

Summertime Haze Air Pollution and Children with Asthma

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In order to investigate associations between summertime haze air pollution and asthma at an individual level, 52, 58, and 56 children (ages 7 to 13) attending a summer "asthma camp" were followed during the last week of June in 1991, 1992, and 1993, respectively. Most of the subjects had moderate to severe asthma. Daily records were kept of the environmental conditions, as well as of subject medication use, lung function, and medical symptoms. Air pollution was found to be significantly and consistently correlated with acute asthma exacerbations, chest symptoms, and lung function decrements. The pollutant most consistently associated with adverse health consequences was ozone (O₃), although associations with sulfates and hydrogen ion suggest a possible role by fine particles as well. Effects were found to be roughly monotonic as a function of O₃ concentration. Regression of morning (8:00 A.M.) to afternoon (5:00 P.M.) peak flow change on O₃ indicated pulmonary function reductions similar to those previously reported for more active children without asthma. Moreover, analyses also indicated an increased risk of an asthma exacerbation and of experiencing chest symptoms of approximately 40% on the highest pollution day, relative to the mean. Based on these relative risk estimates, a rise in the 1-h daily maximal O₃ from 84 ppb to 160 ppb was associated in this group with an increase from 20 to 28 (± 2) in the expected number of unscheduled medications administered/day, and from 29 to 41 (± 3) in the expected total number of chest symptoms/day. Thus, air pollution can be a major contributor to the respiratory problems experienced by children with asthma during the summer months. **Thurston GD, Lippmann M, Scott MB, Fine JM. Summertime haze air pollution and children with asthma.**

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Summertime haze air pollution, including ozone and sulfate aerosol, has been associated with increases in daily aggregate population counts of asthma hospital visits and admissions in various metropolitan areas (1-6). Moreover, some recent chamber experiments have indicated that controlled short-term exposures of individuals with asthma to ozone increase their bronchial reactivity to allergens (7, 8). Diary studies of persons with asthma (9-13) have also provided results linking these separate chamber and aggregate epidemiologic studies by indicating that asthma "panels" do report increased acute aggravated disease incidence as a result of ambient air pollution exposure.

In order to further investigate and quantify the apparent air pollution-asthma relationship on an individual level and in a more closely controlled situation than possible in diary studies, children with asthma attending a summer camp were followed during the last week of June 1991, 1992, and 1993, respectively. Chil-

dren at summer camps have been shown in the past to be suitable subjects for the study of health effects and air pollution, as their exposure and activity patterns can be well defined (e.g., 14, 15). Similarly, "asthma camps," in which children with asthma participate in outdoor activities under careful medical supervision in a campground environment, also provide a suitable setting in which to search for firmer individual-level evidence of air pollution-asthma associations.

The study camp was located in the Connecticut River Valley, which is frequently downwind of the New York City metropolitan area during the summer months, resulting in occasional transported air pollution episodes in an area usually quite low in pollution. During each of the three separate study weeks, detailed daily records were kept by the on-site research staff of the environmental conditions, and by the health staff of each child's medication use, lung function, and respiratory symptoms. This study design thus avoided the question of subjective data-keeping by subjects (e.g., in diary studies). Furthermore, the comprehensive nature of the individual medical records kept for each child, combined with the detailed on-site environmental data, provided a unique dataset with which to evaluate the potential role of ambient summertime haze air pollution in respiratory problems experienced by children with asthma. The key questions addressed in this analysis of these data were whether exposure to summer haze air pollution: (1) increases the frequency of asthma exacerbations, (2) increases the incidence of respiratory symptoms, and/or (3) reduces the normal A.M. to P.M. increase in peak expiratory flow rate (Δ PEFR) in children with asthma.

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METHODS

Subject Health Data Collection

Fifty-two, 58, and 56 children (ages 7 to 13) attended a summer asthma camp held in the Connecticut River Valley during the last week of June, 1991, 1992, and 1993, respectively. Of these children, 113 were white and 53 were nonwhite. While the severity of their asthma ranged from mild to severe, most were moderate to severe, as defined by the National Asthma Education Program Guidelines for the Diagnosis and Management of Asthma (16). For example, 71% were regularly taking inhaled anti-inflammatory medications (i.e., either cromolyn sodium or corticosteroids, or both), as prescribed by their physicians, which is consistent with moderate to severe asthma. The children signed up for activities upon arrival (on Sunday) and had those same activities each day of the study (i.e., Monday through Friday). These activities were not physically strenuous (e.g., archery, drama, nature, riflery, crafts, etc.), so exercise-induced asthma was unlikely to be a complicating factor. Campers departed for home on Saturday. Throughout the study, the children were under 24-h supervision by certified respiratory therapists, who also ensured that the children received their routine medications.

Before breakfast and dinner (at approximately 8:00 A.M. and 5:00 P.M., respectively) on each study day, peak expiratory flow rate (PEFR) was assessed using 60–800 L/min range MiniWright meters (Clemente Clarke, Columbus, OH), and respiratory symptoms were recorded for each child by a respiratory therapist at the Health Lodge. Every child was assigned a peak flow meter for his or her exclusive use during the study week. In each case, the best of three PEFR trials was recorded. The MiniWright meters used were intercompared with measurements made with a calibrated 8-L Collins portable spirometer (W. E. Collins, Braintree, MA) for each child during the 1991 study. A regression of paired MiniWright PEFR values and spirometric PEFR values yielded a high degree of correlation ($r = 0.9$) and a regression slope not statistically different from 1.0. Thus, the MiniWright peak flow measurements employed were functionally equivalent to measurements from a calibrated spirometer. Afternoon symptoms (as reported by the children at 5:00 P.M.) were summed into total daily counts of chest symptoms (cough, phlegm, and wheeze) and head symptoms (sore throat, runny nose, eye irritation) for each child.

In the event that a child experienced an asthma exacerbation, he or she was referred by their group's respiratory therapist to the on-site physician at the Health Lodge for confirmation, who then authorized an inhaled β -agonist on an "as-needed" (*pro re nata*, prn) basis, when appropriate. Each child's normal medications (as prescribed by his or her physician) were maintained throughout the week. The only medications included in this analysis were those unscheduled medications administered in addition to normal medications. All medications were stored and administered at the Health Lodge. As a result, carefully controlled objective records were kept of each child's health throughout the week, including all symptoms, lung function measurements, and both scheduled and unscheduled medication usage.

Environmental Data Collection

Daily air pollution, pollen, and weather measurements were conducted on-site during the three study periods. Pollutants measured included ozone (O_3) and fine particulate matter ($d_p < 2.5 \mu m$). The fine particle samples were collected twice per day (9:00 A.M.–9:00 P.M., 9:00 P.M.–9:00 A.M.), protected from possible neutralization by ambient ammonia, and later extracted and analyzed for particulate strong acidity (H^+) and sulfate (SO_4^{2-}) (17). To avoid possible neutralization of acids on the fine particle samples during handling, the filters were not weighed. Ozone was monitored continuously at the camp (Dasibi 1003-AH, Glendale, CA), and hourly average concentrations computed throughout each study week. On-site calibrations of the monitoring equipment (i.e., concentrations and flows) were performed at the beginning and end of each week, and careful quality assurance records were kept. Pollen samples were collected on-site daily (9:00 A.M.–9:00 P.M.) using a Rotorod sampler which sampled for 60 s per every 10 min. Twenty-four hour pollen sampling, starting at 9:00 P.M. the night before a study day, was employed to ensure sufficient counts, given that pollen levels were expected to be relatively low in summer. The rods were subsequently sent out to be analyzed for pollen counts/ m^3 of air by a certified aerobiologist (Z. Dyer, Santa Barbara, CA). Hourly meteorological data (i.e., temperature and relative humidity) were obtained from a nearby meteorological monitoring

station in Middletown, Connecticut, and were also collected continuously on-site during the 1992 and 1993 study periods.

Data Analysis

The analyses focused on three measures of the possible effects of the atmospheric environment on children with asthma: the number of daily asthma exacerbations (as indicated by the total number of unscheduled β -agonist prn treatments administered on each day); the incidence of respiratory symptoms (i.e., the daily number of head and chest respiratory symptoms reported in the afternoon); and the A.M. to P.M. Δ PEFR. Given the limited number of study days for each child, extensive efforts were made to collect a complete dataset. As a result, there were no missing prn or symptom data. In the very few cases that a peak flow observation was missing, that child's observation was eliminated from the analysis on that day. The daily change in peak flow was examined in order to ascertain whether the normal circadian pattern of peak flow values was altered by environmental factors, and to utilize a metric that intrinsically controlled for possible day-of-week effects (e.g., peak flow "learning curve" effects) over the course of the study week. Absolute differences were evaluated (rather than percent changes) in order to allow more direct intercomparison with past camp study results. In each case, the records were initially analyzed as aggregated group daily counts or means over each of the three study weeks ($n = 5 \text{ d/summer} \times 3 \text{ summers} = 15$) in order to permit a plotting of the results versus the individual environmental variables for visual inspection. Aggregate mean daily counts/child of β -agonist prn treatments and symptoms, as well as daily mean Δ PEFR, were also regressed on the various environmental variables using linear regression methods. Per child means were analyzed (rather than total daily counts, for example) in order to normalize for the fact that slightly different numbers of children were enrolled each year.

The health outcome data were also regressed on the pollutants considered as individual daily values for each child ($n = 166 \text{ subjects} \times 5 \text{ d/subject}$) with an intercept fitted for each subject in order to derive overall effect estimates after controlling for interindividual differences. However, because of small numbers of individual daily counts, total daily β -agonist prn treatments (i.e., numbers of exacerbations requiring medication per day by the children at the camp) and daily head and chest respiratory symptoms counts for each child were each regressed on the various environmental variables using the Poisson modeling approach (using the Statistical Analysis System's Nlin Procedure) to search for associations. Each individual's daily 8:00 A.M. to 5:00 P.M. Δ PEFR was also regressed on the environmental variables, but linear regression (Statistical Analysis System's General Linear Model [SAS GLM]) was employed, as these were not count data. Exploratory regressions including multiple pollutants (e.g., O_3 and SO_4^{2-} simultaneously) were also conducted to further investigate the relative roles of the various air pollutants. However, pollutant interaction terms were not attempted as the high intercorrelation of the various pollutants were greatly reduce the interpretability of such terms. In each model, autocorrelation of the residuals and the correlations of the regression coefficients (in simultaneous regression cases) were evaluated. In this way, the respective role of each pollutant was evaluated, for each of the health outcomes considered, both on an individual child and aggregate group level.

RESULTS

Table 1 presents the mean, maximal, and minimal values for the environmental and health data collected each study week, as well as for the combined data (i.e., 1991–1993). Although the pollen levels were fairly low and stable over the three years, the other environmental conditions experienced were quite varied across the three study periods. Pollen counts were dominated by the Pinus (pine/spruce group) and Graminae (grasses) pollens categories. The peak daily air pollution levels were highest in 1991 and lowest in 1992. For example, the highest daily 1-h maximal O_3 concentration experienced in 1992 (68 ppb) was nearly the same as the lowest concentration in 1991 (65 ppb), which experienced a highest daily 1-h maximal O_3 of 160 ppb. While the pollution concentrations in 1993 were more like those in 1991 (e.g., max $O_3 = 146 \text{ ppb}$), the pattern over the week was quite differ-

TABLE 1
MEANS, STANDARD ERRORS, MINIMUM AND MAXIMUM OF VARIOUS
POLLUTANTS, WEATHER, SYMPTOMS, PEAK FLOWS, PEAK FLOW DIFFERENCES, AND PRN FOR
CAMP STUDIES OF 1991, 1992, 1993, AND 1991-1993 COMBINED

	1991 (n = 5 d, 52 subjects)				1992 (n = 5 d, 58 subjects)				1993 (n = 5 d, 56 subjects)				1991-1993 (n = 15 d, 166 subjects)			
	mean	SE	min	max	mean	SE	min	max	mean	SE	min	max	mean	SE	min	max
1-h max O ₃ , ppb	114.0	5.3	65	160	52.2	8.4	20	68	84.6	17.5	37	146	83.6	10.2	20	160
Afternoon H ⁺ , nmol/m ³	83.7	40.8	22.4	245	44.0	17.2	10.2	106	34.0	10.9	18.2	76.0	53.9	15.2	10.2	245
Afternoon SO ₄ , µg/m ³	10.3	4.3	1.3	26.7	5.7	2.0	1.1	12.6	4.8	2.3	1.7	13.7	7.0	1.8	1.1	26.7
Pollen count, Grns/m ³	20.3	2.8	12.2	28.8	26.0	9.5	8.7	57.1	21.9	6.6	6.0	45.7	22.7	3.7	6.0	57.1
Daily max temp, °F	83.8	2.7	76	92	71.0	2.9	63	78	82.3	3.1	71	88	79.0	2.2	63	92
Total head symptoms/day	19.2	1.1	17	23	19.2	1.5	14	23	12.4	1.7	7	18	16.9	1.2	7	23
Total chest symptoms/day	32.0	4.5	18	41	26.0	1.6	21	30	29.6	2.1	23	35	29.2	1.7	18	41
A.M. Peak flow, L/min	302.5	5.9	60	500	318.8	4.7	100	490	344.1	4.9	80	550	322.4	3.0	60	550
P.M. Peak flow, L/min	320.3	5.9	60	530	341.1	4.6	100	505	365.9	4.6	110	600	343.2	2.9	60	600
ΔPEFR, L/min	18.3	2.9	-140	180	23.9	2.5	-110	200	20.9	2.8	-110	200	21.1	1.6	-140	200
Total β-agonists/d	22.8	3.1	15	31	19.4	3.1	10	27	19.2	1.6	16	24	20.5	1.5	10	31

ent: in 1991 pollution concentrations started relatively low and built up throughout the week, peaking on Day 5 (Friday), while in 1993 the highest pollution concentrations were experienced on the first study day of the week (Monday) and declined throughout that week. Thus, despite the limited number of days available, consideration of these three separate study periods provides a range of air pollution exposure concentration levels and a variety of exposure patterns in which to assess the influence of the atmospheric environment on the health of children with asthma.

Aggregate-Level Evaluation of Environmental-Health Effects Associations

In order to explore the data interrelationships, mean ΔPEFR values and total daily counts of daily symptoms and prn treatments were computed over all children for each study day for comparison with daily environmental values. The correlations between the various environmental factors and the daily mean of each health outcome over the 15 d are presented in Table 2. It is seen that some of the environmental variables are highly intercorrelated (e.g., H⁺ and SO₄²⁻). For this number of daily observations, the critical correlation coefficient is $r_{crit} = 0.43$ for significance at the $p = 0.05$ level (one-way test). Of the environmental exposure-health outcome relationships in Table 2, the strongest and most consistent associations appear to be with O₃. An exception is the poor correlation with head symptoms, which is clearly nonsignificant.

While daily maximal temperature (T_{max}) is highly correlated with O₃ in these data, O₃ is consistently more strongly correlated with the health outcomes measured. An examination of the plots

of the health outcomes versus temperature did not suggest a non-linear relationship (e.g., exponentially increasing effects at high temperature). Also, daily maximal temperatures at the camp were moderated by the presence of an adjacent lake, reaching a maximum of 91° F on only one study day (Day 5, 1991), so extremely hot weather was not experienced during the study.

Relative humidity (RH) is not significantly correlated with any of the health outcomes, although its correlation with lung function approaches significance. Examination of these data revealed that this correlation is driven by the one rain day during the study (on Wednesday of the 1992 study week), on which the RH was 93%. Elimination of this day from the analysis causes the RH-health effects correlations to weaken substantially (e.g., the correlation with ΔPEFR drops to only $r = 0.19$). However, the air pollution-health effects associations were not adversely affected by removing this day (e.g., the O₃ correlation with ΔPEFR becomes $r = -0.39$, and with chest symptoms becomes $r = 0.72$).

As shown in Table 2, O₃ exhibits the highest correlation with ΔPEFR of the environmental variables considered. It can be seen in Figure 1 that, at low ozone, the P.M. peak flow averages roughly 20 to 30 L/min more than the A.M. value, whereas at the highest ozone levels, the diurnal improvement is reduced to roughly 10 to 20 L/min. The 1991 data have consistently high values for O₃ and have generally average to low ΔPEFR, whereas the opposite is generally true of the 1992 data. Together, the 1991 and 1992 data suggest a trend toward lower ΔPEFR values at higher O₃ levels. It is also seen in Figure 1 that the 1993 data, which spanned the entire 1991-1992 O₃ range, confirm the trend implied by the earlier years' data. Pollen is poorly correlated with lung func-

TABLE 2
BIVARIATE PEARSON CORRELATIONS AMONG ENVIRONMENTAL VARIABLES AND
DAILY MEAN VALUES OF MEASURED HEALTH OUTCOMES (n = 15, $r_{crit} = 0.43$)

	Max O ₃	H ⁺	SO ₄ ²⁻	Pollen	Max T	RH	β-Agonist Use	Chest Symptoms	Head Symptoms
Max O ₃	1.00								
H ⁺	0.64	1.00							
SO ₄	0.74	0.97	1.00						
Pollen	-0.15	-0.12	-0.16	1.00					
Max T	0.86	0.47	0.52	-0.17	1.00				
RH	-0.52	-0.10	0.58	-0.13	-0.66	1.00			
β-Agonist use	0.62	0.66	0.71	-0.09	0.55	-0.28	1.00		
Chest symptoms	0.71	0.53	0.59	-0.03	0.56	-0.23	0.54	1.00	
Head symptoms	0.09	0.29	0.27	0.08	-0.21	-0.13	0.11	0.37	1.00
ΔPEFR	-0.43	-0.18	-0.25	-0.07	0.24	0.39	-0.15	-0.05	-0.25

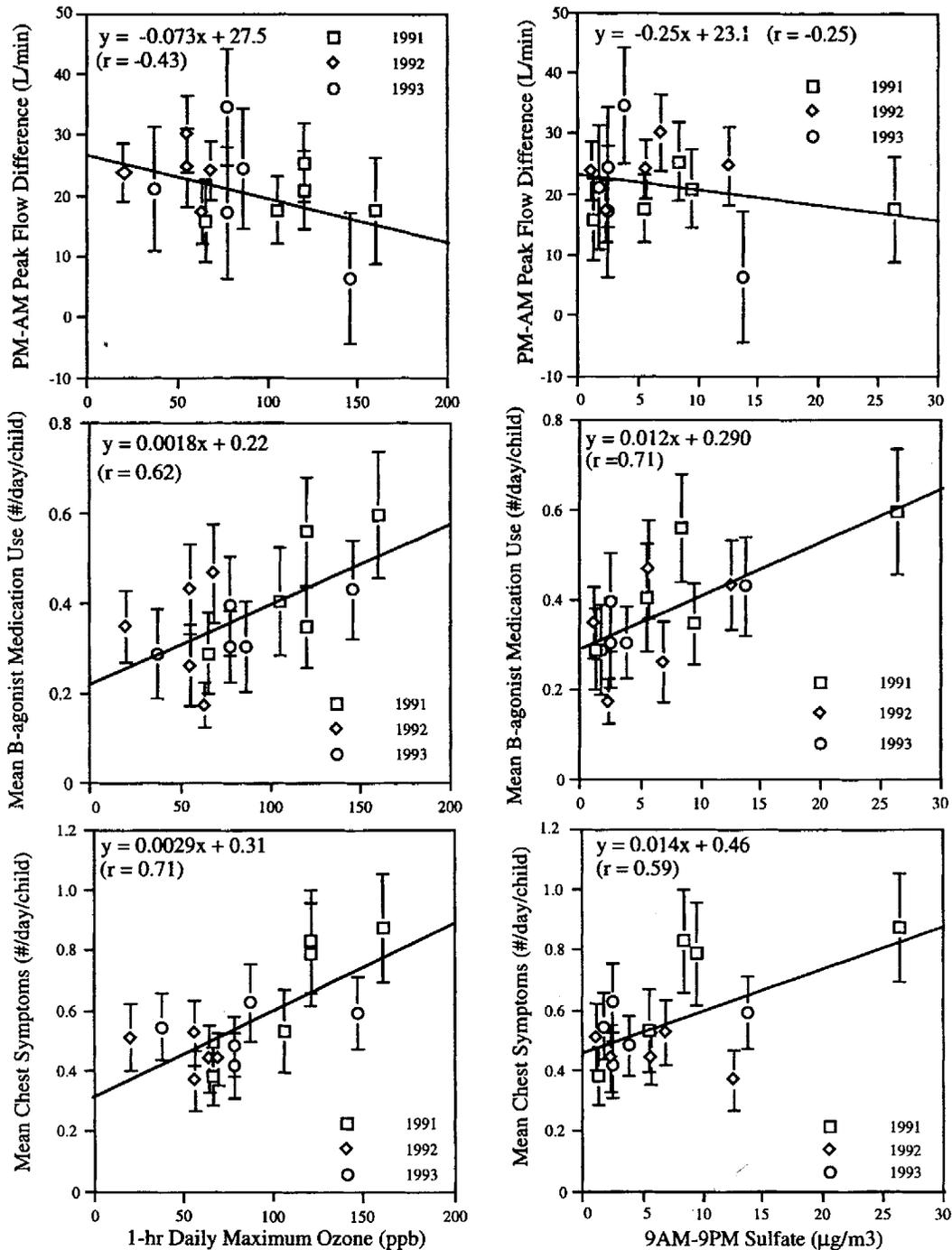


Figure 1. Mean daily morning to afternoon peak flow change, β -agonist medication use, and chest symptoms counts versus ozone and sulfate concentration ($r_{crit} = 0.43$).

tion decrements ($r = -0.07$), which is not surprising, given that pollen counts are relatively low at this time of year. H^+ and SO_4^- also show moderate negative correlations with ΔPEFR ($r = -0.18$ and -0.25 , respectively) but, as seen in Figure 1 for SO_4^- , these are strongly influenced by a single extreme day. For example, removing this day (Day 5, Friday of the 1991 study week), which is also the highest O_3 day of the study, reduces the H^+ correlation to $r = -0.07$ and the SO_4^- correlation to $r = -0.20$, but only slightly reduces the O_3 - ΔPEFR correlation to

$r = -0.41$. Thus, the O_3 - ΔPEFR relationship is seen to be the strongest, as well as the least sensitive to the elimination of the highest pollution day.

Figure 1 also displays the same pairings for counts of daily mean β -agonist prn treatments on each study day. The associations are stronger than was the case for ΔPEFR , and are clearly significant. As shown in Table 2, pollen is again poorly associated with adverse effects ($r = -0.09$). Eliminating the highest pollution day of the study (Day 5) reduces all of the air pollution corre-

TABLE 3
GLM REGRESSION OF INDIVIDUAL CHILDREN'S DAILY Δ PEFR ON DAILY AIR POLLUTION CONCENTRATIONS

Model Specification	Pollutant (units)	Coefficient (L/min/unit pollution)	t Statistic ($t_{crit} = -1.65$)
Single pollutant alone	O ₃ (ppb)	-0.096	-1.92
	SO ₄ ⁼ (μ g/m ³)	-0.36	-1.53
	H ⁺ (nmol/m ³)	-0.64	-1.15
Single pollutant with temperature	O ₃ (ppb)	-0.22	-2.50
	SO ₄ ⁼ (μ g/m ³)	-0.42	-1.46
	H ⁺ (nmol/m ³)	0.08	0.12

lations with β -agonists somewhat (e.g., SO₄⁼ drops to $r = 0.54$), but all three remain significantly correlated with β -agonist prn treatments.

Of the pollutants considered, O₃ also displays the strongest association with daily mean counts of chest (i.e., lower respiratory) symptoms, explaining half the variance in chest symptoms experienced in these children (Figure 1). Also strongly correlated with daily counts of chest symptoms are SO₄⁼ ($r = 0.59$) and H⁺ ($r = 0.53$). However, these latter results are strongly affected by a single day, whereas chest symptoms are seen to rise consistently and monotonically with O₃ concentration. Indeed, excluding Day 5 from the analysis lowers both SO₄⁼ and H⁺ to statistical nonsignificance ($r = -0.30$ and $r = 0.09$, respectively) for this outcome, though O₃ remains clearly significant ($r = 0.60$). As shown in Table 2, pollen is again poorly associated ($r = 0.03$). Thus, while elevated air pollution concentrations in general are seen to be strongly associated with increased chest symptoms experienced by these children with asthma, only the O₃ relationship is consistent enough to still exhibit a significant association after eliminating the highest pollution day.

Regression Analyses of Pollutant Associations with Individual Subjects

In order to determine if the aggregate analyses presented above are consistent with the results that would be obtained had each child's individual daily data been evaluated (rather than daily means of the total for all subjects), these data were analyzed using GLM and Poisson regression models (for the subjects' lung function and for the morbidity counts, respectively).

As shown in Table 3, the GLM procedure, which fit an intercept for each subject and an overall slope for the pollutant, yielded results very consistent with the aggregate analyses. For example, O₃ coefficient is -0.096 L/min/ppb, indicating that there was a 9.6 L/min, or an average 3% decline in PEFR for a 100 ppb

TABLE 4
POISSON REGRESSIONS OF INDIVIDUAL CHILDREN'S DAILY β -AGONIST USE ON DAILY AIR POLLUTION CONCENTRATIONS

Model Specification	Pollutant (units)	Poisson Coefficient	t Statistic ($t_{crit} = 1.65$)
Single pollutant alone	O ₃ (ppb)	0.00454	3.57
	SO ₄ ⁼ (μ g/m ³)	0.0274	4.14
	H ⁺ (nmol/m ³)	0.0580	3.87
Single pollutant with temperature	O ₃ (ppb)	0.00396	1.52
	SO ₄ ⁼ (μ g/m ³)	0.0214	2.63
	H ⁺ (nmol/m ³)	0.0426	2.39

TABLE 5
POISSON REGRESSIONS OF INDIVIDUAL CHILDREN'S CHEST SYMPTOMS COUNTS ON DAILY AIR POLLUTION CONCENTRATIONS

Model Specification	Pollutant (units)	Poisson Coefficient	t Statistic ($t_{crit} = 1.65$)
Single pollutant alone	O ₃ (ppb)	0.00482	4.77
	SO ₄ ⁼ (μ g/m ³)	0.0215	3.86
	H ⁺ (nmol/m ³)	0.0442	3.44
Single pollutant with temperature	O ₃ (ppb)	0.00623	3.02
	SO ₄ ⁼ (μ g/m ³)	0.0144	1.95
	H ⁺ (nmol/m ³)	0.0261	1.55

increase in O₃ daily maximal concentration. This is very similar to the coefficient derived from the aggregate analysis shown in Figure 1 (-0.073 L/min/ppb). Also, as in the aggregate analyses, O₃ was the pollutant most strongly associated with decreases in lung function. First-order autocorrelation was only moderate in these regressions ($|r| < 0.2$). The difference between O₃ and the other pollutants was heightened once daily maximal temperature was included in the regression, indicating a larger t statistic and a coefficient of -0.22 L/min/ppb. Temperature is significantly positively associated with lung function in this simultaneous regression, which agrees with biologic plausibility (see DISCUSSION), but may also be an artifact of the high serial intercorrelation between O₃ and temperature. Converting units for this case yields an O₃ coefficient of -3.7 ml/s/ppb for these children, which is similar in magnitude to the response reported in a previous study that examined A.M. to P.M. Δ PEFR in active children without asthma (-3.4 ml/s/ppb O₃) (14).

Table 4 similarly shows the pollutant coefficients from the Poisson regressions of individual children's daily prn β -agonist medication use in which intercepts have been fit for each child. In this case, it is more difficult to directly compare the coefficients with the aggregate analyses summarized in Figure 1, as the Poisson coefficients are not linear. However, converting the coefficients to relative risks at the mean concentration ($RR = \exp(0.00454 \times 83.6 \text{ ppb}) = 1.46$ for O₃) allows comparisons at the mean. In the case of O₃, this implies a slope at the mean of $0.46 \times 20.5 \text{ counts}/55.3 \text{ subjects}/83.6 \text{ ppb} = 0.0020$ prn β -agonist treatments/day/child/ppb, which is very close to the value shown in Figure 1 for the aggregate analysis (0.0018). Also, all three pollutant metrics' coefficients are strongly significant in the Poisson analysis, just as in the aggregate analysis, and the order of their relative strengths is also the same, with SO₄⁼ being the pollutant metric most strongly associated for this outcome. First-order autocorrelation was weak ($|r| < 0.1$) in these regressions. Adding temperature into the regression noticeably reduces the significance of all of these pollutant coefficients (no doubt because of the high collinearities between the temperature and pollution coefficients, e.g., $r = -0.57$ for SO₄⁼), but the RR estimates at the mean only drop slightly when temperature is included (e.g., by 15%, from 1.46 to 1.39 for O₃).

Table 5 presents the pollutant coefficients from the Poisson regressions of individual children's daily counts of chest symptoms. As for the other modeled outcomes, these results are very consistent with the aggregate results (shown in Figure 1). Of the health outcomes considered in this work, chest symptoms is the metric that yields the strongest associations with the various pollutants (i.e., $t = 4.77$ for O₃ in the Poisson analyses, and $r = 0.71$ in the aggregate analysis). Once again, the Poisson coefficients, when evaluated at the mean, give mean effect estimates similar to those derived via the aggregate linear regressions. For

example, the O_3 RR at the mean implied by the Poisson analysis is $RR = \exp(0.00482 \times 83.6 \text{ ppb } O_3) = 1.50$. This yields a slope of $(0.50 \times 29.2 \text{ mean counts/day} \div 55.3 \text{ children} \div 83.6 \text{ ppb } O_3) = 0.0031 \text{ symptoms/day/child/ppb}$, which is very close to the slope indicated by the aggregate analysis (0.0029). When temperature is introduced into the analysis, O_3 is still the most significant pollutant, and the effect estimate is actually increased.

Simultaneous pollutant regressions were also conducted for the two pollutants which generally had the most significant associations in the various models considered: O_3 and SO_4^{2-} . This was done in order to see how the regression apportioned the previously noted air pollution associations between these two pollutants. In the case of Δ PEFR, the O_3 coefficient was virtually unchanged ($b = -0.94$, $t = -1.16$), whereas SO_4^{2-} declined noticeably (to $b = -0.011$, $t = 0.97$). For β -agonists, the SO_4^{2-} poisson coefficient declined slightly and remained significant ($b = 0.020$, $t = 1.94$), while the O_3 coefficient declined more and became nonsignificant ($b = 0.0017$, $t = 0.90$). For chest symptoms, O_3 dominated, with a nearly unchanged and significant coefficient estimate ($b = 0.0044$, $t = 2.84$), whereas SO_4^{2-} declined noticeably (to $b = 0.0026$, $t = 0.30$). These various results should be interpreted with extreme caution, as these two pollutants were highly correlated with each other over time ($r = 0.74$), causing these pollutants' regression coefficient estimates to also be highly (negatively) correlated with each other in these analyses ($r = -0.76$). Overall, while the strong association between sulfates and increased medication use warrants further investigation, these various exploratory multipollutant analyses generally indicate that O_3 is the air pollutant most strongly and consistently associated with adverse health effects in this population of children with asthma.

DISCUSSION

Summer haze pollutants were found to be significantly and consistently correlated with asthma exacerbations, chest symptoms, and lung function decrements in children attending a summer asthma camp. Regression of Δ PEFR on ozone indicated pulmonary function reductions per ppb O_3 similar to those previously reported for active camp children without asthma (14). However, such summer haze associated reductions may have greater health consequences in children with asthma, given their already compromised respiratory health. Also, the physical activity level of these children was less than in most past camp studies. This would lower their ventilation rates, and therefore their pollution doses and responses, relative to more active subjects exposed to the same pollutant concentration (18). This factor is likely to be the reason that past camp studies of active children (14, 19) have reported O_3 -PEFR regression coefficients nearly double those reported by studies of less active children (20, 21). Thus, once the relatively limited activity levels at this camp are considered, our analyses suggest that greater lung function reductions result from a given air pollution dose to children with asthma than found in past studies of children without asthma. In addition, a coherence of summer haze pollution acute effects was found across the chest symptoms, lung function, and unscheduled inhaled β -agonist medication use (i.e., asthma exacerbation) health outcomes. These results are consistent with past results showing associations between elevated O_3 and particulate matter $\leq 10 \mu\text{m}$ in diameter (PM_{10}) and increased reporting of respiratory symptoms by children with asthma (13), as well as with population-based "ecological" studies, which have similarly indicated an association between summertime haze air pollution and the exacerbation of asthma.

Of the air pollutants considered here, the pollutant most consistently and coherently associated with adverse health consequences appeared to be O_3 . Although H^+ and SO_4^{2-} were also

strongly (and sometimes even more strongly) associated with specific adverse health effects, their association was found to be more dependent on a single extreme day that was high for all the pollutants considered (as well as for temperature). Excluding this day from the analysis had much less effect on the size and significance of the O_3 coefficient, which suggests a more consistent association. The exploratory multipollutant analyses also suggest that O_3 is the pollutant most strongly associated with a range of adverse health effects in this population of children with asthma. Such an association between air pollution and increased inhaled β -agonist use by children with asthma has not been previously reported, though an association between winter air pollution and medication use by adults with asthma has been reported previously (with the strongest degree of association being with H^+) (11). While the O_3 -adverse health associations were the most consistent in this summer study, the fact that the H^+ and SO_4^{2-} associations with medication use were also quite strong may be indicative of a fine particle effect, as well. Future such studies of children with asthma should include fine mass and composition measurements to further investigate this hypothesis.

Overall, the adverse effects noted among these children with asthma were found to be roughly monotonic as a function of O_3 concentration experienced. This is consistent with what we know about both O_3 and asthma, since asthma is worsened by inflammatory insults (22), and O_3 exposure at ambient levels is known to initiate an inflammatory response in the upper airways (23). Moreover, the increase in adverse effects with O_3 concentration is also consistent with past results from both chamber experiments involving persons with asthma (24) and observational epidemiologic studies of hospital admissions (1-6). Collectively, our results, and their coherence with other independent results, are consistent with a causal role by O_3 in the adverse asthma health effects noted in this research.

Other atmospheric environmental factors, including temperature, relative humidity, and pollen, were also considered. Neither pollen nor relative humidity was found to significantly correlate with adverse health effects, but pollen levels were relatively low during these summertime study periods. Temperature did correlate with the health outcome measures, but more weakly than pollution and not in a way consistent with biologic plausibility. For example, the negative temperature- Δ PEFR correlation found is the opposite of that expected based on past pulmonary chamber experiments, which showed that warmer ambient temperatures in the absence of air pollution actually improve lung function in normal and asthmatic subjects (25). Similarly, the incidence of asthma exacerbations generally increases with colder temperatures (16, 26), rather than with warmer temperatures (as would be implied by the bivariate correlations in Table 2). Thus, while statistically significant correlations are found for temperature with decreased lung function and increased numbers of symptoms and asthma exacerbations, in this case these are almost certainly an artifact of the confounding association between temperature and (the even more strongly correlated) air pollution concentrations, rather than causal associations with temperature.

A striking aspect of the noted air pollution associations with increased β -agonist medication use (i.e., increased numbers of asthma exacerbations) and increased chest symptoms is the large magnitude of these effects. Using O_3 as the index pollutant, both the linear and Poisson models indicate an increased relative risk of an asthma exacerbation of about 40% ($RR = 1.37$ and 1.41 , respectively) on the highest pollution day ($O_3 = 160 \text{ ppb}$) versus the average O_3 day during these study weeks ($O_3 = 84 \text{ ppb}$). Similarly, the risk of experiencing chest symptoms estimated by these two models also increased about 40% ($RR = 1.40$ and 1.44 , respectively) on the highest day versus the average O_3 day. In this

population averaging 55 children, this implies that an increase in the 1-h daily maximal O₃ concentration from the mean of 84 ppb to the maximum recorded (160 ppb) was associated with an increase from 20 to 28 (± 2) in the expected number of unscheduled β -agonist medications administered per day, and from 29 to 41 ($\pm 3\%$) in the expected number of chest symptoms reported per day. These estimates are reasonably consistent with the O₃ maximal/mean RRs previously reported for asthma hospital admissions for Buffalo, New York (RR = 1.29 \pm 0.12) and Toronto, Ontario (RR = 1.32 \pm 0.19) (2). They are also consistent with the Houston adult asthma panel study results, which indicated an increase of 80 ppb in the daily maximal O₃ concentration was associated with a 50% increase in the asthma exacerbation rate (10). Although the incidence of asthma problems is not as high during the summer months as at some other times of the year (e.g., during the spring and early autumn pollen seasons), a large portion of summer asthma problems are apparently attributable to summertime haze air pollution.

It is clear from this work that summertime haze air pollution remains a serious health threat to children with asthma, despite the laws and regulations implemented to date to reduce precursor pollutants, such as the nitrogen oxides, hydrocarbons, and sulfur oxides being emitted by industry, power plants, and automobiles. It is relevant that, even in the rural section of eastern Connecticut considered in this work, the daily 1 h maximal O₃ equaled or exceeded the 120 ppb U.S. National Ambient Air Quality Standards (NAAQS) on more than 25% of the study days during the 1991–1993 years (i.e., 4 d of 15 total). However, the monotonic nature of the relationships of O₃ with reduced lung function and increased numbers of asthma symptoms and exacerbations found in this work indicates that these effects extend well below the present 120 ppb concentration level, so that even meeting this standard will apparently not be fully protective for these sensitive individuals. Past medical advice that children with asthma should take care to avoid exposure to air pollutants (27) is further supported by the results of this research.

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