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pH Increase Observed in Exhaled Breath Condensate from Welding Fume Exposure

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Learning Objectives

- Summarize previous reports on the association between changes in the pH of expired breath and common pulmonary disorders, and list the advantages of estimating the pH of exhaled breath condensate (EBC) as a means of studying airway inflammation.
- Describe whether and how exposure to welding fumes in this small-scale study (14 exposed and 8 non-exposed boilermakers) influenced the amount of particulate matter and the pH of EBC samples.
- Identify possible explanations for the findings of this study.

Abstract

Objectives: *We sought to investigate changes in exhaled breath condensate (EBC) pH in healthy workers exposed to welding fumes.* ***Methods:*** *Fourteen exposed participants (median age 39 years, 5 smokers) and 8 nonexposed controls (median age 44 years, 1 smoker) were monitored at an apprentice welding school. Exposure to fine particulate matter less than 2.5 μm ($PM_{2.5}$) was assessed using cyclone samplers. EBC samples were collected at baseline and at the end of the work shift. EBC samples were deaerated using argon and pH values were measured using standard pH microelectrodes.* ***Results:*** *Mean ± SEM $PM_{2.5}$ levels were 1.17 ± 0.18 mg/m^3 for exposed subjects and 0.03 ± 0.01 mg/m^3 for controls. Baseline median (range) EBC pH values for the control and exposed group were similar (P = 0.86), 7.21 (4.91 to 8.26), and 7.39 (4.85 to 7.79), respectively. The exposed subjects had a small-but-marginally significant (P = 0.07) pre- to post-work shift increase in pH of 0.28, whereas the control group showed a minimal increase of only 0.03 (P = 0.56). Compared with the control group, the exposed group had a median cross-shift pH increase of 0.25 (P = 0.49).* ***Conclusions:*** *The aerosolized fine particulate matter contained in metal fumes may be associated with an acute increase in EBC pH values. Further study is necessary to investigate the acute rise in EBC pH after acute exposure to welding fume.* (J Occup Environ Med. *2006;48:353–356*)

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Welding involves joining metals that have been made liquid by heat produced as electricity passes from one electrode to another.[1] This process generates high levels of metal fume comprising primarily fine and ultrafine particles. Epidemiologic studies have shown that exposure to welding fumes has been associated with a variety of respiratory conditions, including metal fume fever, chronic bronchitis, and asthma.[2,3]

Exhaled breath condensate (EBC) presents a novel and noninvasive method to study airway inflammation. Collection is relatively simple to perform, easily repeated, safe, and does not adversely affect the measurement of other pulmonary measurements as seen with bronchoalveolar lavage, induced sputum, and nasal lavage.[4] Its simplicity, tolerability, and safety of collection make it an attractive research and clinical tool to assess pulmonary inflammatory processes. In particular, EBC pH has been shown to be both reproducible and reliable.[5] Previous EBC studies have shown that airway acidification occurs during asthma, cystic fibrosis, and chronic obstructive pulmonary disease exacerbations.[6–8] To date, no study has investigated EBC pH values in healthy subjects exposed to high levels of particulate matter or metal fumes in the occupational setting. In this preliminary study, we hypothesized that welding fume exposure would be associated with pulmonary inflammation as reflected by acute changes in EBC pH values.

Materials and Methods

Study Population

The study was approved by the Institutional Review Board of the Harvard School of Public Health (Boston, MA). Written informed consent was obtained from each subject. The study population consisted of 22 boilermakers (Table 1). Subjects were recruited and monitored at an apprentice welding school (Quincy, MA) in January and February 2004.

Fourteen subjects were exposed during activities at the welding school to metal fume and airborne fine particulate matter from shielded metal arc welding, gas tungsten arc welding, plasma arc cutting, and grinding. The most commonly used base metal was carbon steel. Eight control subjects were exposed primarily to background levels of particulate matter while performing office tasks at the welding school.

Exposure Assessment

The determination of $PM_{2.5}$ using personal exposure monitors has been described previously.[9] Briefly, personal particulate samplers were placed on the lapels of the subjects during their workday. The KTL cyclone (GK2.05SH, BGI Incorporated, Waltham, MA) with a 50% aerodynamic diameter cut point of 2.5 μm was used in line with a Vortex Timer 2 personal sampling pump (Casella USA, Amherst, NH) calibrated at a flow rate of 3.5 L/min. Downstream of the cyclone, particles were collected on a 37-mm polytetrafluoroethylene membrane filter (Gelman Laboratories, Ann Arbor, MI). Samples were collected for a mean of 4.52 ± 0.20 hours. The mass collected on the filter was divided by the air volume sampled to calculate the gravimetric $PM_{2.5}$ concentration.

EBC Collection

EBCs were collected in each subject both at the beginning and the end of their shift using a disposable system. Subjects breathed through a mouthpiece attached to one-way valves at the inhalation and exhalation port. A filter was attached to the inspiratory one-way valve. The expiratory one-way valve also served as a saliva trap. The expiratory valve was attached to disposable corrugated plastic respiratory tubing coiled in an ice bath at approximately 0°C, which served as a condensate trap. Subjects breathed at a normal frequency and tidal volume, wearing a nose clip, for a period of 7 minutes. If subjects felt saliva in their mouths, they were instructed to swallow it. The collecting system was centrifuged manually and the collected samples were aspirated from the tubing using a 22-gauze needle syringe. The condensate (approximately 3–5 mL) was immediately transferred to Eppendorf tubes and stored at −80°C until further processing.

EBC pH values were measured using a commercially available kit for assessment of pH in low ionic strength solutions (Orion Pure Water pH Test Kit, Thermo Electron, Waltham, MA). The low conductivity and limited buffering capacity of EBC causes pH electrodes to drift, producing nonreproducible and inaccurate results. Hence, after the addition of a neutral salt (potassium chloride) to stabilize measurements, samples were deaerated using Argon and pH measurements obtained using a standard pH microelectrode. Samples were blindly validated by two separate laboratories and pH values were found to be well correlated ($R^2 = 0.97$).

TABLE 1
Study Population Characteristics and EBC Results

	Controls (n = 8)	Exposed (n = 14)	P value*
Number (%) of current smokers	1 (13%)	5 (36%)	0.35
Age, years			0.36
Median	44	39	
Range	26–62	27–50	
Years as boilermaker			0.31
Median	17	4	
Range	2–33	2–30	
$PM_{2.5}$ concentration, mg/m^3			<0.01
Mean ± SEM	0.03 ± 0.01	1.17 ± 0.18	
Baseline pH			0.86
Median	7.21	7.39	
Range	4.91–8.26	4.84–7.79	
Δ pH			0.49
Median	0.03	0.28	
Range	−0.41–1.47	−0.43–2.33	
P value†	0.56	0.07	

*Comparing exposed group with control group.
†Comparing post-shift EBC pH with baseline pH.

Statistical Analysis

Statistical analyses were performed using SAS version 9.0 (SAS Institute Incorporated, Cary, NC). Study population characteristics and exposure between the control and exposed group were compared using Fisher's exact test, two-sample *t*-tests, and Wilcoxon rank-sum tests. Data were expressed as mean ± SEM when normally distributed; otherwise, median values were used. Parametric testing was performed on normally distributed data while non-parametric analyses were performed on non-normal data. Within group pH pre- to post-shift changes were compared using Wilcoxon rank-sum tests.

Results

The overall study population demographic, exposure and results data are presented in Table 1. As shown, there was no statistical difference between baseline characteristics of the exposed and control groups. Exposure to $PM_{2.5}$ during the monitoring period was markedly different between the two groups, with mean ± SEM levels of 0.03 ± 0.01 mg/m^3 for controls and 1.17 ± 0.18 mg/m^3 for exposed subjects. Baseline median (range) EBC pH values for the control and exposed group were similar, 7.21 (4.91 to 8.26) and 7.39 (4.85 to 7.79), respectively (P = 0.86). There was a median (range) cross-shift increase in pH of 0.21 (−0.43 to 2.33, P = 0.06) across the entire cohort. The control group had a median (range) cross-shift increase in pH of 0.03 (−0.41 to 1.47, P = 0.56), while the exposed group had a larger increase in pH of 0.28 (−0.43 to 2.33, P = 0.07).

Discussion

EBC is being used as a noninvasive method to study airway inflammation,[4,5] most notably in studies of asthma,[10,11] cystic fibrosis,[10,12] chronic obstructive pulmonary disease,[10] and lung transplantation.[10] These studies consistently have shown that EBC pH is decreased (acidified) in such states of respiratory disease. In documenting a trend for increased cross-shift pH in the exposed group and no such trend in the control group, our study suggests that the aerosolized metals contained in metal fumes may cause an acute increase (alkalinization) in EBC pH values. The trend for cross-shift pH increase in the exposed group was strong (P = 0.07) despite the small size of our study.

Our exposure of interest was fine particulate matter ($PM_{2.5}$) in the form of welding fume, which is composed of various gases and metal-containing fine and ultrafine particles, with 90% of the particles having an aerodynamic mass median diameter less than 1 μm.[1,13] In our study, samples were obtained approximately 4.5 hours after the start of active welding. Active welders were exposed to markedly elevated concentrations of $PM_{2.5}$ compared with the control subjects ($P < 0.01$). We have shown that exposure to similar levels of welding fume does induce acute systemic inflammation, where $PM_{2.5}$ concentrations were found to be statistically associated with elevated levels of C-reactive protein in a similar subject population.[9]

The effect of metals on pH homeostasis has not been investigated. The welding rods used are composed of primarily iron oxides and fluorides and secondarily of complex oxides of manganese, magnesium, potassium, silicon, sodium, titanium, molybdenum, and zinc.[14,15] We postulate that there may be particular effects of these compounds on EBC pH that to date have not been investigated.

The baseline values of the subjects were noted to be more acidic than would be expected from previously published literature.[5] All samples were collected and analyzed in the same fashion, using disposable collection systems, hence eliminating cross-contamination between subjects. Review of questionnaires distributed before testing revealed no known explanation for this, with particular attention paid to medical problems such as lung disease and gastroesophageal reflux disease. Also, there was not a significant correlation between body mass index and baseline EBC pH. 12 EBC samples (27%) were also retested randomly and were found to correlate well with our initial measurements (R^2 = 0.97).

The trend for EBC pH alkalinization in welders after acute exposure, although intriguing, must be noted as being only marginally significant. It is likely that the small sample size was an important contributor to our failure to document statistically significant differences between welders and controls at the 5% level. In addition, correlating changes in EBC pH with other biomarkers of exposure would add to the validity of our findings. Given the simplicity of EBC collection, EBC is potentially attractive for longitudinal sampling, making it useful for monitoring environmental and occupational exposure effects. Further studies are needed to investigate the effect of aerosolized metals in welding fume on EBC pH values and other known biomarkers of exposure.

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