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No short-term respiratory effects among particle-exposed employees in the Stockholm subway

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Objective Exposure to traffic-related air pollution is associated with adverse respiratory effects, but it is not known whether the high exposure to particles prevailing in the subway system may affect the respiratory system. We investigated airway inflammation and lung function among particle-exposed subway employees.

Methods We studied 81 workers. All participants were non-smokers, aged 25–50 years. Three exposure groups were formed according to particulate matter (PM) levels obtained during an occupational hygienic investigation: 30 platform workers [average PM_{2.5} 63 µg/m³ and DataRAM (MIE Inc, Billerica, Waltham, MA, USA) 182 µg/m³], 30 subway drivers (19 µg/m³ and 33 µg/m³), and 21 ticket sellers (10 µg/m³ and 13 µg/m³). We measured the fractional exhaled nitric oxide (FENO) of all workers before and after a workday. We also measured the peak expiratory flow (PEF) and forced expiratory volume in one second (FEV₁) of platform workers and ticket sellers five times a day over two weeks. We calculated the arithmetic means of PEF and FEV₁ during exposed and unexposed time for every individual.

Results There was no significant increase in FENO after work among platform workers, subway drivers or ticket sellers (the means of percentual individual change were -7%, +2% and -4% respectively). The averages of the ratios (exposed to unexposed time) of PEF and FEV₁ were above 1.0 for both ticket sellers (1.016 and 1.002 respectively) and platform workers (1.022 and 1.005).

Conclusions Our observations do not indicate any short-term respiratory effects of particle exposure in the subway among the employees, with respect to airway inflammation or lung function.

Key terms air pollution; lung function; occupational exposure; particulate matter; Sweden; underground.

Epidemiologic studies have demonstrated associations between particles in urban air, mainly derived from traffic, and respiratory-associated morbidity and mortality (1–4) and cardiovascular disease (3, 5). Particulate matter (PM) pollution has been suggested to be the major contributor to these effects (6). A main hypothesis concerning the mechanisms involved is that inhaled particles deposited in the airway epithelium may cause inflammation in lower airways, systemic inflammation, and oxidative stress. Nitric oxide (NO) is endogenously produced when airways are inflamed. The fractional concentration of NO in exhaled breath (FENO) is a marker of airway inflammation and has been used to investigate the relationship

between exposure to air pollutants and airway inflammation (4, 7–9). Exposure to wood smoke among healthy subjects increased alveolar NO three hours after exposure, but there was no difference in the effects of wood smoke versus clean air on FENO at an exhalation flow rate of 50 ml/sec, thus indicating inflammation at the distal parts of the airways rather than the conducting airways (9). Among children with asthma, the FENO was associated with hourly averages of PM_{2.5} from 1 up to 10–12 hours after exposure (7). Short-term exposure to diesel traffic in a central London street induced reductions in the forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) and increased biomarkers of

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inflammation among people with asthma (10). Healthy persons exposed to road tunnel air pollution in Stockholm got airway inflammation, as reflected in bronchoalveolar lavage fluid and bronchial mucosal biopsies, but no reductions in FEV₁ or FVC (11).

However, very little is known about the potential respiratory effects of exposure to particles in the subway system, another source of particulate air pollution. The subway particles contain a high proportion of iron and derive mainly from wheels, rails, and brakes. They are larger than particles generated by combustion engines, mainly in the size range of 1–10 microns (12–14). Transportation workers and commuters are mainly exposed at the underground platforms. Levels of particles with an aerodynamic diameter of <10 µm (PM₁₀) measured on an underground platform in central Stockholm were on average 470 µg/m³, which is a factor five times higher than the corresponding values measured on one of the busiest city streets (15). Exposure to a subway environment for two hours did not induce reductions in lung function or changes in exhaled NO among healthy volunteers in Stockholm (16), but experimental data indicate that subway particles have marked inflammatory properties on the cell level (12, 17, 18) and induce more oxidative stress than street-level particles (18, 19). Since high levels of particles have been reported in the subway system of Stockholm (15), as well as in several other cities in the world (20–23), and previous studies indicate inflammatory effects of these particles, we investigated the potential respiratory effects among particle-exposed employees in the subway.

Methods

Study group

The study group comprised 81 employees of the Stockholm subway. The participants were non-smoking men and women, aged 25–50 years. All subjects had to be currently working. They all participated in an individual medical examination performed once for each person between November 2004 and March 2005. During the same time period, exposure measurements were performed for 44 of the participants, with the first day of exposure measurements usually occurring the same day as the medical examination. Three exposure groups were formed according to the level of exposure to subway particles. There were (i) 30 platform workers (cleaners and ticket collectors whose main working site was on the platforms) who had the highest exposure among the occupational groups studied, (ii) 30 intermediately exposed subway drivers, and (iii) 21 ticket sellers with low exposure (control group).

Background characteristics

At the medical examination in a room adjacent to their workplace, the participants were examined and interviewed about the state of their health and medication use. One physician and one laboratory assistant took part in all examinations. This individual medical examination was done in the morning, right before the start of a work shift, after at least two work-free days. All participants had previously fasted overnight due to the need for the collection of blood samples as part of the medical examination. The results from analyses of blood samples have been presented elsewhere (24). The examination included the recording of weight and height. At the same occasion and in the same room, the first measurements of FENO (all participants) and peak expiratory flow (PEF) and FEV₁ (ticket sellers and platform workers) were recorded. After the medical examination, those who participated in the exposure measurements put on the personal sampling equipment. Individuals who had smoked on a regular basis any time before inclusion in the study were coded as ex-smokers. There was an equal distribution between the occupational groups with regard to the limited numbers of participants with asthma and limited use of inhaled anti-inflammatory medication. No one was on oral anti-inflammatory medication. Table 1 shows the background characteristics of the exposure groups and mean values of FEV₁ registrations for two weeks.

Information on particle exposure

The exposure to particles [measured as PM_{2.5} and by DataRAM (MIE Inc, Billerica, MA, USA)] was investigated by personal sampling during two work shifts for 44 of the participants. More detailed information about the exposure measurements has been presented elsewhere (25). Each sampling shift was about eight hours. The first day of measurements usually occurred the same day as the medical examination and the subsequent day of measurements within the following 1–2 weeks.

To collect PM_{2.5}, we used the cyclone GK2.05 (KTL) (BGI Incorporated, Waltham, MA, USA), with the flow rate 4 l/min, measuring all particles in sizes <2.5 micrometer. The filters used were 37 mm Teflon filters weighed with a balance of sensitivity 0.001 mg in a room with constant temperature (20° C) and 50% relative humidity. Real time particle measurements were performed with the person-borne direct reading instrument DataRAM (type MIE pDR 1000) which is a light scattering instrument that uses a nephelometric method scanning particles in sizes 0.1–10 micrometer. The average of every minute was recorded and stored in a built data logger.

Table 1. Background characteristics of the exposure groups regarding gender, age, body mass index (BMI), previous smoking habits, asthma, inhalable anti-inflammatory medication, and forced expiratory volume in one second (FEV₁).

	Ticket sellers (N=21)				Subway drivers (N=30)				Platform workers (N=30)			
	N	%	Mean	Range	N	%	Mean	Range	N	%	Mean	Range
Gender (male)	13	62			18	60			24	80		
Age			38	25–50			38	25–50			40	25–50
BMI			25	19–35			26	19–35			28	20–38
Ex-smoker	6	29			18	60			6	20		
Asthma	2	9			2	7			3	10		
Daily inhalable anti-inflammatory medication	1	5			2	7			2	7		
FEV ₁ (l/sec)		80 ^a	3.12							81 ^a	3.27	

^a Percent of predicted.

Measurement of fractional exhaled nitric oxide

On the same day as the medical examination, the FENO was investigated among all ticket sellers, subway drivers, and platform workers. The first measurement was done before the start of a work shift after at least two work-free days. The second measurement was taken the same day directly after the end of the work shift. All measurements were made in the same room (an office room with mechanical ventilation, adjacent to the work place) and with the same analyzer. The FENO was measured with the subject in a seated position using a NIOX chemiluminescence analyzer (Aerocrine AB, Stockholm, Sweden) during a single slow exhalation against an oral pressure of 5 cm H₂O. Measurements were taken for 10 seconds aiming at an exhalation flow rate of 50 ml/sec, according to guidelines established by the American Thoracic Society and European Respiratory Society (26). All measurements were taken threefold and the mean concentration (in parts per billion) was registered. The analyzer was calibrated once a week with a certified NO calibration gas.

Measurement of peak expiratory flow and forced expiratory volume in one second

Using a portable Piko-1 electronic PEF and FEV₁ meter, (Medeca Pharma AB, Uppsala, Sweden) measurements were performed on all ticket sellers and platform workers, with the first registration on the same day as the medical examination and the FENO-measurements. All subjects borrowed a Piko-1 meter and made five registrations a day for two weeks, both at work and at leisure time. All registrations were made threefold and the best value out of three was stored and used in the analysis. The Piko-1 meter registered PEF and FEV₁. The subjects got detailed oral and written instructions for the registrations and also practiced how to handle the Piko-1 meter. Before the

first measurement, we checked that their technique of measurement was adequate by using a stationary spirometer that gave values of FVC, FEV₁, PEF and the form of the curve. They received a form to register their working hours.

Statistical methods

To investigate whether the FENO was higher after a workday compared to the baseline value, we calculated the mean of percentual individual change for each group, with standard deviation (SD). We used a two-sided t-test to analyze whether there was a significant percentage change. We also present the arithmetic mean of the FENO in parts per billion for each exposure group before and after work.

For PEF and FEV₁, we compared exposed and unexposed time by calculating the mean of all PEF and FEV₁ measurements at work and during leisure time for each individual. Secondly, we calculated an individual ratio between the mean value at work and leisure time. The arithmetic mean and SD of these individual ratios was calculated for each occupational group. The ratios were normally distributed. A two-sided t-test was performed to analyze whether the PEF and FEV₁ ratios significantly differed from 1.0.

To investigate if there was a trend to a change in PEF or FEV₁ during the working week, we calculated the mean of all measurements for each of the first four days and used a regression analysis to investigate if there was a trend over time.

In addition, we analyzed whether there was a diurnal variation in PEF or FEV₁. We calculated the arithmetic mean and SD of individual ratios between the mean value at daytime and mean value in morning and night, for all study subjects combined.

The Regional Ethics Committee in Stockholm, Sweden, evaluated and approved the study. All study subjects were included following informed consent.

Results

The results from the exposure measurements are shown in table 2. The levels of $PM_{2.5}$ for the platform workers were about six times higher than those of ticket sellers, and about twice as high among subway drivers, with an average $PM_{2.5}$ of $63 \mu\text{g}/\text{m}^3$ for platform workers, $19 \mu\text{g}/\text{m}^3$ for subway drivers, and $10 \mu\text{g}/\text{m}^3$ for ticket sellers. The corresponding DataRAM levels were $182 \mu\text{g}/\text{m}^3$, $33 \mu\text{g}/\text{m}^3$, and $13 \mu\text{g}/\text{m}^3$, respectively.

Table 2. Information on exposure to particles measured as particulate matter ($PM_{2.5}$) and by DataRAM by personal sampling during two work shifts for 44 workers in the Stockholm subway.

	Ticket sellers (N=8)		Subway drivers (N=13)		Platform workers (N=23)	
	Mean	SD	Mean	SD	Mean	SD
$PM_{2.5}$ ($\mu\text{g}/\text{m}^3$)	10	3	19	3	63	12
DataRAM ($\mu\text{g}/\text{m}^3$)	13	3	33	12	182	57

Table 3. Findings of measurements of the fraction of exhaled nitric oxide (FENO) per exposure group, before and after work. The arithmetic mean of FENO in parts per billion (ppb), and mean of percentual individual change with standard deviation (SD).

	Ticket sellers (N=21)		Subway drivers (N=30)		Platform workers (N=30)	
	Mean	SD	Mean	SD	Mean	SD
FENO before work	21.8 ^a	17.2	22.3 ^a	15.5	22.1 ^a	18.0
FENO after work	22.2 ^a	20.3	22.1 ^a	14.4	21.2 ^a	21.0
Percentual individual change in FENO	-4%	25%	+2%	21%	-7%	18%

^a In group.

Table 4. Findings of the mean of Piko-1 meter-registered peak expiratory flow (PEF) and forced expiratory volume in one second (FEV_1) ratios (ratio between work and leisure time) for each occupational group (based on the mean of individual ratios) during a two-week period and standard deviation (SD). P-values are for comparisons between the mean ratio for each group and the ratio 1.0.

Risk marker	Ticket sellers (N=21)			Platform workers (N=30)		
	Mean of ratios	SD	P-value	Mean of ratios	SD	P-value
PEF ratio	1.016	0.039	0.074	1.022	0.048	0.020 ^a
FEV_1 ratio	1.002	0.066	0.914	1.005	0.040	0.524

^a P-value <0.05.

Table 3 shows findings from measurements of FENO for ticket sellers, subway drivers, and platform workers before and after work. There was no significant increase in the mean FENO after a workday, compared to the baseline value, in any of the exposure groups. The mean of percentual individual change in FENO was -4% among ticket sellers, +2% among subway drivers and -7% (significant) among platform workers.

The mean PEF and FEV_1 ratios were above 1.0 for both ticket sellers and platform workers, thus indicating better airflow function during work (table 3). Among the platform workers, the PEF ratio significantly differed from 1.0 ($P=0.020$).

There was no significant trend over time in PEF or FEV_1 during the working week. For PEF, the mean value of exposed and unexposed measures combined were 472, 473, 490, and 476 l/min respectively for days 1–4 ($P=0.666$ for the trend) among ticket sellers and 446, 451, 453, and 458 l/min respectively ($P=0.346$ for the trend) among platform workers. For FEV_1 , the mean values were 3.29, 3.20, 3.31, and 3.23 l/sec respectively for days 1–4 ($P=0.875$ for the trend) among ticket sellers and 3.33, 3.25, 3.25, and 3.25 l/sec respectively ($P=0.8752$ for the trend) among platform workers.

When diurnal variation in PEF or FEV_1 was analyzed using all unexposed measurements during the two-week period, we found no tendency towards better values at daytime compared to morning and night.

Discussion

There were no signs of acute airway inflammation among subway drivers or platform workers who were exposed to particles in the Stockholm subway. Nor were there any signs of negative effects on lung function during work. On the contrary, the comparison between exposed and unexposed time for PEF and FEV_1 indicated better airflow during work. The reason for the general tendency of better airflow at work is unclear. It is notable that this tendency was significant only for PEF among platform workers but not for FEV_1 , which is a more robust measure than PEF. It is possible that some parameter in the work situation trigger the individuals to make a better effort in the measurement situation compared to during leisure time. Diurnal variation is also a possible explanation (27, 28), but additional analyses including only the measurements during leisure time did not confirm this hypothesis. Furthermore, we found no significant trend over time in PEF or FEV_1 during the working week.

The FENO measurements indicated no inflammation after work. It is possible that the period of two days off duty before measuring the baseline value for

the FENO was insufficient to reach baseline, leading to a reduced possibility to detect acute changes. Other potential explanations include the possibility of diurnal variation, which may mask a negative influence of the workplace exposure. A study among 20 asthmatic and 6 healthy children in Germany suggested a diurnal rhythm of FENO in both groups, with a peak in the early morning (29) while two other studies did not report a diurnal pattern (30, 31). It is also possible that the FENO measurements were registered too early after the exposure to register an effect, since the second FENO registration was done directly after the end of the work shift. In a study on exposure to wood smoke (four hours exposure), the effect on alveolar NO was not directly noticeable but only three hours later (9) and, among children with asthma, there was a lag time from 1 up to 10–12 hours for the association between FENO and hourly averages of $PM_{2.5}$ (7). However, in our study there was not even a tendency towards increased FENO levels after exposure for eight hours for the occupational group with the highest exposure. On the other hand, the exposure levels in the highest exposed group in our study were considerably lower than in the study on exposure to wood smoke where the mass concentrations of fine particles were 240–280 $\mu\text{g}/\text{m}^3$. Also, FENO has been shown to be an airway-specific marker of predominantly eosinophilic inflammation associated with asthma (32, 33). However, in the occupational setting it has been shown that there are a substantial proportion of subjects with occupational asthma without eosinophilia (34). The lack of effect on FENO levels in the present study could be a result of the limitations of the FENO technique as a marker for non-eosinophilic airway inflammation. For measurements of FENO, different flow rates have been used to determine the relative contribution of the bronchi and alveolar regions to FENO production (33). Since FENO – at a flow rate of 50 ml/sec – is supposed to indicate inflammation at the conducting airways (9), we may have missed an inflammatory response at the distal parts of the airways.

Normal values (upper limits) of FENO for adult non-smokers range between 24.0–54.0 parts per billion, depending on age and height (35). Levels of FENO are elevated among subjects with asthma symptoms and are positively related to height and age, while smoking and the use of inhaled corticosteroids have been associated with decreased FENO levels (36). Since the comparison in our study was done for FENO values before and after work for each individual, most of these parameters would not influence the results. No participant was smoking and very few were on inhalable anti-inflammatory medication. Intake of nitrate rich food has been shown to increase levels of FENO (37). When FENO before work was registered, the participants had been fasting over night, but food intake was allowed

during the work-day and subsequently the FENO after work could have been affected by intake of food. However, this would not explain the lack of increased levels after work.

The classification into exposure groups was confirmed by personal exposure measurements for about half of the participants. Therefore, the risk of misclassification of exposure is low. The contrast between the highest and lowest exposed workers was high: for $PM_{2.5}$, the exposure levels were about 6 times higher for platform workers (63 $\mu\text{g}/\text{m}^3$) compared to the control group ticket sellers (10 $\mu\text{g}/\text{m}^3$), and for DataRAM (nephelometric $PM_{0.1-10}$) about 14 times higher (182 $\mu\text{g}/\text{m}^3$ and 13 $\mu\text{g}/\text{m}^3$, respectively) (25). The control group had an exposure to $PM_{2.5}$ that was in line with the annual average background levels during daytime above roof across the greater Stockholm area. However, it is possible that the particle levels in the Stockholm subway are too low to induce airway inflammation or airway obstruction among healthy individuals. Many of the studies showing an association between combustion-generated particle exposure and respiratory effects have been performed on subjects with asthma. Particles formed in the subway also differ in size and composition from combustion-related air pollution particulates which might be an explanation for the lack of effect, even though experimental studies indicate inflammatory effects on the cell level of subway particles (12, 17, 18). The source of particulate air pollution in the subway is mainly from mechanical wear of wheels, rails, and brakes resulting in relatively large particles, which is typical for particles generated by mechanical wear, with a high content of metals, mainly iron, and with properties that considerably differ from those of combustion-generated air pollution. The number concentration of ultra-fine particles and nitrogen oxides are lower in the subway compared to road environments where particles and gases are emitted from gasoline and diesel engines.

Our negative findings are supported by a recent study in Stockholm with 20 healthy volunteers who were exposed to a subway environment for two hours (mean levels of $PM_{2.5}$ and PM_{10} were 77 $\mu\text{g}/\text{m}^3$ and 242 $\mu\text{g}/\text{m}^3$, respectively) and an office environment (16). No significant changes between subway and office environment were observed in regard to VC, FVC, FEV_1 , PEF or exhaled NO, and no signs of cellular response in the lower airways assessed by bronchoscopy were found after exposure, regardless if cells were retrieved from peripheral or central airways. In an earlier study by the same research group using the same study design, the exposure to particles derived from city traffic (two hours exposure to air pollution in a road tunnel) increased the amount of inflammatory cells in bronchoalveolar lavage fluid of healthy individuals but no significant changes in lung function (VC, FVC and FEV_1) occurred

as a result of exposure (11). Since the exposure levels regarding PM_{2.5} and PM₁₀ from city traffic were in the same levels (median concentrations of PM_{2.5} and PM₁₀ were 64 µg/m³ and 176 µg/m³, respectively) as in the study among volunteers in the subway environment one could have expected signs of cellular inflammatory response in the lower airways after exposure to the subway environment as well. The lack of effect may be due to the differences in particle characteristics between the subway and road tunnel environments. In our study, the highest exposed group platform workers had similar exposure levels (mean levels of PM_{2.5} and PM_{0.1–10} were 63 µg/m³ and 182 µg/m³, respectively) as in the two aforementioned studies, but the exposure time was longer, 8 as opposed to 2 hours. In a previous investigation among the same study group of employees in the Stockholm subway, we found elevated plasma concentrations of the inflammatory marker PAI-1 and a tendency to elevated plasma concentrations of hs-CRP among platform workers, relative to employees with low exposure, but the differences observed could not definitely be linked to particle exposure as such, and we found no short-term effects of particle exposure on blood markers of inflammation and coagulation (24). These results are in accordance with the absence of short-term effects on airway inflammation in the present study. The participants in the occupational groups studied were mainly in good health and few had asthma. The results might have been different if we would have had the possibility to include only asthmatics.

A strength of the study is the personal measurements that showed a high exposure to airborne subway particles for platform workers relative to the control group and the background levels of particles. Sampling time of FENO and the choice of method for studying airway inflammation could have affected the outcome, although the method used is well established. The study could exclude a decrease in the ratio of FEV₁ during work and leisure time with 1.2% or more with 95% certainty, and similarly a reduction in the PEF ratio with 1.5% and a change in FENO with 5%, with 95% certainty.

In conclusion, we found no indication of short-term respiratory effects of particle exposure in the subway system among the employees, concerning negative effects on lung function or airway inflammation. However, we cannot rule out the effects of long-term exposure.

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