

Medication Use Modifies the Health Effects of Particulate Sulfate Air Pollution in Children with Asthma

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Previous controlled studies have indicated that asthma medication modifies the adverse effects of sulfur dioxide (SO₂) on lung function and asthma symptoms. The present report analyzed the role of medication use in a panel study of children with mild asthma. Children from Sokolov (*n* = 82) recorded daily peak expiratory flow (PEF) measurements, symptoms, and medication use in a diary. Linear and logistic regression analyses estimated the impact of concentrations of sulfate particles with diameters less than 2.5 μm, adjusting for linear trend, mean temperature, weekend (versus weekday), and prevalence of fever in the sample. Fifty-one children took no asthma medication, and only 31 were current medication users. Most children were treated with theophylline; only nine used sprays containing beta-agonist. For the nonmedicated children, weak associations between a 5-day mean of sulfates and respiratory symptoms were observed. Medicated children, in contrast, increased their beta-agonist use in direct association with an increase in 5-day mean of sulfates, but medication use did not prevent decreases in PEF and increases in the prevalence of cough attributable to particulate air pollution. Medication use was not a confounder but attenuated the associations between particulate air pollution and health outcomes. **Key words:** air pollution, asthma, asthma medication, beta2-agonist, children, particles, peak expiratory flow, respiratory symptoms, sulfates. *Environ Health Perspect* 105:430–435 (1997).

Particulate air pollution has been implicated in the incidence and severity of respiratory disease. Acute effects of particles on respiratory symptoms have been demonstrated in panel studies (1–7), and decreases in lung function have been observed (1,2,4–8). Asthmatic patients have reported increasing their beta-agonist use in association with particulate air pollution (2,4,7,8). These acute effects of particulate matter particles of 10 μm or less in aerodynamic diameter (PM₁₀) have been observed in children with respiratory symptoms (1,4,5), in children without respiratory symptoms (1), and in asthmatic patients (2,5,7), but some studies have failed to show consistent associations between particulate air pollution and lung function (9–11) or any respiratory symptoms (9,10) during particulate air pollution episodes. These differences in response may be due to differences in the panel characteristics or in the air pollution exposures. Subjects with preexisting chronic respiratory disease are considered to be subgroups of the population that are sensitive for health effects. Under conditions in which pollutant values are near or below the recommended guidelines, symptomatic children appeared to be the most sensitive subgroup (1,2), whereas studies of asthmatic patients have failed to show consistent associations (9–12).

These latter results were unexpected because most subjects with asthma have hyperreactive airways that respond to non-

specific external stimuli (13). However, experimental studies on young adults with mild asthma have shown that routinely used asthma medications such as theophylline and beta-agonist were able to attenuate or reverse the effects of sulfur dioxide (SO₂) on lung function (14–16) and symptoms (16). Therefore, regular asthma medication as well as additional doses during particulate air pollution episodes may compensate for the adverse effects of exposure to outdoor air pollutants. A panel study of severe asthmatics suggests that increased levels of particulate air pollution result in improved lung function tests, possibly due to increased medication use (17). The present report analyzes the role of medication use in a panel of mildly asthmatic children from Sokolov, the Czech Republic. The panel provided a unique opportunity to analyze the role of asthma medication in modifying acute responses to particulate air pollution. A consistent inverse association between respiratory health and 5-day means of air pollutants has been observed, and elevated levels of particulate air pollution have been associated with an increased prevalence of beta-agonist use (8). Only one-third of the total cohort used asthma medication, and the group was large enough for us to conduct a stratified analysis. This paper addresses two main questions: Do children who are treated with asthma medication differ from untreated asthmatic children in

their general characteristics and their responses to particulate air pollution? Does medication use confound the effects of particulate air pollution observed in a panel of asthmatic children?

Materials and Methods

Study area. Sokolov is a city of approximately 60,000 inhabitants, located in a hilly region in the northwest of the Czech Republic. A power plant located 5 km west of the city and small-scale industry are the primary sources of winter air pollution. Glass and china manufacturing plants are scattered within 20 km of Sokolov. Brown coal (lignite) is used widely in both power production and domestic heating. The high sulfur and ash content of the coal produces high SO₂ and particulate air pollution in the winter.

Study population. The panel of children from Sokolov was the largest of three panels in a study conducted in Erfurt and Weimar in eastern Germany and Sokolov in the Czech Republic (6). Children with asthma who regularly attended outpatient clinics in Sokolov or Chodov (15 km northeast of Sokolov) were recruited. Participating children lived within a 25-km radius of Sokolov, the majority within 5 km. A questionnaire on the history of respiratory disease was distributed at the beginning of the study and completed by a parent or a guardian. A local physician examined each child and assessed the asthma and allergy status. Asthma was defined as “chronic inflammatory disorder of the airways associated with variable airway obstruction that is often reversible either spontaneously or with treatment, and causes an associated increase in airway responsiveness to a variety of stimuli” (18). A history of bronchitic symptoms was defined as a history of

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cough, bronchitis, excessive phlegm production, or spastic bronchitis. Written informed consent was obtained from parents before their children were enrolled in the study. Data were collected between January 1991 and June 1992. The analyses presented here are restricted to the winter of 1991–1992 (15 November–4 February 1992) to allow the analysis of individual time series with generalized linear models. Eighty-two children aged 6–14 years old at the end of 1991 participated during the period of analysis.

Lung function was assessed daily by measuring peak expiratory flow (PEF) rates with a Mini Wright Peak Flow meter (range 60–800 liter/min). PEF measurements during the first 2 weeks were discarded to eliminate learning effects. A detailed description of the study design is given elsewhere (8,19). Participants recorded the highest of these PEF measurements before taking medication in the morning and in the evening. If the subject took medication, a second measurement was made 10 min after the dose. Reports of cough during the night before, cough during the day, dyspnea at rest, dyspnea at night, dyspnea on exertion, runny nose, phlegm, fever, school absence, and time spent outdoors were collected in the diary. Use of asthma medication (including time, amount, and name of drug) was also recorded. Prescriptions containing theophylline were converted to milligram of active drug. Beta-agonist use was coded as number of puffs.

Air pollution data. Pollutants [SO_2 , nitrogen dioxide (NO_2), and total suspended particles (TSP)] and meteorological variables (temperature, relative humidity, barometric pressure, wind speed, and wind direction) were measured at one central site. Acid aerosols were sampled with a size-selective impactor and ammonia denuder. Concentrations of sulfates were determined by ion chromatography, and acidity was determined by pH measurement of 24-hr samples of particles with an aerodynamic diameter less than 2.5 μm . PM_{10} was measured at the same location and on the same schedule. Daily measurements of PM_{10} and acid aerosols were only available during the winter of 1991–1992. A detailed description of the exposure assessment is given elsewhere (20,21).

Episodes of elevated air pollution lasting longer than 7 days occurred repeatedly during the winter of 1991–1992 in Sokolov (8). Air pollution was dominated by SO_2 , with a mean concentration of 100 $\mu\text{g}/\text{m}^3$ (maximum: 383 $\mu\text{g}/\text{m}^3$) during the period of analysis. TSP had a mean concentration of 83 $\mu\text{g}/\text{m}^3$ (maximum: 325 $\mu\text{g}/\text{m}^3$) and PM_{10} a mean concentration of

55 $\mu\text{g}/\text{m}^3$ (maximum: 171 $\mu\text{g}/\text{m}^3$). Concentrations of sulfate fine particles averaged 8.8 $\mu\text{g}/\text{m}^3$ (maximum: 23.8 $\mu\text{g}/\text{m}^3$). Particle strong acidity (PSA) was on average below the detection limit (22), despite high SO_2 concentrations. The highest air pollution concentrations were observed between the middle of November 1991 and the middle of December 1991. During the following 5 weeks, air pollution was much lower in Sokolov. At the end of January 1992, SO_2 concentrations stayed above 200 $\mu\text{g}/\text{m}^3$ for 12 days. On the first day of this air pollution episode (25 January 1992), the highest PSA concentration (4.8 $\mu\text{g}/\text{m}^3$) was detected. This value was confirmed by an independent measurement by a second sampler (20). The concentrations of SO_2 and particle measurements were highly correlated; for example, sulfate (SO_4) concentrations were highly correlated with SO_2 ($r = 0.79$) and PM_{10} ($r = 0.80$). PM_{10} was strongly correlated with TSP ($r = 0.90$) and SO_2 ($r = 0.75$). No data on ozone concentrations were available for Sokolov during the winter of 1991–1992 because of low levels. These analyses are therefore restricted to the effects of particulate and sulfur pollution. To simplify the presentation in the following section, results are presented only for SO_4 as a general indicator of particulate and sulfur pollution. SO_4 was previously shown to be the air pollution indicator most strongly and consistently associated with PEF in the larger panel study (6,8).

Statistical analysis. Previous analyses of panels of asthmatic subjects have used time-series methods to evaluate the association between the mean day-specific health outcomes and air pollution (6,8). In this study, the impact of medication use on subject-specific time series was analyzed with generalized linear models (23,24). Models for binary and normally distributed data were estimated with control for a linear trend, 24-hr mean temperature, and weekend (versus weekday). To control for viral infections that may have coincided with high exposures to air pollution at the end of January 1992, additional analyses adjusted for the mean prevalence of fever in the cohort. A detailed analysis of possible confounding of the association between respiratory health and air pollution by viral infections has been published elsewhere (8). Missing observations were assumed to be missing completely at random and were omitted. Because repeated measurements were taken on each individual, a variance-covariance structure that took into account that the error-term was associated with the outcome measured on the previous day was considered. Analyses were restricted

to the 82 patients who contributed more than 21 observations (average: 76.8 observations) during the period of analysis; 95% confidence intervals were calculated on the basis of robust standard errors. Previous analyses suggested that the strongest associations between health outcomes and air pollution were attributable to the concentrations of sulfate fine particles (8). SO_4 was chosen to present analyses with regard to medication use because it measured the particle fraction attributable to SO_2 , the major air pollutant of the area. Same-day and 5-day mean (current plus 4 previous days) SO_4 was used to compare immediate and delayed impact of air pollutants. In the case of missing exposure data, the mean of the available measurements was taken. Cough included reporting of cough during the day or cough during the night before. Dyspnea included dyspnea at rest, on exertion, or at night. Beta-agonist and theophylline use were summarized in a binary variable, which was 1 if theophylline or beta-agonist use was recorded. Associations between medication use and symptoms were evaluated by inclusion of an indicator for medication in the logistic models with control for a linear trend, 24-hr mean temperature, weekend (versus weekday), and 5-day mean of SO_4 .

Results

The cohort of 82 children was divided into those who did ($n = 51$) or did not ($n = 31$) use asthma medication during the period 15 November 1991–14 February 1992 (Table 1). Children who took medication were reported to have a diagnosis of asthma more frequently, but the prevalence of bronchitic symptoms was similar. The medicated children were slightly younger, had lower mean PEF, and reported a higher prevalence of symptoms than nonmedicated children. The prevalence of cough, dyspnea, and phlegm was more than three times higher among medicated children, and they reported fever more frequently and were absent from school more often during the period of analysis than nonmedicated children.

Exacerbation of asthma in 22 children was treated with theophylline only. One child used beta-agonist alone, and eight children used both types of medication. Two of the children were receiving continuous therapy, one with theophylline only and one with theophylline and beta-agonist (Fig. 1). All other children took asthma medication infrequently as needed. There were shortages of beta-agonist during the whole study period, which might explain the low prevalence of beta-agonist use (rather than a preference for a different approach to asthma therapy). Cortisone was

not prescribed for any of the children during the study period. None of the children used aerosol medication with combinations of beta-agonist and cortisone. The nonmedicated children included 26 subjects who reported medication use during other peri-

ods but not during the analysis period. The medicated children ($n = 31$) provided 2,422 person-days out of the total 6,294 person-days recorded during the 3-month period. Theophylline was used on 588 person-days and aerosol sprays on only 111 person-days.

Table 1. Characteristics of patients from Sokolov

	Medication use		
	All	None	During period of analysis ^a
Number of patients	82	51	31
Age (mean years)	9.8	9.9	9.5
Gender	50 m/32 f	30 m/21 f	20 m/11 f
Asthma	69 (86%)	41 (80%)	28 (93%)
Bronchitic symptoms	69 (86%)	42 (82%)	27 (87%)
Peak expiratory flow (mean)	296 l/min	307 l/min	278 l/min
Symptom on more than 20% of days			
Any	44 (54%)	17 (33%)	27 (87%)
Cough	34 (41%)	10 (20%)	24 (77%)
Dyspnea	12 (15%)	1 (2%)	11 (36%)
Phlegm	11 (13%)	3 (6%)	8 (26%)
Runny nose	28 (34%)	13 (25%)	15 (48%)
School absence on more than 20% of days	14 (17%)	5 (10%)	9 (27%)
Fever on more than 5% of days	9 (11%)	4 (8%)	5 (16%)
No symptom during whole period	0	0	0

^a15 November 1991–14 February 1992.

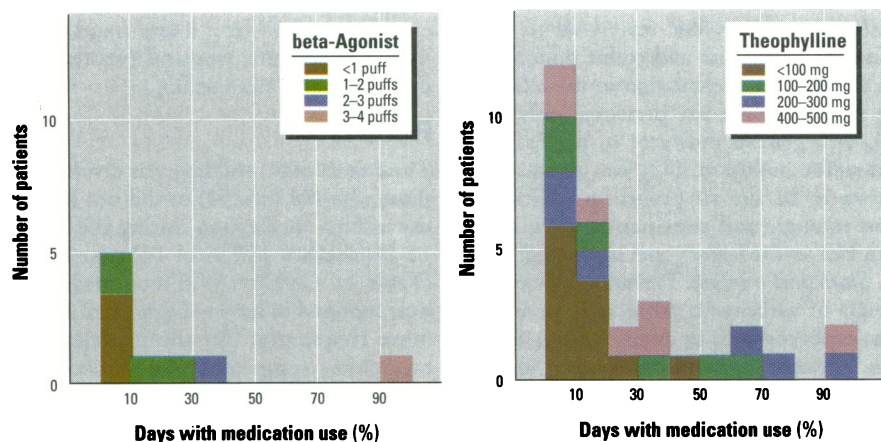


Figure 1. Frequency and dose of medication use for the medicated children from Sokolov.

Table 2. Comparison of effect estimates^a for concurrent SO₄ concentrations expressed for an increase of 8 μg/m³

	Medication use		
	All	None	During period of analysis ^b
Change in PEF (95% confidence intervals)			
PEF [l/min]	-0.48 (-1.59,0.63)	0.02 (-1.46,1.49)	-1.21 (-3.28,0.85)
Odds ratio (95% confidence intervals)			
Any symptom	1.01 (0.97,1.05)	1.07 (0.98,1.18)	0.92 (0.83,1.02)
Cough	1.04 (0.92,1.18)	1.08 (0.96,1.23)	1.01 (0.92,1.12)
Dyspnea	1.03 (0.88,1.20)	1.05 (0.77,1.44)	0.99 (0.83,1.17)
Phlegm	1.04 (0.92,1.18)	1.11 (0.92,1.34)	0.97 (0.87,1.09)
Runny nose	1.07 (1.00,1.14)	1.13 (1.03,1.24)	1.01 (0.93,1.10)
School absence	0.99 (0.91,1.07)	0.92 (0.79,1.08)	1.07 (0.96,1.19)
Fever	1.35 (0.92,1.97)	1.23 (0.78,1.94)	1.52 (0.95,2.44)
beta-Agonist use	1.07 (0.91,1.25)	—	1.08 (0.88,1.32)
Theophylline use	1.01 (0.95,1.08)	—	1.03 (0.89,1.18)

PEF, peak expiratory flow.

^aAdjusted for temperature, a linear trend, and weekend (vs. weekday).

^b15 November 1991–14 February 1992.

Separate analyses for medicated and nonmedicated children were conducted to evaluate differences in response to particulate air pollution. Table 2 presents the results of the multivariate regression analyses of same-day SO₄ concentrations on lung function, symptoms, and medication use. All analyses adjusted for a linear trend, 24-hr mean temperature, and an indicator for weekend (versus weekday). The regression coefficients or odds ratios are given for an increase of one interquartile range of SO₄ (8 μg/m³). Exposure to SO₄ on the same day was not strongly associated with decreased lung function, increased prevalence of respiratory symptoms, or increased absence from school in the nonmedicated or medicated children or in the total cohort. A decrease in PEF was observed only for the medicated children. The estimates for SO₄ were slightly larger for respiratory symptoms in nonmedicated children than in medicated children, but the association was not statistically significant. Evidence for a possible association between fever and same-day SO₄ concentrations was found in both subgroups. The prevalence of beta-agonist use among the medicated children was not associated with concurrent exposure to SO₄.

Table 3 presents the results of the multivariate regression analyses, with a 5-day mean to quantify cumulative effects of SO₄ concentration. All effect estimates were multiplied by one interquartile range of the 5-day mean of SO₄ (6.5 μg/m³) and can be compared directly with those in Table 2. The responses to cumulative exposure to SO₄ differed between medicated and nonmedicated children. The decrease in PEF associated with increased levels of a 5-day mean of SO₄ was four times larger in medicated children than nonmedicated children. It accounted nearly entirely for the association observed in the total cohort. While an odds ratio larger than 1 was observed for cough in both subgroups, an increase in the prevalence of dyspnea in association with SO₄ was observed only in the nonmedicated children. The association between a 5-day mean of SO₄ and the prevalence of fever was most pronounced in the medicated subgroup, for whom an increase in runny nose was observed as well. There was a statistically significant association between beta-agonist use and a 5-day mean of SO₄. Large standard errors associated with the effect estimates for the nonmedicated children, despite the fact that 51 panelists belonged to the subgroup, indicated that the group included a sample with large variability in their responses to particulate air pollution. Half of the nonmedicated children took asthma medication in the

Table 3. Comparison of effect estimates^a for a 5-day mean of SO₄ concentration expressed for an increase of 6.5 µg/m³

	Medication use		
	All	None	During period of analysis ^b
Change in PEF (95% confidence intervals)			
PEF [l/min]	-3.25 (-5.50,1.00)	-1.35 (-3.69,0.99)	-5.62 (-9.93,-1.30)
Odds ratio (95% confidence intervals)			
Any symptom	1.07 (0.95,1.20)	1.10 (0.92,1.31)	1.05 (0.86,1.29)
Cough	1.19 (1.05,1.34)	1.27 (1.01,1.60)	1.16 (1.00,1.34)
Dyspnea	1.09 (0.91,1.31)	1.18 (0.98,1.41)	1.04 (0.83,1.29)
Phlegm	1.01 (0.86,1.19)	1.18 (0.80,1.76)	0.88 (0.70,1.12)
Runny nose	1.16 (0.99,1.36)	1.16 (0.94,1.44)	1.17 (0.94,1.47)
School absence	1.05 (0.87,1.27)	1.06 (0.77,1.46)	1.05 (0.85,1.31)
Fever	1.71 (1.11,2.64)	1.36 (0.82,2.26)	2.26 (1.11,4.61)
beta-Agonist use	1.45 (1.09,1.92)	—	1.46 (1.08,1.98)
Theophylline use	0.99 (0.80,1.22)	—	0.99 (0.77,1.26)

PEF, peak expiratory flow.

^aAdjusted for temperature, a linear trend, and weekend (vs. weekday).^b15 November 1991–14 February 1992.**Table 5.** Qualitative summary of the group characteristics and observed effects

	Nonmedicated children (n = 51)	Medicated children (n = 31)
Grade of asthma	Slight	Moderate
Symptom prevalence	Low	High
Medication use	None	If needed
Hypothesized reactivity to external stimuli	Low	Moderate
Observed associations between health outcomes and SO ₄ concentrations		
Peak expiratory flow	None	Decrease
Respiratory symptoms	Increase in dyspnea	Increase in cough
Medication use	—	Increase

year preceding the analyses, but not during this specific study period. The associations observed between symptoms and a 5-day mean of SO₄ were largely attributable to this subgroup.

Treatment with medication as an indicator for either theophylline or beta-agonist use did not confound the association between the health outcomes and the exposure to SO₄ as shown in Table 4 for the 5-day mean of SO₄. Increased symptoms and decreased PEF were strongly associated with increased medication use. All symptoms except runny nose were associated with increased medication use. The children appeared to adjust their medication use according to their perception of their health. The strongest associations were found for dyspnea at night and at rest, which were symptoms indicating an exacerbation of asthma. However, adjustment for medication use did not modify the associations with the 5-day mean SO₄ concentration (Table 4 compared with Table 3 results).

Viral infections at the end of January 1992 may have coincided with an episode of particulate air pollution and potentially confounded the association between health outcomes and SO₄ exposures (8). Additional analyses adjusting for the prevalence of fever in the sample were conducted in

order to assess possible confounding. The association between the PEF and SO₄ was not altered in these additional analyses (Fig. 2A). However, associations between phlegm/runny nose and SO₄ concentrations were reduced in the nonmedicated children but not in the medicated children after adjustment for fever (Fig. 2B). The effect estimates for the association between health outcomes and medication use were not confounded by the prevalence of fever.

Discussion

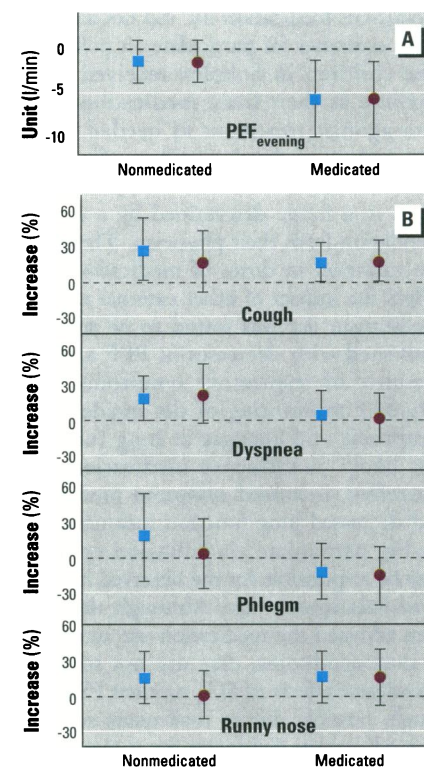
Previous analyses showed decreased PEF rates and increased prevalence of respiratory symptoms and beta-agonist use in association with increased 5-day means of sulfate fine particle concentrations in children with mild asthma from Sokolov, the Czech Republic (6,8). Concentrations of sulfate fine particles may serve as an indicator pollutant in an atmosphere with a complex mixture of air pollutants dominated by high SO₂, moderate levels of particulate matter, and low acidity (8,20,21).

An analysis of these same data for a 3-month period during the winter of 1991–1992 stratified by medication use, suggested that nonmedicated children (51 panelists) differed substantially from children who took medication (31 panelists) in

Table 4. Effect estimates^a for 5-day mean of SO₄ concentrations expressed for an increase of 6.5 µg/m³ and any medication use estimated jointly in one model for all children

	SO ₄	Medication use
Change in PEF (95% confidence intervals)		
PEF [l/min]	-3.19 (-5.40,-0.98)	-14.9 (-22.3,7.50)
Odds ratio (95% confidence intervals)		
Any symptom	1.08 (0.95,1.23)	4.31 (2.60,7.13)
Cough	1.21 (1.08,1.36)	3.67 (2.05,6.56)
Dyspnea	1.08 (0.87,1.33)	12.30 (5.43,27.9)
Phlegm	1.00 (0.81,1.24)	2.39 (1.32,4.32)
Runny nose	1.16 (0.99,1.36)	1.20 (0.91,1.57)
School absence	1.05 (0.87,1.27)	2.36 (1.40,3.98)
Fever	1.64 (1.05,2.54)	2.48 (1.05,5.86)

PEF, peak expiratory flow.

^aAdjusted for temperature, a linear trend, and weekend (vs. weekday).**Figure 2.** Effect estimates for peak expiratory flow (PEF) and respiratory symptoms in association with a 5-day mean of SO₄ concentrations without (■) and with (●) adjustment for prevalence of fever.

their general characteristics and their responses to particulate air pollution (Table 5). The children treated with asthma medication had more severe asthma as indicated by a high prevalence of respiratory symptoms, which presumably led to more frequent absence from school. Although the medicated children increased their beta-agonist use in association with an increased 5-day mean concentration of SO₄, the strongest decrease in PEF was observed in this subgroup. Despite a higher

prevalence of respiratory symptoms among medicated children, effect estimates quantifying the association between SO_4 and respiratory symptoms appeared to be larger for nonmedicated children. Although results are presented only for SO_4 , similar results were found for SO_2 , TSP, PM_{10} , and particle acidity as in previous analyses (8). Only weak associations were observed with TSP and PM_{10} and health outcomes, even after adjustment for medication use.

Chamber studies have indicated that medication use attenuates or reverses the effects of air pollutants on health outcomes in asthmatic volunteers (14–16). Therefore, medication use can be a confounder, as has been suggested by Silverman et al. (17). No confounding by medication use was observed in this study, since controlling for concurrent medication use did not alter the effect estimates for particulate air pollution. The children in Sokolov received theophylline as their basic medication, with beta-agonist treatment as needed. They kept asthma medication at home for emergencies, which resulted in variation of the doses in a range determined by a recommendation from their physician. Therefore, the variation in doses of medication may reflect the impact of other external stresses. Medication use was found to be strongly associated with decreases in PEF and the presence of respiratory symptoms. The intensive monitoring of the incidence of symptoms and changes in lung function was likely to influence medication use. Therefore, increased symptom prevalence and decreased lung function measurements during particulate air pollution episodes may be responsible for the observed increases in beta-agonist use. Although the children adjusted the medication use according to their symptoms, they did not suppress the adverse effects of SO_4 on their PEF and cough, possibly due to inadequate supplies of medication. Evidence for a protective effect of medication use was found for dyspnea, which increased in association with exposure to SO_4 only in nonmedicated children. Dyspnea was the strongest predictor for medication use. Thus, this study suggests that medication use diminishes the effects of ambient particulate air pollution on asthmatics. However, it should be stressed that under Western treatment regimens (18) and with adequate availability of medication, the medicated children may not have shown associations between SO_4 and health outcomes.

The associations between health outcomes and elevated levels of SO_4 may be confounded by coinciding viral infections (25). In a longitudinal study of children who reported wheezing or persistent

cough, exacerbation of symptoms and severe decreases in PEF were, in 80% of the cases, associated with the presence of viruses detected by polymerase chain reaction (26). In order to eliminate this possibility, regression results adjusted for the prevalence of fever in the sample are presented here. The association of decreased PEF and increased SO_4 were not confounded by viral infections. However, the effect estimates calculated for SO_4 and symptoms were attenuated for nonmedicated children. Of all groups, the actively medicated children had the highest prevalence of fever; nonetheless, the observed associations between cough and a 5-day mean of SO_4 were not altered. Although the impact of viral infection coinciding with an episode of particulate air pollution cannot be ruled out entirely (8), the possibility of confounding does not weaken the role of medication as an effect modifier.

Pope et al. (2) compared a school-based sample of children with respiratory symptoms to a panel of asthma patients. Asthma patients showed polynomially distributed lag structures for PM_{10} and PEF, which suggests that a 5-day moving average would show bigger effect estimates than concurrent exposure to PM_{10} . The school-based sample showed an immediate effect of particulate air pollution on PEF and symptoms, but the asthma panel did not. One possible explanation for these differences is beta-agonist use, which increased in the asthma panel in association with increasing PM_{10} .

The observed health effects and their potential modification by medication use were associated with air pollution originating from the burning of lignite. Two epidemiological studies [from Pope et al. (2) and the results presented here] suggest that effect estimates for particulate air pollution on symptoms may be underestimated when medication is used by asthmatic patients.

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