Final Peformance Report: 5 K01 OH00172-03

Environmental and Occupational Health

University of Arizona College of Public Health

Tucson, Arizona 85719-4197

Biomarkers of Smoke Exposure Among Firefighters

December 14, 2001

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Sponsors: NIOSH

Grant Number: 5 K01 OH00172-03

Abstract

Objective: Evaluate smoke exposure during overhaul and sensitive biomarkers of smoke exposure in firefighters.

Background: Firefighters frequently remove their self-contained breathing apparatus during overhaul (seeking and extinguishing hidden fire) despite potentially injurious smoke exposure. Preliminary work demonstrated decline in diffusing capacity (DLCO) associated with number of fires fought, while spirometry, usually the only test of lung function used in firefighter surveillance, remained stable. These findings suggested possible chronic injury due to smoke exposure. We proposed to validate these findings through evaluation of firefighters with biomarkers of lung injury potentially more sensitive to smoke exposure than spirometry, including serum Clara cell protein, alveolar surfactant-associated protein A, radiological (inhaled ^{99m}TcDTPA), and induced sputum (cell count, TNF-α, O_2^-) tests.

Specific aims: 1) Characterize smoke exposure during overhaul.

2) Use biomarkers to measure acute (≤2 hours) pulmonary effects in firefighters after overhaul.

3) Explore the use of serum biomarkers as surveillance tools for chronic (≥1 year) pulmonary effects in firefighters.

4) Determine the ability of air purifying respirators to reduce pulmonary effects of smoke exposure during overhaul.

Study design: A cohort of 105 Phoenix and Tucson firefighters underwent baseline evaluation including exposure questionnaires, spirometry, DLCO, and measurement of serum biomarkers. Within this group, 26 Phoenix and 25 Tucson firefighters were monitored for smoke exposure during overhaul of residential structural fires, and in addition received post-exposure evaluation using the same set of biomarkers. Phoenix firefighters used air-purifying respirators during overhaul, while Tucson firefighters did not wear respiratory protection during overhaul. Acute changes in serum biomarkers and spirometry in Phoenix and Tucson firefighters were compared to determine the efficacy of using air-purifying respirators during overhaul.

Outcome: Serum biomarkers provided sensitive measures of acute pulmonary injury in firefighters, and served as well to evaluate the efficacy of workplace interventions designed to reduce smoke exposure. Air-purifying respirators did not prevent changes in lung status associated with low-level smoke exposure.

Significant Findings:

Smoke exposure during overhaul was found to include potentially harmful concentrations of carbon monoxide, aldehydes, and to a lesser degree, benzene, NO_2, SO_2, and PNAs (Bolstad-Johnson et al., 2000; Burgess et al., 2001). It was hypothesized based on these measurements that as long as carbon monoxide concentrations were not excessively high, cartridge respirators would provide adequate protection during overhaul. However, adverse changes in FEV_1, FVC, and both serum pneumoproteins occurred in Phoenix firefighters despite the use of cartridge respirators (Burgess et al., 2001, subsequently referred to as the 'overhaul paper'. These changes, with the possible exception of serum Clara cell protein, were not felt to be secondary to exertion alone, as demonstrated in the Nanson et al. (2001) paper. Also, use of respiratory protection in a small unpublished study described in the overhaul paper resulted in an increase in FEV_1 and FVC, so this was also felt not to explain the adverse findings. Correlation between changes in specific biomarkers and products of combustion revealed a dose-response relationship that strengthened our proposed causal link between smoke exposure and adverse lung effects.

The radiological (inhaled ^{99m}TcDTPA) test was not found to be useful in this study, given the extreme variability in the measurements of lung transfer, and they were not described in the overhaul paper. The serum pneumoproteins were felt to provide a much better measurement of lung inflammation and permeability. The use of induced sputum provided an excellent means of measuring lung inflammation through evaluation of cytokine concentrations (Burgess et al., 2002). Specifically, low-level smoke exposure was associated with a marked drop in interleukin 10 (IL-10), a cytokine that suppresses inflammation, one hour following cessation of overhaul, while levels of interleukin 8 and tumor necrosis factor alpha (TNF-α) did not change significantly in this time period. Since IL-10 suppresses the production of a number of pro-inflammatory cytokines, the decline in IL-10 may be a significant mechanism by which smoke exposure causes inflammation. Measurement of sputum macrophage superoxide (O_2^-) production were carried out on a few firefighters, but technical difficulties prevented measurement of this product in a sufficient number of firefighters to allow for statistical analysis. Macrophages collected in sputum do not adhere to plastic in the same manner as do macrophages collected by bronchoalveolar lavage or lung lavage.

Usefulness of findings:

We were able to demonstrate concentrations of a number of airborne toxicants during overhaul that exceeded recommended exposure limits, clearly demonstrating the need for respiratory protection. This alone is of great importance, because firefighters traditionally do not wear respiratory protection during overhaul because the products of combustion during this phase are not visible. We demonstrated that use of cartridge respirators during overhaul did not prevent acute respiratory effects. Again, based on the industrial hygiene measurements such respiratory protection was expected to be protective. These findings demonstrate the need to include biomarkers of effect in evaluation of worker exposures to complex mixtures, such as those found in smoke. Serum pneumoproteins were found to be an excellent means of measuring lung inflammation, which complemented the use of spirometry, which only measures airflow within the lung. Finally, the use of induced sputum provides a means to evaluate changes in inflammatory mediators within the lung, and changes in IL-10 may play a significant role in the increase in lung inflammation seen with smoke exposure.

List of publications:

Bolstad-Johnson DM, Burgess JL, Crutchfield CD, Storment SB, Gerkin RD. Characterization of firefighter exposures during fire overhaul. *American Industrial Hygiene Association Journal* 2000;61:636-641. (Note: not funded by NIOSH. This study was supported by the Phoenix Fire Department and was a preliminary study for the NIOSH supported research)

Burgess JL, Nanson CJ, Bolstad-Johnson DM, Gerkin R, Hysong TA, Lantz RC, Sherrill DL, Crutchfield CD, Quan SF, Bernard AM, Witten ML. Adverse respiratory effects following overhaul in firefighters. *Journal of Occupational and Environmental Medicine* 2001;43:467-473.

Nanson CJ, Burgess JL, Robin M, Bernard AM. Exercise alters serum pneumoprotein concentrations. *Respiration Physiology* 2001;127:259-265.

Burgess JL, Nanson CJ, Gerkin R, Witten ML, Hysong TA, Lantz RC. Rapid decline in sputum IL-10 concentration following occupational smoke exposure. *InhalationToxicology* 2002;14:101-108.

Burgess JL, Witten ML, Nanson CJ, Hysong TA, Sherrill DL, Quan SF, Gerkin R, Bernard AM. Serum pneumoproteins: a cross-sectional study in public safety personnel. (submitted)

Relation of publications to specific aims:

The overhaul paper listed above addresses three of the four specific aims: 1) Characterize smoke exposure during overhaul; 2) Use biomarkers to measure acute (≤2 hours) pulmonary effects in firefighters after overhaul; and 4) Determine the ability of air purifying respirators to reduce pulmonary effects of smoke exposure during overhaul. Specific aim 1 was addressed through personal monitoring of firefighters during overhaul for carbon monoxide, nitrogen dioxide, sulfur dioxide, hydrogen cyanide, formaldehyde, acetaldehyde, acrolein, benzaldehyde, glutaraldehyde, isovaleraldehyde, hydrochloric acid, sulfuric acid, benzene, and respirable dust. Specific aim 2 was addressed through measurement of baseline and post-exposure spirometry and serum pneumoproteins, specifically Clara cell protein and surfactant associated protein A. Specific aim 4 was addressed through the use of air purifying respirators in Phoenix firefighters. For specific aim 1, Bolstad-Johnson et al. (2000) also provides information, and for specific aim 2, Nanson et al. (2001) provides information on the possible confounding effects of exercise.

The only aim not well addressed in the published papers was specific aim 3. To address this aim, we were able to find additional funding to support a cross-sectional study comparing serum pneumoproteins in firefighters and police. This paper has been submitted for publication, and will be described in the following technical report. Repeat measurement of serum pneumoproteins (not submitted for publication) revealed that between-run variations in serum pneumoproteins was excessive, and therefore annual medical surveillance given currently available ELISA tests is not feasible.

TECHNICAL REPORT FOR SPECIFIC AIM 3: Serum Pneumoproteins: A Cross-sectional Study in Public Safety Personnel

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This publication was supported by Grant Numbers 1 K01 OH00172 from the National Institute for Occupational Safety and Health and 1 P30 ES06694 from the National Institute for Environmental Health Sciences. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of these agencies.

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List of Abbreviations

CC16: Clara cell protein

DL_{CO}: Diffusing capacity of the lung to carbon monoxide

FEV_1: Forced expiratory volume in one second

FVC: Forced expiratory volume

SP-A: Surfactant associated protein A

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Abstract

Background: Serum pneumoproteins provide a measure of lower respiratory tract injury, increasing with acute exposure to pulmonary toxicants and decreasing with chronic exposure.

Methods: To evaluate the effects of chronic occupational smoke exposure, 105 firefighters were compared with 44 police controls in a cross-sectional study using spirometry, diffusing capacity of the lung, serum Clara cell protein (CC16) and serum surfactant-associated protein A (SP-A) measurements.

Results: There were no significant differences in age, gender, height, spirometry (FVC and FEV_1) and diffusing capacity between the two groups. Serum SP-A was lower in firefighters (260.1 ± 121.2 μg/L) than police (316.0 ± 151.4 μg/L, $p = 0.019$). Serum CC16 was also lower in firefighters (8.39 ± 3.11 μg/L) than police (10.56 ± 4.20 μg/L, $p < 0.001$), although this difference lost statistical significance when adjusted for confounders.

Conclusion: Serum pneumoproteins may be useful as early biomarkers of chronic respiratory injury in occupationally exposed groups.

Key words: Clara cell-specific protein, pulmonary surfactant associated protein, spirometry, police, firefighters

Significant Findings

This research revealed that serum pneumoprotein measurements differed between firefighters and police, while spirometry and diffusing capacity measurements were not statistically different. This research supports the findings of previous studies suggesting that spirometry alone is inadequate for completely assessing lung status. Early sub-clinical emphysematous changes may occur as a result of occupational smoke exposure that are not revealed by standard spirometry testing.

Usefulness of Findings

Medical surveillance testing should be augmented through the use of biomarkers of lung status at an alveolar level. If between-run variability in ELISA assays of serum pneumoproteins could be overcome, serum pneumoproteins could serve this need. At the time of the study, we understood that ELISA testing for Clara cell protein and surfactant associated protein A were not commercially available, and were only provided in research laboratories.

Scientific Report

Introduction

Smoke contains substances known to be injurious to the lung including aldehydes, acid gases, sulfur dioxide, oxides of nitrogen, particulates, and free radicals [Burgess et al., 1979; Brandt-Rauf et al., 1988; Lowry et al., 1985; Gold et al., 1978; Pryor, 1992]. Firefighters are exposed to these substances as a routine part of their job activities. Use of self-contained breathing apparatus (SCBA) has markedly decreased occupational smoke exposure. However, firefighters continue to have low-level smoke exposure during times when SCBA are not worn [Bolstad-Johnson et al., 2000].

Spirometry is used for annual medical surveillance in firefighters, both as a part of the Occupational Safety and Health Administration (OSHA) respiratory protection standard and also as a longitudinal surveillance tool. Older studies of firefighters demonstrated an accelerated rate of decline in lung function [Peters et al., 1974; Sparrow et al., 1982; Douglas et al., 1985], although more recent studies observed mixed results [Tepper et al., 1991; Musk et al., 1977; Musk et al., 1982; Horsfield et al., 1988]. The latter findings are attributed in part to increased use of respiratory protection. However, a recent study of Seattle firefighters demonstrated an increased longitudinal decline in diffusion capacity of the lung to carbon monoxide (DL_{CO}), associated in part with annual number of fires fought, despite lack of corresponding changes in spirometry [Burgess et al., 1999]. These findings raise the hypothesis that lower respiratory tract injury, and possibly a subclinical loss of alveolar tissue, is occurring in firefighters as a result of occupational exposure, and that spirometry is inadequate to measure this adverse respiratory effect.

Serum pneumoproteins are proteins produced in the lung that diffuse into the systemic circulation. Clara cell protein (CC16) is the best studied, and is a 16 kDa protein released from nonciliated pulmonary epithelial cells (Clara cells) in the lung. With acute lung injury involving disruption of the bronchoalveolar/capillary barrier, CC16 levels increase in the blood [Hermans et al., 1999; Jorens et al., 1995; Bernard et al., 1997; Burgess et al., 2001]. With chronic exposure, including smoking, silica exposure and foundry dust exposure, serum CC16 levels decrease [Hermans et al., 1996]. These changes often occur without or potentially before

alterations in spirometry. Surfactant-associated protein A (SP-A) is a 36 kDa protein produced by Clara cells and type II alveolar cells [Veldhuizen et al., 1994]. Its roles in the lung include stabilizing pulmonary surfactant [Wright et al., 1995], up-regulation of pulmonary macrophage phagocytosis and nitric oxide production [Blau et al., 1997; Weikert et al., 1997], and potentially viral inactivation [Ghildyal et al., 1999]. It has not previously been used to evaluate the chronic respiratory effects of occupational exposure to inhaled toxicants.

Police have similar demographic characteristics to firefighters, and have been used in epidemiological studies as a control population without significant smoke exposure [Demers et al., 1994; Kern et al., 1993]. The purpose of this study was to evaluate the use of serum CC16 and SP-A in relation to occupational smoke exposure in a cross-sectional study of firefighters and police.

Methods

This study was approved by the University of Arizona Human Subjects Committee. Volunteers were recruited from the City of Phoenix Fire Department and the City of Tucson Fire and Police Departments. After obtaining informed consent, subjects completed a self-administered questionnaire and answered verbal questions about their last occupational exposure to smoke (for both firefighters and police), recent exercise, and current smoking, including cigarettes, cigars, or pipes. Recent exercise was defined as a positive response to the question: "Have you exercised or engaged in strenuous activities today?"

For serum pneumoproteins, blood was obtained from each subject by venipuncture and collected in uncoated tubes. Each sample was allowed to clot for a minimum of 8 hours at 4° C. Samples were then centrifuged at 3000 rpm for 10 minutes. Serum was decanted and stored at -20° C until analysis was completed. CC16 and cystatin C (a marker of glomerular filtration rate) were measured by Latex immunoassay-LIA. CC16 was measured in a blind randomized manner using rabbit anti-protein 1 antibody (Dakopatts,Glostrup, Denmark) and purified CC16 as a standard [Bernard et al., 1991]. The serum samples were pre-treated by heating at 56°C for 30 min and treated with polyethylene glycol (16%, vol/vol, 1/1) and trichloroacetic acid (10%, vol/vol, 1/40) to avoid possible interference by complement, rheumatoid factor, or chylomicrons. All samples were analysed in duplicate at two different dilutions. The assay has a detection limit of 0.5 μg/l and an average analytical recovery of 95%, with the intra- and interassay coefficients of variation ranging from 5 to 10%. The assay has been validated by comparison with a monoclonal antibodies based sandwich type ELISA [Hermans et al., 1998]. SP-A was measured by an ELISA inhibition assay similar to that described by Doyle et al. [1997] using a polyclonal antibody raised against alveolar proteinosis derived SP-A (Chemicon, Temecula, CA). All samples were assayed in duplicate at 4 serial dilutions.

Pulmonary function testing was done with a Keystone Pulmonary Function System (Louisville, CO) calibrated daily. Measurements were made in accordance with testing criteria of the American Thoracic Society [American Thorasic Society, 1987 update; American Thorasic Society, 1987] and corrected for temperature and barometric pressure. Maximum acceptable forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) measurements were reported and used for data analysis. For diffusing capacity of the lung to carbon monoxide

(DL_{CO}), a minimum of two measurements was conducted, with at least five minutes between trials. Measurements were considered adequate if inspiration reached ≥ 90% of FVC within 2 seconds and the subject's breath was held for an interval of 9-11 seconds. Testing was continued until two tests were obtained that were within 10%. The acceptable maneuver yielding the highest test value was used for data analysis.

Comparisons between Phoenix firefighters, Tucson firefighters, and Tucson police were done using one-way ANOVA. For multiple regression analysis (STATA 6.0, College Station, TX), data for firefighters and police were initially analyzed separately. Bivariate analysis was first used to determine variables significant at the $p = 0.10$ level in predicting the outcome variables (FVC, FEV_1, SP-A, and SCC16). Second, for models in which firefighters and police were combined, only terms significant bivariately in the firefighter and/or police analyses were considered. The least significant terms were taken out sequentially, unless the removal changed any of the other significant coefficients greater than 10%. A town variable (Tucson v. Phoenix) was left in all models to account for potential differences in non-occupational exposures and reporting. For FEV_1 and FVC, age, height, gender, and race were kept in the models. For CC16 and SP-A, age and the contribution of a recent exercise and job (firefighter or police) interaction were included in each initial model, but allowed to drop out if not significant. SP-A measurements were log-transformed prior to bivariate analysis in police, but not for firefighter or combined police and firefighter models.

Results

Study participants included 105 firefighters, 52 from Phoenix and 53 from Tucson, and 44 Tucson police officers. Characteristics of the study populations are listed in Table I. There were no significant differences in age, height, gender, and minority status between the groups. In addition, there were no significant differences in FVC, FEV_1, or DL_{CO}. For spirometry, 143 (97%) of 147 subject measurements met ATS criteria and were included in the analysis. For DL_{CO}, 143 (97%) of 147 subject measurements met ATS criteria and were included in the analysis. Serum CC16 was lower in firefighters (8.39 ± 3.11 μg/L) than police (10.56 ± 4.20 μg/L, $p < 0.001$) as was SP-A (260.1 ± 121.2 μg/L v. 316.0 ± 151.4 μg/L, respectively, $p = 0.019$). This difference persisted when the analysis was limited to nonsmokers. Neither serum CC16 nor SP-A concentrations were significantly different between Tucson and Phoenix firefighters.

Of the 44 police, 5 were Special Weapons and Tactics (SWAT) team members that underwent strenuous exercise in an obstacle course immediately prior to testing. Compared to the other police, the SWAT team members demonstrated a non-significant increase in serum CC16 (10.42 ± 0.71 μg/L v. 11.68 ± 0.42 μg/L, respectively, $p = 0.137$) and SP-A (311.9 ± 25.0 μg/L v. 348.3 ± 52.7 μg/L, respectively, $p = 0.460$).

For firefighters, information on annual use of respiratory protection is listed in Table II. Bivariate analysis revealed a statistically significant difference in serum CC16 concentrations in firefighters with occupational smoke exposure within one day as compared with all other firefighters, and a statistically significant difference in serum SP-A concentrations in firefighters with occupational smoke exposure within three days as compared with all other firefighters. In Tucson, 3 (6%) firefighters reported occupational smoke exposure within one day of testing, and 10 (20%) reported occupational smoke exposure within 3 days of testing. In Phoenix, 6 (12%) firefighters reported occupational smoke exposure within one day of testing, and 8 (16%) reported occupational smoke exposure within 3 days of testing.

The results of multiple regression analysis combining firefighters and police with FVC as the dependent variable are listed in Table III. Job (firefighter v. police) was not significant bivariately and so was not included in the model. The independent variables; ever smoked cigarettes, usual phlegm production, colds usually going to the chest, lung trouble before age 16 and chronic bronchitis were included in the initial model but were not statistically significant.

Age, height, gender, and recent exercise (on the same day of the study) were significantly associated with FVC. In a model limited to firefighters, the same independent variables remained statistically significant except for gender, and no respirator use variables were significantly associated with FVC.

The results of multiple regression analysis combining firefighters and police with FEV_1 as the dependent variable are listed in Table IV. Job (firefighter v. police) was not significant bivariately and so was not included in the model. The independent variables; tightness in chest and shortness of breath with exposure to dust or animals and present asthma were included in the initial model but were not statistically significant. Age, height, recent exercise, and dyspnea with exertion were significantly associated with FEV_1. In a model limited to firefighters, age and height remained statistically significant, and no respiratory protection variables were significant predictors of FEV_1.

The results of multiple regression analysis combining firefighters and police with serum SP-A as the dependent variable are listed in Table V. The independent variables; ever had asthma, ever wheezing, wheezing with shortness of breath and chest tightness upon awakening within 12 months were included in the initial model but were not statistically significant. Recent occupational smoke exposure ($\leq$ 3 days), and job (firefighter v. police) were statistically significant predictors of serum SP-A concentration. The association with job and occupational smoke exposure remained statistically significant when the analysis was limited to nonsmokers. When the analysis was limited to firefighters, recent smoke exposure remained statistically significant, and use of respiratory protection was not significantly associated with serum SP-A concentrations.

The results of multiple regression analysis combining firefighters and police with serum CC16 as the dependent variable are listed in Table VI. The independent variables allergies during the past year, usual cough, and high blood pressure were included in the initial model but were not statistically significant. The independent variables; dyspnea with exertion, regular exercise, job (firefighter v. police), job * exercise interaction, and serum cystatin C were significant predictors of serum CC16 concentration, as was recent occupational exposure to smoke ($\leq$ 1 day), although the coefficient for this latter variable was opposite that expected. When the analysis was limited to nonsmokers, only dyspnea with exertion lost statistical significance. When the analysis was limited to firefighters, serum cystatin C concentration

remained statistically significant while occupational smoke exposure within one day, dyspnea on exertion, and recent exercise lost statistical significance. The percentage of time spent without respiratory protection in entry/ventilation was statistically significant, although the coefficient was opposite the expected direction.

Discussion

Our study found reduced concentrations of serum pneumoproteins in firefighters as compared with police. Serum SP-A concentrations were on average 18% lower in firefighters than police, and this difference remained consistent when adjusted for occupational smoke exposure within 3 days. Serum CC16 concentrations were also lower in firefighters than police, but the contribution of job lost statistical significance when adjusted for occupational smoke exposure within one day, dyspnea with exertion, recent exercise, and serum cystatin C, a marker of glomerular filtration rate. These findings contrasted with the lack of significant differences in FVC and FEV_1 between firefighters and police.

When analysis was limited to firefighters, FVC, FEV_1, and serum SP-A were not affected by frequency of use of respiratory protection. This is consistent with the previous study of Seattle firefighters, where estimates of time spent fighting fires without respiratory protection were not associated with changes in DL_{CO} [Burgess et al., 1999]. Serum CC16 decreased as reported percentage of time without respiratory protection during the entry/ventilation phase increased, contrary to expectations. However, the respiratory protection variables evaluated in this study could not be validated, and they may not have been representative of overall occupational smoke exposure.

Serum pneumoproteins increase in conditions disrupting the alveolar-capillary barrier. In our model including both firefighters and police, recent exercise caused a statistically significant increase in serum CC16, consistent with the increase in epithelial permeability seen in exercising subjects studied with the radioisotope 99mTc-DTPA [Lorino et al., 1989]. Of interest, this increase was of lesser magnitude in firefighters than police. There are a number of potential explanations for this finding. First, the exercise may have been of greater intensity in police. This possibility is supported by the fact that 5 (11%) of the police subjects were SWAT team members who had their annual qualifying exam involving an obstacle course shortly before evaluation for this study. An alternate hypothesis is that with exercise serum CC16 increases less in subjects in better aerobic condition, and that firefighters are in better physical condition than police. This possibility is supported by the lack of increase in serum CC16 found with exercise alone in a study of European cyclists [Broeckaert et al., 2000]. No association was found between exercise and serum SP-A concentrations. Given the larger molecular size of SP-

A in comparison with CC16, it may be less likely to diffuse across the alveolar/capillary barrier with minor changes in permeability.

Both serum CC16 and SP-A have been shown to increase with greater lung permeability. Serum CC16 has been shown to increase acutely following respiratory exposures including smoke in firefighters [Bernard et al., 1997] and ozone in cyclists [Broeckaert, et al., 2000]. Serum levels of SP-A have been found to increase in smokers [Nomori et al., 1998; Kida et al., 1997], acute respiratory distress syndrome [Doyle et al., 1997; Kuroki et al., 1998], progressive systemic sclerosis patients with interstitial lung disease [Takahashi et al., 2000], and post-mortem in individuals that have drowned, received trauma to the chest, or were burned in fires [Ishida et al., 2000]. As in our study, serum SP-A was not affected by age or gender [Nomori et al., 1998]. Of additional interest, alveolar fluid concentrations of SP-A and CC16 were increased in nonsmoking asbestos-exposed workers as compared with non-asbestos exposed controls, whereas in smokers, asbestos exposure increased lavage fluid concentrations of CC16 but not SP-A [Lesur et al., 1996].

It is our hypothesis that serum levels of CC16 and SP-A decrease with chronic occupational exposure due to loss of cells in the distal airways and alveoli. CC16 has been studied more extensively as a marker of exposure to respiratory toxicants. CC16 is the major secretory product of Clara cells, which contain most of the lung cytochrome P450 activity and are thus sensitive to toxicant-induced lung injury [Richards et al., 1990]. Studies have documented a decline in serum levels with exposure, including cigarette smoke [Bernard et al., 1994] and silica [Bernard et al., 1994] and foundry dust [Hermans et al., 1996]. With silica exposure and foundry dust exposure, serum levels declined while spirometry and chest radiographs remained unchanged relative to the respective control groups. No published studies could be found evaluating the use of serum SP-A as a marker of chronic occupational exposure.

At present, there are clear limitations to the use of serum pneumoproteins for medical surveillance. Spirometry has a long history of use, with multiple studies in occupationally exposed and control populations, and established standards for determination of impairment. However, the clinical significance of serum pneumoprotein concentrations in a single individual is not known. In addition, our current study is cross-sectional. Longitudinal medical surveillance studies are necessary to study clinical correlates of decline in serum pneumoproteins

with chronic exposure, and to evaluate inter-individual as compared with intra-individual variability.

In conclusion, we have demonstrated that in our study population, firefighters have lower serum CC16 and SP-A concentrations than police, although the difference in serum CC16 levels was confounded by other variables. Along with previous cross-sectional studies demonstrating similar findings with a variety of exposures [Hermans et al., 1996; Bernard et al., 1994; Bernard et al., 1994], our current study raises the possibility that measurement of serum pneumoproteins could provide a useful addition to medical surveillance evaluations of firefighters and other populations exposed to respiratory toxicants.

Acknowledgement

We would like to thank the firefighters from Tucson Fire Department and Phoenix Fire Department who participated in this study, and without whom this research would not have been possible. Special thanks go to Assistant Chief E.A. Geare of the Tucson Fire Department and Assistant Chief Stephen Storment of the Phoenix Fire Department for their recommendations and invaluable assistance in completing the study.

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Table I. Cross-sectional comparison: firefighters and police.

		Phoenix Fire	Tucson Fire	Tucson Police
Participants		52	53	44
Age (years)		39.5 ± 7.0	40.1 ± 7.4	41.4 ± 7.2
range		23-56	25-55	27-54
Height (meters)		1.80 ± 0.07	1.78 ± 0.08	1.77 ± 0.09
Male gender		48 (92%)	51 (96%)	39 (89%)
Race/ethnicity	White	31 (60%)	37 (70%)	35 (80%)
	Hispanic	18 (35%)	12 (23%)	6 (14%)
	Black	2 (4%)	2 (4%)	2 (5%)
	Other	1 (2%)	2 (4%)	1 (2%)
Current smoker		2 (4%)	3 (6%)	1 (2%)
Ever smoker		9 (17%)	9 (17%)	13 (30%)
Exercise on day of study		12 (23%)	21 (40%)	16 (36%)
Dyspnea with exertion		1 (2%)	1 (2%)	5 (12%)
FVC (L)*		5.46 ± 0.83	5.40 ± 0.76	5.17 ± 0.82
FEV_1 (L)*		4.20 ± 0.58	4.14 ± 0.60	3.97 ± 0.65
DLCO (ml/min/mmHg)*		42.55 ± 6.47	44.39 ± 6.65	41.72 ± 7.94
Serum CC16 (μg/L)†		8.31 ± 3.28	8.47 ± 2.96	10.56 ± 4.20
Serum SP-A (μg/L)		251.5 ± 109.8	268.6 ± 131.9	316.0 ± 151.4
Serum Cystatin C (μg/L)†		881.8 ± 164.1	987.7 ± 195.7	891.1 ± 162.4

* For lung function studies, results were limited to 143 subjects meeting ATS criteria.

† Significant difference among groups by one-way ANOVA, p = 0.003

Table II. Annual time spent in firefighting activities and use of respiratory protection

Phase of firefighting*	Phoenix	Tucson	Combined
Rescue			
Annual hours	5.0 ± 8.0	2.1 ± 2.7	3.4 ± 5.9
No respiratory protection (percent time)	5.2%	8.3%	6.9%
Entry/ventilation			
Annual hours	5.7 ± 11.7	3.5 ± 3.7	4.5 ± 8.4
No respiratory protection (percent time)	14%	26%	20%
Extinguishment			
Annual hours	5.6 ± 8.9	4.5 ± 4.4	5.0 ± 6.9
No respiratory protection (percent time)	4.6%	13.5%	9.2%
Overhaul			
Annual hours	15.0 ± 23.7	20.8 ± 76.8	17.9 ± 56.3
No respiratory protection (percent time)	62.0%	53.8%	58.0%
Support/standby			
Annual hours	16.3 ± 28.6	19.1 ± 76.7	17.9 ± 60.1
No respiratory protection (percent time)	79.6%	90.0%	85.1%

* The phases of firefighting include rescue which involves searching for and saving fire victims, entry/ventilation which involves gaining access to a burning building and smoke removal, extinguishment which involves putting out visible flames, overhaul which involves searching for and putting out hidden sources of combustion and support/standby which involves working or awaiting assignment near the fire scene.

Table III. Regression model for FVC in firefighters and police (n =139).

Variable	Coefficient (L)	SE	p Value	partial R^2
Age (years)	-0.016	0.007	0.022	0.039
Height (meters)	5.808	0.654	<0.001	0.374
Male gender	0.523	0.208	0.013	0.046
Minority status	-0.117	0.110	0.290	0.008
Exercise on day of study	0.331	0.105	0.002	0.070
Town*	0.107	0.104	0.306	0.008
Constant	-4.979	1.148	<0.001	

* Work location: Tucson = 0, Phoenix =1

Total R^2 for the model is 0.503

Table IV. Regression model for FEV_1 in firefighters and police (n = 139).

Variable	Coefficient (L)	SE	p Value	partial R^2
Age (years)	-0.025	0.005	<0.001	0.135
Height (meters)	3.980	0.529	<0.001	0.301
Male gender	0.309	0.169	0.069	0.025
Minority status	-0.028	0.089	0.751	0.001
Exercise on day of study	0.190	0.085	0.026	0.037
Dyspnea with exertion*	-0.463	0.195	0.019	0.041
Town†	0.050	0.084	0.557	0.003
Constant	-2.341	0.928	0.013	

*Defined as shortness of breath when hurrying on the level or walking up a slight hill

† Work location: Tucson = 0, Phoenix =1

Total R^2 for the model is 0.450

Table V. Regression model for serum SP-A in firefighters and police (n = 149).

Variable	Coefficient (μg/L)	SE	p Value	partial R^2
Occupational smoke exposure within 3 days	78.45	30.04	0.010	0.031
Firefighter	-58.32	26.53	0.029	0.028
Town*	-12.93	25.12	0.608	0.003
Constant	306.67	19.47	<0.001	

* Work location: Tucson = 0, Phoenix =1

Total R^2 for the model is 0.083

Table VI. Regression model for serum CC16 in firefighters and police (n = 145).

Variable	Coefficient (μg/L)	SE	p Value	partial R^2
Male gender	2.22	1.05	0.037	0.032
Occupational smoke exposure within 1 day	-2.14	1.01	0.035	0.032
Dyspnea with exertion*	-3.06	1.37	0.027	0.035
Exercise on day of study	3.55	1.03	0.001	0.081
Firefighter	-1.38	0.84	0.103	0.019
Firefighters with recent exercise	-3.87	1.24	0.002	0.067
Serum cystatin C (μg/L)	0.0056	0.002	<0.001	0.089
Town†	0.59	0.65	0.365	0.006
Constant	2.52	1.76	0.154	

*Defined as shortness of breath when hurrying on the level or walking up a slight hill

† Work location: Tucson = 0, Phoenix =1

Total R^2 for the model