours worked, and –9.8 mls/100 hours worked after adjustment for age, baseline FEV_1 and cigarette smoking status. The median number of hours worked during the two-year study was 110 hours during FY1 and 290 hours during FY2. The range of hours worked was wide, varying from not working at a gas-fired plant during the interval to working over two thousand hours at a gas-fired boiler. Therefore, the negative association between yearly FEV_1 and hours worked at a gas-fired boiler may indicate more than a 200 ml decrease in FEV_1 in a worker working over two thousand hours at a gas-fired boiler. The association between yearly FEV_1 and working on a gas-fired plant was extremely robust. The association was unchanged after controlling for: 1) confounders (age, baseline FEV_1 and cigarette smoking status), 2) work hours at other types of plants, and 3) the use of a respirator.

There were negative associations found between yearly FEV_1 and hours worked at an oil and coal-fired plant and "ever" working at an oil or coal-fired plant during the year follow-up interval. Earlier studies have shown both an acute (i.e. across shift) as well as a short-term (i.e. over 4 weeks) decrement in lung function among boilermaker construction workers working on an oil-fired boiler. The present study extends these findings to long-term changes (i.e. over 2 years) in workers engaged in the same type of work. Together, these studies provide support for a consistent association between exposure to fuel-oil combustion particulates and adverse effects on lung function.

Usefulness of findings

These results provide evidence that boilermaker construction workers working on gas, oil and coal-fired boilers experience an annual decrease in lung function. Evidence of a chronic health effect among boilermaker construction workers is important since there are tens of thousands of boilermakers currently work on these types of boilers. Based on these findings, strategies to reduce exposure among boilermakers are necessary.

Publication:

Hauser R, Eisen, EE, Pothier L, Christiani DC. A prospective study of lung function among boilermaker construction workers exposed to combustion particulates. Amer J Ind Med (In Press)

This publication explicitly addresses specific aim #1. It presents the results of the relationship between annual lung function and occupational exposures among boilermaker construction workers.

Specific Aim #2: *To determine whether host characteristics (airway responsiveness, serum IgE, blood eosinophils and atopy) are risk factors for the development of an acclerated decline in lung function in workers with chronic intermittent exposure to fuel-oil ash.*

Abstract

In a recent study on boilermaker construction workers, we found a significant association between combustion particulate exposure and longitudinal decline in lung function. In the present study, we investigated whether host characteristics, such as methacholine

airway responsiveness and atopy can explain a portion of the heterogeneity in longitudinal lung function response to combustion particulate exposures in this cohort of boilermaker construction workers. This study is part of an ongoing prospective study of lung function among 118 boilermaker construction workers. Exposure during the two-year interval was assessed with a detailed work history questionnaire. Spirometry measurements were performed annually to assess lung function decline. Measured baseline host characteristics included methacholine airway responsiveness, skin prick test for atopy, peripheral blood eosinophil counts, and serum total and specific IgE. Airway responsiveness was measured as the provocative concentration of methacholine that caused a 20% fall in FEV_1 (PC_{20}-FEV_1) and the least squares slope of the dose response plot of FEV_1 against concentration of methacholine. A generalized estimating equation (GEE) approach was used to account for the repeated measures design and to investigate whether there was effect modification by host characteristics of the relationship between annual decline in FEV_1 and occupational exposure to combustion particulates. Increased airway responsiveness was associated with a lower baseline FEV_1 and with a steeper rate of decline in FEV_1, although the latter association was not statistically significant. Although we found a high prevalence of airway hyperresponsiveness, (39% had hyperresponsive airways, defined as a $PC_{20}FEV_1 < 8$ mg/mL), we did not find that hyperresponsiveness modified the association between annual FEV_1 and hours worked at either gas-fired, coal-fired or oil-fired boilers.
The high prevalence of boilermakers with hyperresponsive airways may suggest an association with chronic occupational exposure to combustion particulates. Although we found a significant inverse association between airway hyperresponsiveness and percent predicted FEV_1, airway responsiveness did not increase the magnitude of the association between annual lung function and working at gas-fired, coal-fired or oil-fired plants. These results suggest that rather than acting as an effect modifier, airway

hyperresponsiveness may be a primary consequence of long-term exposure to combustion particulates.

Significant Findings for specific aim #2.

We found a statistically significant and strong relationship between airway hyperresponsiveness and baseline FEV_1 percent predicted below 80%. Those subjects with a baseline FEV_1 below 80% predicted were nearly six times more likely to have hyperresponsive airways. In addition, annual FEV_1 in boilermakers with hyperresponsive airways (PC20 < 8 mg/mL) was 154.6 mLs lower than in nonresponsive boilermakers.

This study provided little support for interactions between host characteristics and exposure to combustion particulates among boilermaker construction workers. The stratum specific data showed little consistency across fossil fuels. We would expect that if there were modification by host characteristics it would have a similar modifying effect across fuel types. These data do not show a consistent pattern of effect modification by airway responsiveness. The exposure response relationships for FEV1 decline were stronger for coal work hours among the hyperresponsive, whereas they were weaker for gas-fired and oil-fired work hours among the hyperresponsive. In all cases, the confidence intervals between the two groups overlapped, suggesting that the stratum specific relationships did not differ significantly from each other.

We additionally stratified by positive/negative serum specific IgE test and regressed yearly FEV1 on hours worked at each type of plant in separate models, adjusting for age, baseline FEV1 and cigarette smoking (yes/no). These analyses also did not show a consistent pattern (data not shown). For instance, among those with positive specific IgE, there was a significant negative association between yearly FEV1 and hours worked at an oil fired plant, while among those with negative specific IgE there was a significant negative association between yearly FEV1 and gas and coal-fired work hours. The stratum specific data for IgE (IgE>100 Ku/L), eosinophils (>275) and skin test also failed to show consistent relationships. There appeared to be no effect measure modification by total or specific IgE, eosinophilia and skin test response of the relationship between yearly FEV1 and hours worked at a specific type of fuel-fired boiler.

Although we did not find a consistent 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 (39%) subjects with hyperresponsive airways (i.e. $PC_{20}FEV1$ below 8 mg/ml). In comparison to other studies of occupational cohorts, the percentage of subjects in this cohort with hyperresponsive airways is extremely large.

<u>Usefulness of findings for specific aim #2</u>

The lack of a modification of lung function response by host characteristics suggests that the host factors measured in the present study do not predict chronic effects of occupational exposures while working on combustion fired boilers. However, the high prevalence of airway hyperresponsiveness among this cohort is troubling and remains unexplained. We are planning on following these individuals to determine whether the high prevalence of airway hyperresponsiveness is associated with occupational exposures.

Publication:

Hauser R, Eisen EA, Pothier L, Lewis D, Bledsoe T, Christiani DC. Airway hyperresponsiveness and host characteristics among boilermaker construction workers. Amer J Respir Crit Care Med (Submitted)

This manuscript explicitly addresses specific aim #2. It reports on host characteristics among boilermaker construction workers. In addition, the manuscript presents data on whether host characteristics modify the relationship between occupational exposure among boilermakers and annual decrements in lung function.