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EXPOSURE TO CONCENTRATED AMBIENT AIR PARTICLES ALTERS HEMATOLOGIC INDICES IN HUMANS

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*Descriptions of changes in hematological indices have contested the premise that the biological effects of suspended particulate matter (PM) are restricted to the lung. Employing approximately 40 hematologic parameters reflecting blood cells, chemistries, mediators, and coagulation factors, we tested the hypothesis that exposure to concentrated ambient air particles (CAPs) can be associated with changes in hematologic indices in normal humans. Twenty healthy young volunteers were exposed to either filtered air (*n = *5) or CAPs (*n = *15) with a mean PM mass of 120.5 ± 14.0 μg/m*^{3} *and a range from 15.0–357.6 μg/m*^{3}*. Hematologic indices were measured. Changes in all parameters are expressed as the absolute value either immediately after or 24 h after exposure. Differences between responses of those individuals exposed to filtered air and CAPs were tested using the* T*-test of independent means. If significant differences between the two groups were suggested by the* T*-test (*$p < .10$*), the relationship was further evaluated employing linear regression techniques. Regression analysis verified significant linear relationships between particle mass the individual was exposed to and (1) decrements in WBC count 24 h later, (2) decreases in lactate dehydrogenase (LDH) concentration 24 h later, and (3) elevations in fibrinogen levels 24 h later. There were no changes in either inflammatory mediators in the blood or indices of coagulation/fibrinolysis other than fibrinogen. We conclude that exposure of healthy volunteers to CAPs can be associated with decreases of both white blood cell (WBC) count and LDH and increased concentrations of fibrinogen in the blood.*

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Inhalation of suspended particulate matter (PM) has presented a challenge to the lower respiratory tract in humans for thousands of years (Pabst & Hofer, 1998). Epidemiologic studies had previously established an association between exposures to air pollution particles and both human mortality and morbidity. Episodes of extreme acute particulate pollution in the Meuse Valley of Belgium in 1930 (Firket, 1931), Donora, PA, in 1948 (Ciocco & Thompson, 1961), and London, England, in 1952 (Ministry of Public Health, 1954) demonstrated that extremely high particulate levels can be associated with a dramatic increase in mortality. Approximately 10 yr ago, several epidemiologic studies (using the technique of time-series analysis) demonstrated an association between exposures to ambient air pollution particles at levels currently observed in cities worldwide and indices of acute human morbidity and mortality (Dockery et al., 1993). These health effects are observed at particle concentrations below the previous U.S. Environmental Protection Agency air quality standard of 150 $\mu g/m^3$ (the upper limit for PM_{10} currently promulgated by as a primary National Ambient Air Quality Standard) set to protect public health.

Ambient air pollution particles can be formed either directly through mechanical processes, through an aggregation of fine particles, or by condensation of gases/vapors. These substances exist in either a liquid or solid phase while in the atmosphere. This description includes a large number of particles varying widely in size and composition. The diversity of particle characteristics is dependent on the sources, regional geography, season, and conditions of climate. Air pollution particles originating from natural sources can be derived from pollen, plant debris, volcanic eruptions, sea spray, wildfires, reactions between natural gaseous emissions, and dispersion of soil and rock debris by wind and automobiles. Dusts of anthropogenic origin emanate from the incomplete combustion of carbon-containing materials at power plants, smelters, incinerators, cement kilns, home furnaces, fireplaces, and by motor vehicles.

The initial assumption was that elevations in human morbidity and mortality after exposure to these particles resulted from a lung injury in susceptible subjects with preexisting cardiopulmonary disease but was likely to be inconsequential in healthy individuals. Descriptions of changes in hematologic indices (Peters et al., 1997; Seaton et al., 1999) have suggested that biological effects of PM may also affect the vascular system. Changes in red blood cell counts, hematocrit, and hemoglobin were reported to be associated with particle inhalation (Nadziejko et al., 1997). Similarly, fibrinogen concentrations in the blood can be increased after inhalation of concentrated ambient air particles (CAPs) (Ghio et al., 2000). In addition, exposure to diesel exhaust elevates blood neutrophils and platelets (Salvi et al., 1999).

Employing approximately 40 hematologic parameters reflecting blood cells, chemistries, mediators, and coagulation factors, we tested the hypothesis that exposure to CAPs can be associated with changes in hematologic indices in normal humans. In this study, 20 healthy young volunteers were

exposed to either filtered air (n = 5) or CAPs (n = 15). Hematologic indices were selected as a result of this prior investigation supporting some change associated with exposure to particles. Additional electrolytes and biochemistries were quantified. Changes in hematologic indices were measured following a 2-h exposure to ambient particles.

MATERIALS AND METHODS

Ambient Aerosol Exposure System

Particles between the sizes of 0.1 and 2.5 μm present in the Chapel Hill, NC, air were concentrated using a Harvard/EPA ambient fine particle concentrator (HAPC) consisting of three-stage virtual impactors. The principles by which this concentrator works and specific methodology have been previously described (Sioutas et al., 1995, 1997; Ghio et al., 2000).

Particle Characterization

In the Chapel Hill area of North Carolina, ambient particulate mass is driven primarily by mobile sources such as automobiles and is similar in size distribution and chemical composition to that found in many east coast cities, albeit at lower concentrations. Concentration of particles found in Chapel Hill air 6- to 10-fold by the HAPC allows controlled exposure of humans to similar concentrations of particles as seen in many major metropolitan areas (Ghio et al., 2000).

Air was sampled just prior to entering the HAPC and again just before entering the chamber from the inlet duct. Particles were collected on preweighed 47-mm Teflon filters (2 μm pore, Gelman Sciences, Ann Arbor, MI) at a flow rate of 10 L/min for 2 h during the exposure. Filters were weighed on an electrobalance (Mettler UMT2) in a temperature (20°C) and humidity (45%) controlled room. The end net filter weight, sampling time, and flow rate were used to calculate the particle concentration in micrograms per cubic meter.

Study Population

Volunteers responding to a newspaper advertisement were prescreened over the telephone using the following criteria: age between 18 and 40 yr old; nonsmokers for at least 5 yr prior to study; no history of allergies or respiratory diseases (food allergy, hay fever, dust allergies, rhinitis, asthma, chronic bronchitis, chronic obstructive pulmonary disease, tuberculosis, hemoptysis, or recurrent pneumonia); and not presently on any medication prescribed by a physician (except birth control pills). A urine pregnancy test was performed on all female subjects, and a positive result excluded the subject from further participation in this study.

Prior to participation in the study, subjects were informed of the procedures and potential risks and each signed a statement of informed consent.

The protocol and consent form were approved by the University of North Carolina School of Medicine Committee on the Protection of the Rights of Human Subjects. The screening procedures for each subject included a Minnesota Multiphasic Personality Inventory, medical history, physical examination, and routine hematologic and biochemical tests.

Exposure to Filtered Air or CAPs

Each volunteer had a single exposure to either filtered air or CAPs. Using telemetry and oximetry, subjects were monitored continuously for abnormalities of rate, rhythm, and arterial saturation. Total exposure time was two hours. Subjects entered the exposure chamber (200 ft^3), sat on a recumbent bicycle ergometer, and exercised for 30 min of each hour. The schedule included 15 min of exercise on a cycle ergometer alternating with 15 min rest. This was repeated four times. Exercise intensity, that is, cycle ergometer workload, was adjusted so that subjects breathed at a ventilatory rate, normalized for body surface area, of 25 L/m^2-min. In most subjects, this was about 50 L/min (i.e., a VO_2 of approximately 1.0 L/m). A cycle ergometer work setting of 75 to 100 W achieved such a physiological response. During the 2-h exposure, particle concentrations were monitored continuously at the inlet duct of the chamber by using a tapered element oscillating microbalance (TEOM, series 1400a, Rupprecht & Patashnick, Inc., Albany, NY). The TEOM was used to monitor a consistency or short-term excursion of exposure concentration. The average exposure concentrations were determined by filter samples as described earlier.

Venipuncture and Assays

Venous blood was sampled from an antecubital site immediately before, immediately after, and 24 h after the exposure. Both serum and plasma were obtained and stored at –80°C.

Hematologic indices were selected as a result of prior investigation suggesting some change associated with exposure to particles. Additional electrolytes and biochemistries were quantified. Measurements are listed in Table 1. Blood cell values were quantified by cell impedance using a Coulter model Gen-S. Electrolytes were measured employing ion-selective electrodes. Other biochemistry values were measured using colorimetric or kinetic methodologies on a Roche BMC Modular. C reactive protein was quantified using an immunoturbidometric assay on a Roche Integra. Commercially available enzyme-linked immunosorbent assay (ELISA) kits (R & D, Minneapolis, MN) were used in assays for interleukin (IL)-6, tumor necrosis factor, and endothelin-1. Paired antibody methodology was employed to develop immunoassays to measure protein C, prothrombin, factor VII, factor IX, plasminogen, tissue plasminogen activator (all from Enzyme Research Labs, South Bend, IN), plasminogen activator inhibitor (Oncogene Science, Cambridge, MA), and D dimers and von Willeband factor (both from Diagnostica Stago, Asnieres-Sur-Seine, France). Changes were calculated be subtracting that value

TABLE 1. Hematologic measurements

Blood cell values
Hematocrit, platelet count
White blood cell count, percentage and absolute number of neutrophils, eosinophils, and lymphocytes
Biochemistries
Sodium, potassium, chloride, glucose, blood urea nitrogen, creatinine
Calcium, phosphorus
Total protein, albumin
Bilirubin, alkaline phosphatase, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transpeptidase
Uric acid
C-reactive protein
Mediators
Interleukin-6, tumor necrosis factor
Endothelin-1
Coagulation factors
Fibrinogen, D dimers
Protein C, van Willeband factor, prothrombin, factor 7, factor 9
Plasminogen, tissue plasminogen activator, plasminogen activator inhibitor

prior to any exposure from that either immediately after or 24 h after, providing an absolute difference rather than percentage change.

Statistics

Data are expressed as mean values ± standard error. Changes in all parameters are expressed as the absolute value either immediately after or 24 h after exposure. Since particle exposure of the volunteer and the blood values investigated are both continuous variables, it is proper to regress the two rather than treat exposure as a binary function (i.e., exposed or not). Therefore, we used a *T*-test of independent means as a screen prior to application of regression methodology. As the *T*-test test was a screen, a *p* value of less than .10 was allowed as significant. If significant differences between the two groups were suggested by the *T*-test ($p < .10$), the relationship was further evaluated employing linear regression techniques. Two-tailed tests of significance were employed.

RESULTS

Study Population and Exposure

The subject population included 20 volunteers (14 males and 6 females; 25.3 ± 0.8 yr old). All were students at the time of this investigation. As gender differences were not considered for outcome, subjects were not matched by this variable. There were 5 exposures to filtered air and 15 exposures to CAPs (mean PM mass of 120.5 ± 14.0 μg/m^3). There was a substantial range in CAPs exposures reflecting the variation outside the facility,

TABLE 2. Changes in blood cell values with exposure to filtered air and CAPs

Parameter	Prior to exposure	Difference immediately after	Difference 24 h after
Hematocrit (%)			
Filtered air	44 ± 2.9	–0.4	–0.6
CAPs	42 ± 3.2	–0.1	–1.0
Platelets ($\times 10^{-3}$/μl)			
Filtered air	230 ± 12.3	–2.3	+9.2
CAPs	256 ± 19.4	–2.4	–2.7
White blood cell count ($\times 10^{-3}$/μl)			
Filtered air	5.8 ± 0.44	+1.36	+0.78
CAPs	5.5 ± 0.93	+0.91	–0.21
PMNs (%)			
Filtered air	58 ± 10.7	+6.0	–4.3
CAPs	56 ± 8.9	+6.8	–1.2
Absolute number of PMNs ($\times 10^{-3}$/μl)			
Filtered air	3.4 ± 0.26	+1.27	+0.49
CAPs	3.1 ± 0.42	+0.96	–0.29
Eosinophils (%)			
Filtered air	2 ± 3.5	–0.4	+0.2
CAPs	3 ± 1.8	–0.5	–0.5
Absolute number of eosinophils ($\times 10^{-3}$/μl)			
Filtered air	0.1 ± 0.08	–0.02	+0.02
CAPs	0.1 ± 0.08	0.00	–0.03
Lymphocytes (%)			
Filtered air	32 ± 8.1	–5.0	+3.4
CAPs	33 ± 5.5	–5.0	+1.1
Absolute number of lymphocytes ($\times 10^{-3}$/μl)			
Filtered air	1.9 ± 0.27	+0.18	+0.34
CAPs	1.8 ± 0.12	–0.15	0.08

with individual exposures ranging from 15.0 to 357.6 μg/m^3. Taking into account time of exposure and ventilation rates (i.e., 50 L/min), the greatest exposure for any individual is estimated to approximate a total dose of over a milligram.

Changes in Blood Cell Values

Evaluation of hematocrit demonstrated no significant difference between changes in those individuals exposed to CAPs relative to filtered air (Table 2). Changes in the white blood cell counts were lower among volunteers exposed to CAPs 24 h following exposure (T = –1.84; p = .08). Plotting change in white blood cell counts and PM levels verified some component of a linear relationship between them (r = .56; p = .01; Figure 1). Changes in percentage and absolute numbers of neutrophils, eosinophils, and lymphocytes were not significantly different between those exposed to CAPs and filtered air (Table 2). Similarly, the platelet count did not appear to be significantly affected by inhalation of PM.

Changes in Chemistries

Among the electrolytes, only changes in chloride 24 h after the exposure suggested remarkable differences between those inhaling CAPs relative to filtered air ($T = 1.78$; $p = .09$). However, linear regression revealed no relationship between differences in chloride and the level of CAPs ($r = .0224$; $p = .93$). There were also significant differences in creatinine between the two populations 24 h after exposure ($T = 2.14$; $p = .05$) but again no relationship was observed when plotted against PM concentration. No differences were noted between volunteers exposed to CAPs and filtered air in values of blood urea nitrogen, blood sugar, total protein, albumin, and phosphorus (Table 3). Changes in calcium immediately after exposure were significantly different between the two groups ($T = –1.85$; $p = .08$). No relationship between these changes and particle levels was observed when plotted against PM.

Significant differences between those individuals exposed to CAPs and filtered air were also demonstrated for GGT immediately after ($T = –1.87$; $p = .08$) and lactate dehydrogenase (LDH) 24 h after ($T = –2.20$; $p = .02$). While no relationship could be verified for gamma glutamyl transpeptidase changes when plotted against particle concentrations, some linear association between LDH changes and PM values was evident ($r = .58$, $p = .008$; Figure 2).

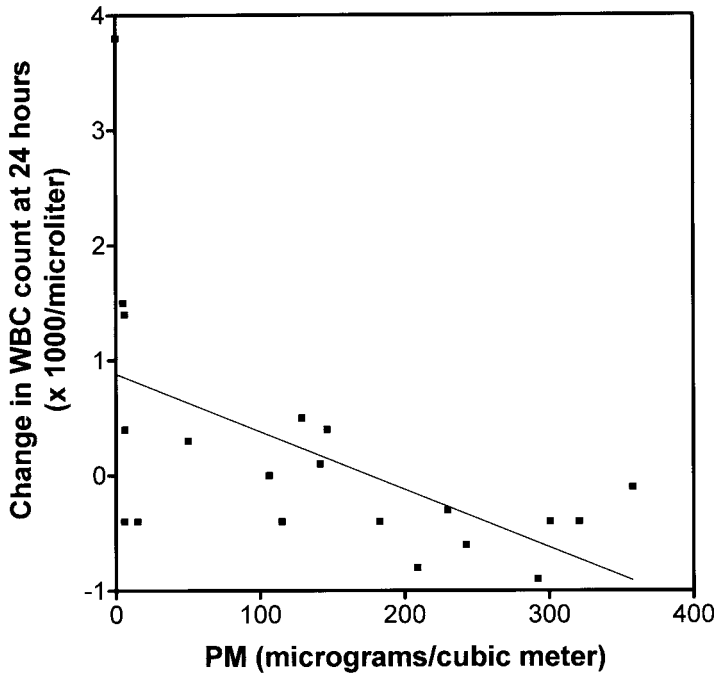

FIGURE 1. Changes in white blood cell (WBC) count 24 h following exposures to filtered air and CAPs. Regression supported a significant linear relationship between particle level and decrements in WBC count 24 h later.

TABLE 3. Changes in chemistries with exposure to filtered air and CAPs

Parameter	Prior to exposure	Difference immediately after	Difference 24 h after
Sodium (mEq/L)			
Filtered air	140 ± 0.8	–0.6	–1.4
CAPs	140 ± 2.4	+0.1	+0.2
Potassium (mEq/L)			
Filtered air	4.1 ± 0.15	+0.14	0.00
CAPs	4.3 ± 0.29	+0.09	–0.08
Chloride (mEq/L)			
Filtered air	105 ± 1.5	–2.6	0.0
CAPs	104 ± 2.2	–1.2	+0.8
BUN (mg/dL)			
Filtered air	11 ± 2.1	+0.4	0.0
CAPs	13 ± 3.2	–0.1	+0.4
Creatinine (mg/dl)			
Filtered air	1.0 ± 0.16	+0.04	–0.11
CAPs	1.0 ± 0.11	+0.03	+0.04
Blood glucose (mg/dl)			
Filtered air	98 ± 26.6	+0.4	+3.8
CAPs	89 ± 10.0	+7.5	+0.1
Calcium (mg/dl)			
Filtered air	9.5 ± 0.23	+0.34	+0.10
CAPs	9.8 ± 0.47	+0.12	+0.02
Phosphorus (mg/dl)			
Filtered air	3.5 ± 0.40	+0.02	+0.24
CAPs	3.7 ± 0.38	+0.03	+0.31
Total protein (g/dl)			
Filtered air	7.1 ± 0.2	+0.22	–0.10
CAPs	7.2 ± 0.2	+0.09	–0.07
Albumin (g/dl)			
Filtered air	4.4 ± 0.16	+0.16	–0.10
CAPs	4.3 ± 0.25	+0.13	+0.03
LDH (U/L)			
Filtered air	121 ± 7.4	+7.2	+2.4
CAPs	131 ± 5.7	+3.2	–7.4
Bilirubin (mg/dl)			
Filtered air	0.6 ± 0.16	+0.02	–0.06
CAPs	0.7 ± 0.23	–0.04	–0.03
AST (IU/L)			
Filtered air	21 ± 2.2	+1.6	–0.4
CAPs	23 ± 3.6	+0.7	–0.9
ALT (IU/L)			
Filtered air	20 ± 3.9	+0.2	–0.4
CAPs	17 ± 8.2	0.0	–0.3
GGT (IU/L)			
Filtered air	27 ± 8.4	+1.0	+0.6
CAPs	20 ± 7.1	+0.2	–0.3
Alkaline phosphatase (IU/L)			
Filtered air	52 ± 19.8	+3.4	+1.0
CAPs	71 ± 26.8	+0.6	–1.1
Uric acid (mg/dl)			
Filtered air	4.1 ± 1.57	–0.14	+0.02
CAPs	4.6 ± 1.35	–0.13	–0.01

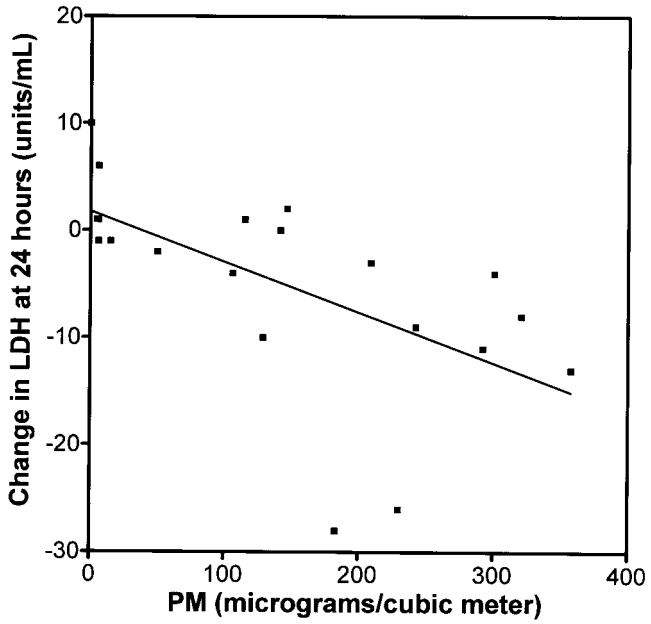

FIGURE 2. Decrements in blood lactate dehydrogenase (LDH) levels 24 h following exposures to filtered air and CAPs. Regression supported a significant linear relationship between particle level and decrements in the concentration of LDH 24 h later.

Changes in Mediators and Coagulation Factors

Except for fibrinogen ($T = 2.02$; $p = .03$), changes in both mediators and coagulation factors were unaffected by exposure (Tables 4 and 5). There was a linear component to the relationship between changes in fibrinogen concentration in the plasma and levels of particles the individual had been exposed to ($r = .59$, $p = .006$; Figure 3).

DISCUSSION

Ambient air pollution particles have been reported to elicit several changes in blood cells including decreases in red cell number (Liao et al., 1999; Seaton et al., 1999) and elevations in white blood cell counts (Pope et al., 1999; Seaton et al., 1999). The decrement in circulating white blood cells after CAPs observed in this investigation is in contrast to previous reports of elevations following exposures to particles (Pope et al., 1999; Seaton et al., 1999). An increase in white blood cell counts has been assumed to reflect the inflammatory state after inhalation of PM. In vitro exposure to particles can be associated with release of both granulocyte–macrophage colony-stimulating factor (GMCSF) and IL-6 from the alveolar macrophage (Suwa et al., 2002). Similarly, diesel exhaust can stimulate the expression of GMCSF in human airway epithelial cells (Bayram et al., 1998; Ohtoshi et al., 1998). This

TABLE 4. Changes in mediators with exposure to filtered air and CAPs

Mediator	Prior to exposure	Difference immediately after	Difference 24 h after
C-reactive protein (mg/L)			
Filtered air	1.3 ± 0.3	+0.21	–0.23
CAPs	1.2 ± 0.2	+0.26	–3.35
Interleukin-6 (pg/ml)			
Filtered air	1.6 ± 0.27	+0.18	–0.22
CAPs	1.0 ± 0.20	+0.04	–0.10
Tumor necrosis factor (pg/ml)			
Filtered air	0.8 ± 0.02	+0.40	+1.18
CAPs	0.8 ± 0.14	+0.67	+0.07
Endothelin-1 (pg/ml)			
Filtered air	1.6 ± 0.19	+0.18	–0.22
CAPs	1.0 ± 0.13	+0.04	–0.10

release is thought to be responsible for some portion of the elevation of white blood cell count observed, with the GMCSF accelerating the maturation of granulocyte precursors and their release into the blood. However, other agents included among components of PM can also be associated with decrements in the number of white blood cells, albeit after parenteral introduction (Martensson et al., 1989; Short et al., 1999). Decreases in white blood cell count following exposures to these agents reflect the extravasation of neutrophils into the lower respiratory tract. This mechanism could also account for decreases in the white blood cell (WBC) count observed after CAPs exposure, as an influx of leukocytes into the lower respiratory tract following CAPs has been previously demonstrated (Ghio et al., 2000). The incursion of neutrophils out of the blood into the lung would support the time-dependency of the decrement in WBC count, since an inflammatory influx after PM exposure is not immediate but certainly evident at 24 h.

Changes in chloride, creatinine, calcium, and gamma-glutamyl transpeptidase (GGT) following PM exposure have not been previously described. Linear regression did not verify any relationship between such changes and concentration of CAPs therefore challenging any possible association. However, lactate dehydrogenase (LDH) values decreased following CAPs and there was a significant correlation with PM. Potential sources of LDH include red blood cells, liver, kidneys, stomach, pancreas, myocardium, and skeletal muscle. Injury to any of these tissues after CAPs has not been reported, and it is not obvious why LDH should decrease following exposure to PM. One possible reason for such a decrement is that LDH can change after exposure to metals. LDH activity decreases with metal availability and increases with chelators in vitro (Breccia et al., 2002). Exposure of lactate dehydrogenase to iron/ethylenediamine tetraacetic acid (EDTA)/ascorbate oxidation system leads to a time-dependent enzymatic inactivation as well as fragmentation of the protein. The greatest inactivation of this enzyme appears to occur at

concentrations above 10 μ*M* of metal (Alonso-Llamazares et al., 1992). An association between iron and LDH can also be observed in vivo, with animals provided iron-depleted diets demonstrating elevated serum values of LDH (Stangl & Kirchgessner, 1998). All metals in the air are associated with particles (Schroeder et al., 1987), and greater exposure to PM frequently can reflect higher burdens of metals in the lower respiratory tract (and perhaps systemically). Therefore, elevated concentrations of PM and metals could affect a decrease in LDH.

Comparable to the results of previous investigation following retrieval of lavage fluid in healthy volunteers exposed to ambient air pollution particles (Ghio et al., 2000), there were no significant increases in inflammatory mediators in the blood after CAPs exposure. This is in striking contrast to the elevation of these same mediators in cultured cells derived from the lower respiratory tract following exposures to specific particles. Concen-

TABLE 5. Changes in coagulation factors with exposure to filtered air and CAPs

Factors	Prior to exposure	Difference immediately after	Difference 24 h after
Fibrinogen (g/dl)			
Filtered air	2.9 ± 0.24	+0.06	–0.17
CAPs	2.9 ± 0.27	+0.08	+0.02
D dimers (ng/ml)			
Filtered air	133 ± 18	+24.6	+22.4
CAPs	181 ± 48	–7.1	+4.9
Protein C (μg/ml)			
Filtered air	6.5 ± 0.44	+0.15	+0.18
CAPs	6.6 ± 0.44	+0.10	–0.12
van Willeband factor (%)			
Filtered air	143.5 ± 15.28	–20.14	+23.65
CAPs	153.2 ± 14.75	–5.61	+13.16
Prothrombin (μg/ml)			
Filtered air	107.0 ± 5.33	+6.32	+8.28
CAPs	136.0 ± 3.18	+6.49	+5.45
Factor 7 (μg/ml)			
Filtered air	166 ± 8.9	+30.6	+39.4
CAPs	176 ± 10.3	+13.1	–4.4
Factor 9 (μg/ml)			
Filtered air	6.3 ± 0.49	–0.58	–0.90
CAPs	5.9 ± 0.75	–0.12	–0.06
Plasminogen (IU/ml)			
Filtered air	0.94 ± 0.13	–0.04	+0.07
CAPs	0.95 ± 0.18	–0.01	–0.03
Tissue plasminogen activator (ng/ml)			
Filtered air	13.81 ± 0.89	–1.08	–0.84
CAPs	6.43 ± 0.55	–0.18	–0.39
Plasminogen activator inhibitor (ng/ml)			
Filtered air	23.0 ± 1.96	–6.3	+8.3
CAPs	22.0 ± 0.89	–6.9	–0.7

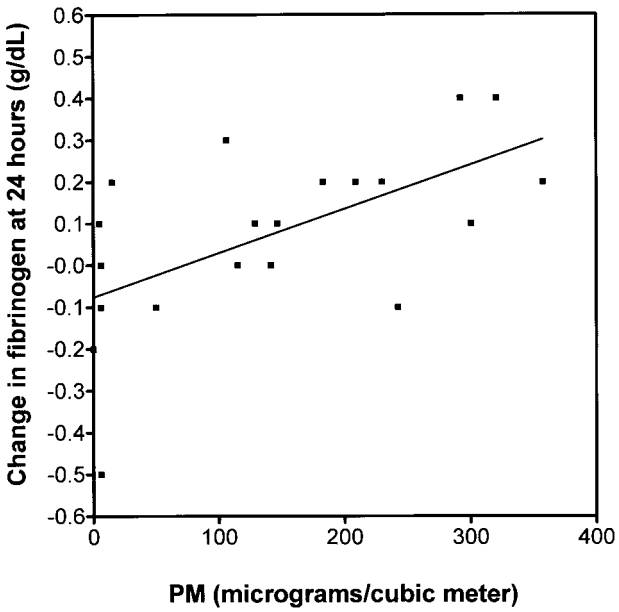

FIGURE 3. Changes in fibrinogen concentration 24 h following exposures to filtered air and CAPs. Regression supported a significant linear relationship between particle level and increases in fibrinogen concentrations 24 h later.

trations of mediators can be greatly increased in the supernatant of respiratory epithelial cells exposed in vitro to ambient air pollution particles (Carter et al., 1997; Fujii et al., 2001). In addition, the instillation of an aqueous extract of PM resulted in an elevation of inflammatory mediators in bronchoalveolar lavage fluid (Ghio & Devlin, 2001). Adverse health effects following exposure to ambient air pollution particles have been considered to possibly have some relationship to an increased expression of proinflammatory mediators in the lower respiratory tract, which are released into the circulation. These mediators are postulated to direct an influx of neutrophils and macrophages into the lung and also to initiate a systemic inflammatory response. Direct measurement of these mediators in the blood has demonstrated elevations in humans. Particles stimulate AM to produce proinflammatory cytokines, and these cytokines (i.e., TNF) can be present in the blood of subject during an episode of acute atmospheric pollution (van Eeden et al., 2001).

Ambient air pollution particles have been previously reported to affect changes in blood fibrinogen in humans (Seaton et al., 1999; Ghio et al., 2000; Pekkanen et al., 2000). Blood concentrations of fibrinogen can also increase after exposure of an animal model to diesel exhaust particles (Cassee et al., 2002). In this investigation, there were no changes in any parameter reflecting coagulation/thrombolysis except for fibrinogen. The increase in this glycoprotein is considered to potentially contribute to the association

of ambient PM with thrombotic events (Yarnell et al., 1991). Other particles have comparable effects on these indices (Mattsby & Rylander, 1978; Fernandez Rego et al., 1991). Currently, plasma fibrinogen levels appear to be a sensitive systemic marker of exposure to an ambient air pollution particle. A mechanism accounting for the effect of particles on fibrinogen has not been delineated.

We conclude that exposure of healthy volunteers to CAPs can be associated with decreases of both the WBC count and the LDH concentration in the blood. Neither has been previously reported. In addition, this study verifies that CAPs can increase the concentration of fibrinogen. It is uncertain whether these changes in blood indices following particle exposure constitute adverse health effects (American Thoracic Society, 2000). It is likely that they reflect a normal response of the host rather than an injury. Their value may lie in a function as biomarkers of particle exposure. Finally, there were no significant changes in either cytokines or any index of coagulation/fibrinolysis other than fibrinogen.

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