Personal PM$_{2.5}$ Exposure and Markers of Oxidative Stress in Blood

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Ambient particulate air pollution assessed as outdoor concentrations of particulate matter $\leq$ 2.5 $\mu$m in diameter (PM$_{2.5}$) in urban background has been associated with cardiovascular diseases at the population level. However, the significance of individual exposure and the involved mechanisms remains uncertain. We measured personal PM$_{2.5}$ and carbon black exposure in 50 students four times in 1 year and analyzed blood samples for markers of protein and lipid oxidation, for red blood cell (RBC) and platelet counts, and for concentrations of hemoglobin and fibrinogen. We analyzed protein oxidation in terms of $\gamma$-glutamyl semialdehyde in hemoglobin (HGBGS) and 2-aminoacldipic semialdehyde in hemoglobin (HBAAS) and plasma proteins (PLAAS), and lipid peroxidation was measured as malondialdehyde (MDA) in plasma. Median exposures were 16.1 $\mu$g/m$^3$ for personal PM$_{2.5}$ exposure, 9.2 $\mu$g/m$^3$ for background PM$_{2.5}$ concentration, and 8.1 $\times$ 10$^{-6}$/m for personal carbon black exposure. Personal carbon black exposure and PLAAS concentrations were positively associated ($p < 0.01$), whereas an association between personal PM$_{2.5}$ exposure and PLAAS was only of borderline significance ($p = 0.061$). A 3.7% increase in MDA concentrations per 10 $\mu$g/m$^3$ increase in personal PM$_{2.5}$ exposure was found for women ($p < 0.05$), whereas there was no significant relationship for the men. Similarly, positive associations between personal PM$_{2.5}$ exposure and both RBC and hemoglobin concentrations were found only in women ($p < 0.01$). There were no significant relationships between background PM$_{2.5}$ concentration and any of the biomarkers. This suggests that exposure to particles in moderate concentrations can induce oxidative stress and increase RBCs in peripheral blood. Personal exposure appears more closely related to these biomarkers potentially related to cardiovascular disease than to ambient PM$_{2.5}$ background concentrations.

**Key words:** carbon black, fibrinogen, hemoglobin, lipid peroxidation, particulate matter, platelets, protein oxidation, red blood cells. *Environ Health Perspect* 111:161–165 (2003). [Online 31 October 2002]
doi:10.1289/ehp.5646 available via [http://dx.doi.org/](http://dx.doi.org/)

Epidemiologic studies have shown that particulate air pollution in the urban environment is associated with an increased risk in human mortality and morbidity, especially that caused by cardiopulmonary diseases (Dockery et al. 1993; Peters et al. 2001; Pope et al. 2002). One of the proposed mechanisms is increased oxidative stress. This is assumed to be mediated partly by particle-induced inflammation in the lungs, causing macrophages to release reactive oxygen species (ROS), and partly by transition metals on the particle surface capable of generating ROS through the Fenton reaction (Donaldson et al. 1997; Li et al. 1997). The atherosclerotic process is thought to involve oxidation of low-density lipids, and a recent intervention study has shown that progression of arteriosclerosis can be reduced in heavily smoking men by supplementing with a combination of antioxidant vitamins C and E (Salonen et al. 2000). Long-term exposure to particles could thus possibly increase the risk of developing atherosclerotic plaques through increased oxidation of low-density lipids. Other possible mechanisms are short-term effects such as increased blood viscosity due to lung inflammation (Peters et al. 1997) or a direct effect of inhaled particles on the concentration of several hematologic parameters such as platelets and red blood cells (RBCs) (Salvi et al. 1999; Seaton et al. 1999). There is increasing evidence that abnormalities in blood rheology are related to various cardiovascular diseases (Koenig and Ernst 1992). A large epidemiologic study found blood viscosity to predict cardiovascular events as efficiently as low-density lipoproteins (LDL), cholesterol, and blood pressure (Lowe et al. 1997).

In most studies assessing particulate air pollution and health, outdoor monitoring of the urban background of particulate matter $\leq$ 2.5 $\mu$m in diameter (PM$_{2.5}$) or particulate matter $\leq$ 10 $\mu$m in diameter (PM$_{10}$) concentrations have been used as indicators for particle exposure. However, people spend most of their time indoors, and indoor sources of air pollutants are numerous (Jenkins et al. 1992; Ozkaynak et al. 1996). This makes risk assessment based mainly on outdoor measurements uncertain because the outdoor particle concentrations used to estimate exposure in health studies may not reflect true population exposures to particulate matter (Ozkaynak et al. 1996). Monitoring personal exposure in relation to adverse health effects may be difficult. However, by means of biomarkers mechanistically related to relevant health effects, it may be possible to assess relevant exposure to particulate matter and the involved sources.

Our aim in this study was to examine the effect of personal exposure to fine particles on levels and damage to several components of the blood. We investigated this in 50 students living and studying in central Copenhagen by measuring the personal PM$_{2.5}$ exposure in 2-day periods followed by collection of blood samples. This was repeated four times in 1 year. We analyzed the blood samples for markers of protein and lipid oxidation, for RBCs and platelet counts, and for concentrations of hemoglobin and fibrinogen.

**Materials and Methods**

**Experimental design.** We measured personal exposure to PM$_{2.5}$ and carbon black in 50 students living and studying in central Copenhagen. To account for seasonal variation, we repeated the measurements four times in one year. Five-week measuring campaigns were conducted in November 1999 (autumn), January–February 2000 (winter), April–May 2000 (spring), and August 2000 (summer). Measurements were conducted over 2-day periods for each subject, with five subjects being monitored from Monday morning to Wednesday morning and five subjects being monitored from Wednesday morning to Friday morning. In each 2-day monitoring period, urban background concentrations of PM$_{2.5}$ were also measured on a roof of a building on the Copenhagen University campus.

The subjects were recruited through a notice in the local university paper. They were all nonsmokers, living and studying in central Copenhagen, and were between 20 and 33 years old, with a median age of 24 years. There was an even distribution of males and females. Not all of the 50 subjects could participate in all four seasons. Therefore, new subjects were recruited so that 50 subjects participated in each season. In all, 68 subjects participated, of whom 31 subjects participated in all four campaigns (corresponding to 124 measurements), 12 subjects participated...
in three campaigns (corresponding to 36 measurements), 10 subjects participated in two campaigns (corresponding to 20 measurements), and 15 subjects participated in only one campaign (corresponding to 15 measurements). Altogether, we collected 195 measurements, which were all included in the subsequent statistical analysis. Morning blood samples were collected at the end of each 2-day campaign. The local ethics committee approved the study protocol, and the subjects gave written informed consent before entry into the study.

**Air sampling and analysis.** The particles were sampled with a system from the International Gravity Bureau (BGI, Toulouse, France) (Kenny and Guzman 1997), a KTLM P3,5 cyclone developed for the European EXPOLIS study (Jantunen et al. 1998), a BGI400 pump (BGI Inc., Waltham, MA, USA) (flow 4 L/min), and a battery for 48-hr operation. The equipment for personal sampling was placed in a backpack, which the subjects carried or placed nearby when they were indoors. Sampling was done on 37-mm Teflon filters (Biotech Line, Lyng, Denmark). Before and after sampling the filters were weighed on a Micro weight MT5 from Mettler-Toledo (Glostrup, Denmark) after conditioning for 24 hr in the laboratory. We determined the detection limit to about 26 µg, defined as three times the standard deviation on the blank, which typically amounted to 5–20%. On the basis of eight parallel measurements, repeated six times, the coefficient of variation was calculated as 14.4%.

We measured the reflectance (carbon black) of the PMS filters on a Model 43 Smokestain Reflectometer (Diffusion Systems LTD, London, UK). On each filter the reflectance was measured with triple determinations in five different spots. The 15 measurements were averaged and transformed into the absorption coefficient ($a$, per meter) using the following formula (ISO 1993):

$$ a = (A/2V) \times \ln(R_0/R) $$

where $A$ is the area of the stain on the filter paper (square meters), $V$ the volume sampled (cubic meters), $R$ the intensity of reflected light from the exposed filter, and $R_0$ is the intensity of reflected light from a clean filter. The coefficient of variation was 22.2% on the basis of eight parallel measurements repeated five times. Three carbon black measurements were below the detection limit of 0.01 × 10^–6/m. To include these measurements in a logarithmic model, we gave them the value of 0.007 × 10^–6/m, estimated according to the formula: detection limit/√2, suggested by Hornung and Reed (1990).

**Hematologic measurements.** RBC and platelet count as well as hemoglobin and fibrinogen concentrations were measured at the Department of Clinical Biochemistry, Copenhagen University Hospital. After venous puncture, blood samples for determination of hemoglobin concentration and RBC and platelet counts were collected in sodium citrate tubes (Becton Dickinson Vacutainer Systems, Plymouth, UK). The blood samples were then stored at room temperature until they were measured within 3 hr on a Sysmex SE 9000 analyzer (Sysmex, Long Grove, IL, USA). For measurement of fibrinogen concentration, we collected the blood samples in K$_3$EDTA tubes (Becton Dickinson Vacutainer Systems) and analyzed them within 3 hr on an ACL Futura coagulometer (Beckman Coulter, Fullerton, CA, USA). We used a commercially available kit (ABX Diagnostics, Montpellier, France) to measure concentrations of plasma protein. Plasma protein concentration was a significant predictor of the hemoglobin concentration ($p < 0.05$) and a borderline predictor of the RBC count ($p = 0.10$). This indicates that dilution and/or concentration of the blood has an effect on the hematologic parameters measured. To eliminate this source of error, we conducted all the analyses on data corrected for plasma protein (hematologic parameter/gram plasma protein).

**Protein and lipid oxidation.** For analysis of protein and lipid oxidation biomarkers, the blood samples were collected in sodium heparin tubes (Termo Veniject glass tubes, Leuven, Belgium). Plasma and RBCs were collected after centrifugation (1,500 g) and stored at –80°C until analysis. We assessed protein oxidation by the concentration of γ-glutamyl semialdehyde in hemoglobin (HBBGS) and 2-aminoacidic semialdehyde in hemoglobin (HBAAS) and in plasma proteins (PLAAS), as described previously (Daneshvar et al. 1997). Analyses were done in single measurements. For the PLAAS and HBAAS measurements, the intraday coefficient of variation (CV) is 2%, and the interday CV is 7%. For HBBGS the interday CV is 2%, and the interday CV is 8%. Total MDA in plasma was determined by HPLC in doublet measurements as previously described (Lauridsen and Mortensen 1999). The MDA measurements have been found to have an interday CV of 6% and an interday CV of 11%. In all four analyses we included an internal standard in every run, and if this internal standard differed more than 10% compared to the expected value, the run was repeated.

**Statistics.** All statistical analyses were done using SAS software (version 8e; SAS Institute, Cary, NC). We used mixed model repeated-measures analysis (Proc MIXED) to describe concentrations of the hematologic parameters (RBC, hemoglobin, platelets and fibrinogen) as well as oxidation of protein (HBBGS, HBAAS and PLAAS) and lipid (MDA) as a function of various predictors. As explanatory variables (predictors) we included season, average outdoor temperature, sex, and, in three separate models for each dependent variable, the exposure markers personal PM$_{2.5}$ exposure, personal carbon black exposure, and background PM$_{2.5}$ concentration. The interaction between the exposure marker in question and sex was included in each model to analyze whether sex modified a possible association between the exposure marker and the dependent variable. Subject nested in sex was included as a random factor to

Table 1. Hematologic parameters and exposure markers overall and by sex.

| Parameter                          | All          | Men          | Women         | p-value$^a$ |
|-----------------------------------|--------------|--------------|---------------|-------------|
|                                   | Median       | Q25–Q75      | Median        | Q25–Q75     | No.       | Median       | Q25–Q75      | No.       | p-value$^a$ |
| RBC count (x 10^12/g protein)     | 61.5         | 58.8–67.7    | 65.4          | 60.9–69.2   | 96        | 58.0         | 55.5–61.5   | 91        | < 0.0001    |
| Hemoglobin (µmol/g protein)       | 114          | 106–126      | 122           | 112–128     | 96        | 109          | 103–116     | 91        | < 0.0001    |
| Platelet count (x 10^9/g protein) | 3.14         | 2.62–3.80    | 2.77          | 2.44–3.13   | 95        | 3.57         | 3.20–4.16   | 91        | < 0.0001    |
| Fibrinogen (nmol/g protein)       | 130          | 99–159       | 103           | 86–130      | 67        | 153          | 130–187     | 70        | < 0.0001    |
| HBAAS (nmol/mg protein)           | 38.0         | 32.0–45.1    | 35.0          | 29.0–41.0   | 95        | 41.6         | 35.7–51.0   | 91        | 0.0021      |
| MDA (nmol/mg protein)             | 45.0         | 39.0–52.4    | 42.0          | 36.0–50.0   | 95        | 48.0         | 42.0–57.0   | 91        | 0.0003      |
| PLAAS (nmol/mg protein)           | 20.0         | 18.0–23.0    | 19.0          | 18.0–19.0   | 98        | 21.0         | 19.0–25.0   | 92        | < 0.0001    |
| Personal PM$_{2.5}$ exposure (µg/m³) | 16.1        | 10.0–24.5    | 14.9          | 9.7–25.0    | 90        | 18.8         | 10.9–24.3   | 90        | 0.69        |
| Urban background PM$_{2.5}$ (µg/m³) | 9.2         | 5.3–14.8     | 9.1           | 5.3–15.3    | 83        | 9.7          | 6.2–12.9    | 74        | 0.54        |
| Personal carbon black (10^5/m³)   | 8.1          | 5.0–13.2     | 8.1           | 4.2–13.0    | 92        | 8.1          | 5.4–13.3    | 85        | 0.55        |

$^a$The p-value for the difference between men and women was calculated by mixed-model regression, with sex as the predictor and subject number nested in sex as random factor. $^b$The urban background monitoring station was placed on a roof of a building on the Copenhagen University campus site.
account for factors that could possibly lead to an (within-subject) inherent basis concentration in the dependent variable that was not included in the model. A backward selection was applied, and in the final model only significant factors were included. The dependent variables were logarithmically transformed to obtain variance homogeneity and normal distribution of the residuals. The models are therefore not linear in the original scale, and model estimates represent slopes in the logarithmic analysis. To calculate the predictive value of an X unit increase in the predictors, we used the following formula: $[\exp(\text{model estimate} \times X)] - 1 \times 100$.

We used similar models to test for associations between the exposure markers, with the natural logarithm of personal PM$_{2.5}$ exposure as dependent variable and personal carbon black exposure or background PM$_{2.5}$ concentration as predictors. Subject number was included as random factor.

Results

Descriptive statistics. Results on hematologic parameters, oxidation products, and exposure markers are shown overall and by sex in Table 1. The hematologic parameters and the protein oxidation products were significantly different in men and women ($p < 0.005$), with RBC and hemoglobin being highest in men and platelets, fibrinogen, HBGGS, HBAAS, and PLAAS being highest in women. There were no significant sex differences in MDA concentrations or in any of the three exposure markers: personal PM$_{2.5}$ exposure, personal carbon black exposure, or background PM$_{2.5}$ concentration.

Relationship between exposure markers and the oxidation products. The relationships between concentrations of PLAAS and personal exposure to PM$_{2.5}$ and carbon black, respectively, are depicted in Figure 1. The personal carbon black exposure and PLAAS concentration was significantly and positively related ($p = 0.009$) with a 4.1% increase in PLAAS per $1 \times 10^{-3}/m$ increase in personal carbon black exposure (Table 2). The relationship between personal PM$_{2.5}$ exposure and PLAAS was of only borderline significance ($p = 0.061$) with a 1.6% increase in PLAAS per 10 µg/m$^3$ increase in personal PM$_{2.5}$ exposure (Table 2). PLAAS was not significantly associated with the background PM$_{2.5}$ concentration. Neither HBAAS nor HBGGS was significantly associated with any of the three exposure markers (Table 2). For the three protein oxidation products, season was a significant predictor ($p < 0.05$). Average outdoor temperature was excluded in the backward selection.

In the MDA model the estimates for personal PM$_{2.5}$ exposure were significantly different in women and men ($p = 0.015$), with an increase of 3.7% in MDA concentration per 10 µg/m$^3$ increase in personal PM$_{2.5}$ exposure in women and no significant relationship for the men. Season and average outdoor temperature were excluded from the model due to insignificance. There were no associations between MDA and personal carbon black exposure or background PM$_{2.5}$ concentration (Table 2).

Relationship between exposure markers and hematologic parameters. The relationship between the personal exposure to PM$_{2.5}$ and the concentrations of RBC and hemoglobin in men and women is depicted in Figure 2. The interaction between sex and personal PM$_{2.5}$ exposure was significant for both the RBC model ($p = 0.048$) and for the hemoglobin model ($p = 0.019$). For the RBC model there was a significant positive association with personal PM$_{2.5}$ exposure in women ($p = 0.009$) with a 2.3% increase in RBC per 10 µg/m$^3$ increase in personal PM$_{2.5}$ exposure, whereas there was no significant association with personal PM$_{2.5}$ exposure in men (Table 2). Similar results were obtained in the hemoglobin model, with an increase of 2.6% in hemoglobin per 10 µg/m$^3$ increase in personal PM$_{2.5}$ exposure in women ($p = 0.003$) and no association in men (Table 3). In both models season and average outdoor temperature were removed from the initial model due to insignificance. No relationships could be distinguished with either RBC or hemoglobin when including personal carbon black exposure or background PM$_{2.5}$ concentration instead of personal PM$_{2.5}$ exposure in the model (Table 2). Platelet counts and fibrinogen concentration were not significantly associated with the season, the average outdoor temperature, or with the exposure markers (Table 2).

Relationship among the three exposure markers. The background PM$_{2.5}$ concentration was a predictor of personal PM$_{2.5}$ exposure ($p = 0.03$) with an increase of 12% in personal exposure per 10 µg/m$^3$ increase in background PM$_{2.5}$. The personal carbon black exposure was also a predictor of personal PM$_{2.5}$ ($p < 0.0001$) with an increase of 30% in personal PM$_{2.5}$ exposure per 1 $\times 10^{-3}/m$ increase in personal carbon black exposure.

![Figure 1](image1.png)

**Figure 1.** Relationships between 2-aminoadipic semialdehyde in plasma proteins and the personal exposure to (A) carbon black and (B) PM$_{2.5}$, respectively. The PLAAS values are adjusted with respect to season and sex.

| Outcome variables | Personal exposure to PM$_{2.5}$ (µg/m$^3$) | Personal exposure to PM$_{2.5}$ (µg/m$^3$) | Background concentration of PM$_{2.5}$ (µg/m$^3$) |
|------------------|------------------|------------------|------------------|
|                  | Estimate | p-Value | Estimate | p-Value | Estimate | p-Value |
| RBC count (× 10$^{9}$/g protein) | (Results in Table 3) | 0.0003 | 0.75 | 0.0008 | 0.36 |
| Hemoglobin (µmol/g protein) | (Results in Table 3) | 0.0004 | 0.65 | 0.0005 | 0.53 |
| Platelet count (× 10$^{9}$/g protein) | 0.0008 | 0.37 | 0.0009 | 0.51 | 0.0008 | 0.49 |
| Fibrinogen (nmol/g protein) | 0.0006 | 0.69 | −0.0027 | 0.29 | 0.0004 | 0.84 |
| PLAAS (pmol/mg protein) | 0.0016 | 0.081 | 0.0041 | 0.0039 | 0.0004 | 0.76 |
| HBGGS (pmol/mg protein) | 0.0001 | 0.94 | 0.0024 | 0.25 | −0.0020 | 0.29 |
| HBAAS (pmol/mg protein) | 0.0006 | 0.64 | 0.0022 | 0.20 | −0.0021 | 0.29 |
| MDA (pmol/mg protein) | (Results in Table 3) | 0.0018 | 0.30 | 0.0012 | 0.52 |

Estimate, model estimate. In the mixed regression models, the outcome variable was transformed by the natural logarithm. Sex exposure marker (personal exposure to PM$_{2.5}$ or reflectance, or background PM$_{2.5}$ concentration), campaign number, average outdoor temperature, and the interaction between exposure marker and sex were set as explanatory variables in 24 separate models. Due to insignificance, the interaction between the exposure marker and sex was excluded from all models, except for three models (described in "Results", the relationship between a) RBC count and personal exposure to PM$_{2.5}$, b) hemoglobin and personal exposure to PM$_{2.5}$, and c) MDA and personal exposure to PM$_{2.5}$. Average outdoor temperature was excluded from all models due to insignificance.
Discussion

The design of this study, with repeated measurements and inclusion of both men and women, caused the variability in the measured blood components to be determined mainly by differences across the individual subjects and across sex. However, after controlling for differences across subjects and sex, we found significant associations between particulate air pollution and biomarkers of oxidative stress as well as hematologic factors. These associations suggest that personal exposure to fine particles in ambient and/or indoor air can lead to changes and damage to several components of the blood.

There is accumulating evidence that particles are capable of inducing oxidative stress, shown in vitro (Prahala et al. 2001) and in vivo (Han et al. 1999). In most of these experiments the particle exposure doses used are many times higher than the exposures seen in this study, and the oxidative markers reflect damage that is quickly removed. We found a significant relationship between the personal carbon black exposure and PLAAS as well as a borderline significant association between personal PM$_{2.5}$ exposure and protein oxidation in plasma (PLAAS). Aminoadipic semialdehyde (AAS) is an oxidation product of lysine and reflects changes in protein damage over a few days after exposure. The results are in agreement with an earlier study conducted on Copenhagen bus drivers, which found the concentration of PLAAS to be significantly higher in bus drivers from rural/suburban areas compared with bus drivers from central Copenhagen compared with bus drivers from rural/suburban areas (Astrup et al. 1999). Although concentrations of PLAAS in blood can also be influenced by a number of other factors such as diet and age (Daneshvar et al. 1997; Young et al. 1999), this indicates that, even at low concentrations, exposure to particles can cause an increased oxidative stress in the peripheral blood.

Carbon black stems primarily from incomplete combustion, which usually contains toxic substances. Consequently, it has been suggested that carbon black may be a better indicator of the health effect of fine particles than the weight measurement (Horvath 1996; Muir and Laxen 1995). The method responds mainly to particles in the sub-micrometer range, which to a large extent will be ultrafine particles. The association with PLAAS was stronger for the personal carbon black exposure than for PM$_{2.5}$, which could indicate that the ultrafine fraction has the strongest influence on the oxidation of plasma proteins. In recent years several studies have investigated the relationship between personal exposure and indoor-outdoor monitoring of PM$_{2.5}$ or PM$_{10}$ and many of these studies, including this study, find only weak or no relationship between personal exposure and outdoor concentrations (Koistinen et al. 2001; Ozkaynak et al. 1996; Sorensen M. Unpublished data). This could indicate that measurements of personal exposure include particle fractions that are not included in the background PM$_{2.5}$ concentration and that these fractions are capable of inducing oxidative stress and other adverse health effects.

The personal PM$_{2.5}$ exposure was significantly related to lipid peroxidation measured as MDA in women only. A possible explanation may be that the women in this study were exposed to higher concentrations of PM$_{2.5}$ than were men (Table 1). However, the difference in the median values of personal PM$_{2.5}$ exposure was small (3.9 µg/m$^3$) and insignificant, and this is most likely not the only explanation. We also found an increase in RBC and hemoglobin in women as a result of the personal PM$_{2.5}$ exposure (Table 3). The production of RBC is controlled by erythropoietin secreted into the
blood by cells in the kidneys and, to a lesser extent, the liver. Erythropoietin synthesis is induced by the transcription factor hypoxia-inducible factor 1 (HIF-1). Besides induction by hypoxia, HIF-1 has been induced in vivo and in vitro by the transition metals cobalt, nickel, and manganese (Chandel et al. 2000; Jasmin and Solymoss 1975; Goldberg et al. 1988). We therefore suggest that the observed increase in RBC concentrations is caused by an HIF-1 induction of erythropoietin, caused by transition metals on the surface of particulate matter. An increase in RBC would cause an increase in blood viscosity, which is a risk factor for cardiovascular events (Donaldson et al. 2001; Lowe et al. 1997). The blood viscosity is determined by several factors besides the RBC concentration, such as plasma viscosity and RBC aggregation. Another study found an increase in plasma viscosity of exposed subjects during air pollution episodes as measured by total suspended particulates, sulfur dioxide, and carbon monoxide (Peters et al. 1997). Peters et al. (1997) found that the increase in plasma viscosity was higher in women than in men for the three exposure markers TSP, SO₂, and CO (when treated as continuous variables). The difference was largest for CO, where only the group of women showed significant odd ratios. This suggests a difference in response to particulate air pollution in women and men. The baseline RBC concentrations is normally higher in men than in women because of the higher concentrations of testosterone in men, which stimulates erythropoietin release, and because of loss of blood during menstruation in women. However, we do not expect that differences in the menstrual cycle can explain the associations seen in this study, as the time of participation was chosen at random, thereby excluding potential systematic errors. This could make the capacity to react to toxicologic influences higher for women than for men.

The present data and the increases in plasma viscosity reported during air pollution episodes (Peters et al. 1997) contrast with a recent study that found negative correlations between estimated personal PM₁₀ exposure and hemoglobin concentrations, RBCs, packed cell volume, platelets, fibrinogen, and factor VII in both sexes (Seaton et al. 1999). The offered explanation for those findings was sequestration of RBCs in the peripheral vessels due to particle-induced alteration in adhesive properties. However, in that study the personal exposure was estimated using a mathematical model based on activity diaries and comparative measurements of ambient PM₁₀ at multiple sites, and the subjects were all > 60 years old. A study with controlled exposure of human volunteers with a mean age of 24 years found an increase in platelet and neutrophil concentrations in peripheral blood after 1 hr of exposure to 300 µg/m³ PM₁₀ (generated from an idling diesel engine) in an exposure chamber (Salvi et al. 1999). In addition, several studies have shown positive associations between plasma fibrinogen concentrations and particulate matter (Ghio et al. 2000; Pekkanen et al. 2000). Thus, the effect of age on the response to particle exposure may be significant. This effect needs to be confirmed by further studies.

This study was carried out in a relatively clean environment, with a mean personal PM₁₀ exposure of 16.1 µg/m³. It is uncertain whether the results translate to locations where the personal exposure is higher. However, the dose-response curves presented in Figures 1 and 2 show no signs of deviating from a possible linearity at higher doses.

In conclusion, the associations between particulate exposure and oxidative damage markers and RBCs suggest that particulate air pollution has measurable effects in the blood compartment. Such oxidative stress may be involved in the atherosclerotic process, and increased RBC may affect blood viscosity, suggesting a possible mechanistic relationship with cardiovascular disease. Moreover, the associations were confined to the personal exposure, whereas ambient background concentrations were poorly related to the investigated biomarkers.

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