Air Pollution and Exacerbation of Asthma in African-American Children in Los Angeles

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Significant increases in asthma morbidity and mortality in the United States have occurred since the 1970s, particularly among African-Americans. Exposure to various environmental factors, including air pollutants and allergens, has been suggested as a partial explanation of these trends. To examine relations between several air pollutants and asthma exacerbation in African-Americans, we recruited a panel of 138 children in central Los Angeles. We recorded daily data on respiratory symptoms and medication use for 13 weeks and examined these data in conjunction with data on ozone (O_3) nitrogen dioxide (NO_2), particulate matter (PM_{10} and $PM_{2.5}$), meteorological variables, pollens, and molds. Using generalized estimating equations, we found associations between respiratory symptom occurrence and several environmental factors. For example, new episodes of cough were associated with exposure to PM_{10} (OR = 1.25; 95% CI = 1.12–1.39; interquartile range [IQR] = 17 $\mu g/m^3$, 24-hour average), $PM_{2.5}$ (OR = 1.10; 95% CI = 1.03–1.18; IQR = 30 $\mu g/m^3$, 12-hour average), NO_2, and the molds *Cladosporium* and *Alternaria*, but not with exposure to O_3 or pollen. The factors PM_{10} and O_3 were associated with the use of extra asthma medication. For this population several bioaerosols and air pollutants had effects that may be clinically significant. (Epidemiology 2001;12: 200–208)

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Numerous reports have documented significant increases in asthma morbidity and mortality in the United States beginning in the 1970s, with African-Americans disproportionately affected.[1–3] Part of the racial disparity in these trends is undoubtedly associated with conditions of poverty.[4] Exposure to various environmental factors, including indoor and outdoor pollutants and allergens, has been postulated as a partial explanation of increasing incidence of asthma, which may be exacerbated by factors associated with socioeconomic status. Several epidemiologic investigations have used panel data to document associations of ozone (O_3) and particulate matter with asthma exacerbation.[5–9] Other investigations have demonstrated relations between ambient pollution and hospital admissions or emergency room visits for asthma.[10–14] None of these studies, however, focused exclusively on minority populations.

Our specific objective was to determine whether several air pollutants, including particulate matter, O_3, and bioaerosols, are associated with exacerbation of asthma in this population of African-American children, and if so, whether there was any interaction with the children's asthma severity, socioeconomic status, respiratory infections, reported allergic status, or medical management.

Data and Methods

The Study Population

Eligible subjects were African-American children, 8 to 13 years of age, who had physician-diagnosed asthma that required asthma medication during the preceding year in the absence of a respiratory infection, and who did not have any other chronic condition that required regular administration of corticosteroids. In a pilot study,[15] we found that no single institution served a large number of low-income, asthmatic African-American children in central Los Angeles; therefore, for this investigation we recruited from several public and private hospitals, urgent care clinics, and group practices. Such diverse recruitment sources ensured variation in household income and socioeconomic status, access to medical care, and asthma severity. Several recruitment approaches were employed, including in-person encounters during clinic visits and telephone contacts with potentially eligible patients, all using standardized protocols.

To increase the number of children in the study likely to be exposed to high levels of O_3, we broadened our

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recruitment area to include Pasadena (approximately 30 miles east of the main study area), which has O_3 levels typically twice those of metropolitan Los Angeles. In Pasadena, we recruited participants through telephone calls made by school nurses.

Health Data

Data collected from the participants included (1) parental responses to an intake questionnaire that provided information on the children's medical histories, asthma severity and known triggers, allergic status, medical management, family structures and demographics, and potential indoor exposures, as well as (2) a 13-week daily diary in which the children recorded asthma symptoms, medication use, respiratory infections, peak expiratory flows, and physician visits. Study staff went to each participant's home within a few weeks of enrollment to administer the intake questionnaire to the child's parent or legal guardian. All participants were carefully instructed on daily diary completion and peak flow meter use, and each received a return visit for re-training approximately 2 weeks after the start of the study, which took place from August through October 1993. To enhance compliance, study staff made additional home visits throughout the study period, and the parents or caregivers were telephoned weekly about changes in the children's respiratory status.

To improve the accuracy of the recording of medication use during the daily data collection, the parent or guardian of each study participant was asked to produce all of the child's prescribed medications. With this information, the interviewers established a daily baseline asthma-medication level for each participant. Any excess in medication beyond this *regular* level on any given day was then defined as *extra* medication, which was recorded as a dichotomous variable. At the end of each week, the participants returned the diary forms to the study coordinator in pre-addressed, stamped envelopes.

Covariates

Daily data for ambient air pollution, meteorological factors, pollens, and molds were collected during the 13-week study period. Ozone, particulate matter less than 10 'm in diameter (PM_{10}), and nitrogen dioxide (NO_2) were measured daily at two fixed-site monitoring stations operated by the South Coast Air Quality Management District in downtown Los Angeles and Pasadena. Both hourly and 24-hour average PM_{10} data were collected daily at both sites using model FH62I-N β-attenuation monitors (Andersen Instruments, Smyrna, GA). Supplemental monitoring was undertaken under contract to the California Air Resources Board to include daytime (8 am to 8 pm) concentrations of fine particles ($PM_{2.5}$ or particles with mean aerodynamic diameter <2.5 μm) using a proprietary medium-volume gravimetric sampling system at the Los Angeles site only. There were 26 days on which $PM_{2.5}$ concentrations were reported to be higher than those for the corresponding 12-hour PM_{10} measurements at the Los Angeles site. Since these days were not randomly distributed but occurred when $PM_{2.5}$ was particularly high, analyses using the fine particle metric were potentially problematic. These elevated readings may have been due to measurement error, to differences in sample collection efficiency, or to other factors. (Alternatively, it is possible, although in our opinion less likely, that there may have been difficulties with the PM_{10} data, which were collected as part of a statewide air quality monitoring network.) To examine the general reliability of the fine particle data, we compared $PM_{2.5}$ concentrations in Los Angeles to those measured gravimetrically every 6th day at North Long Beach and Azusa, which are 7.5 miles south and 9 miles east of downtown Los Angeles, respectively. The correlations for the 13 concurrent data points between Los Angeles and the other two sites were between 0.6 and 0.7, suggesting that the $PM_{2.5}$ data collected in Los Angeles were broadly representative of local exposures, although we had no direct way to assess this assumption. Consequently, we conducted only limited analyses using $PM_{2.5}$. As a sensitivity analysis, we examined regression models using the full $PM_{2.5}$ dataset as well as a dataset restricted to those days on which the $PM_{2.5}$ concentration was less than that of PM_{10}.

Daily meteorological data collected at the Los Angeles airport and obtained from the National Climatic Data Center (Asheville, NC) included maximum and minimum temperature, relative humidity, precipitation, and dew point. Daily pollen and mold samples were collected at a private allergy clinic in Los Angeles (several miles west of the downtown Los Angeles monitoring site) with a Roto Rod device (Multidata, Minnetonka, MN) set to sample 30 seconds every 10 minutes throughout each 24-hour interval. The samples were interpreted by a counter certified for pollens and spores by the American Academy of Allergy, Asthma and Immunology's Aeroallergen Network following Network guidelines. These data were examined in both aggregated (*ie* concentrations of total pollens) and disaggregated forms (*ie* pollen counts from grasses, trees, and weeds, and several mold spore counts, specifically *Alternaria* and *Cladosporium*).

Statistical Methods

Two sets of related adverse outcomes were examined: (1) symptoms of asthma, including shortness of breath, cough, and wheeze; and (2) daily use of extra medication. For symptoms, both the daily probability of each symptom and the probability of a new onset of a symptom episode were examined. We defined new onset of a symptom as the 1st day, after at least 1 day without any symptoms, on which any of the three symptoms listed above was reported. Multivariate regression analysis used in the full study was similar to that used in the pilot phase.[15] In brief, we used generalized estimation equations (GEE) to estimate the effects of air pollution on symptoms and medication use while controlling for meteorological and temporal factors.[16] The GEE corrects for the correlation and lack of independence of an individ-

ual's responses by using quasi-likelihood methods and robust variance estimators. Also, the GEE model should correct for any serial correlation in the data. The latter attribute is less important in the analysis of symptom episodes, which are less likely than daily symptom probabilities to be subject to serially correlated error terms.

Previous studies of air pollution and asthma have indicated that temperature and humidity may play a role in asthma exacerbation,[12] so these covariates were examined in the regression models, in which lags of 0 to 3 days were considered. Study day and indicator variables for weekend (*vs* weekday) were also examined in the symptom analysis.

Once we obtained the "*best*" regression model, based on chi-squared goodness-of-fit statistics, we entered each pollutant, mold, and pollen measure separately. We matched subjects in Los Angeles and Pasadena with ambient pollution concentrations measured at their respective city monitors. We considered single-day lags of up to 3 days and a 4-day moving average (average of lags 0–3) for all of these measures of exposure. For pollutants found to be associated with symptoms, additional analysis was conducted in which the population was stratified to examine whether it included particularly susceptible subgroups. Regressions were re-run after stratifying by location (Los Angeles *vs* Pasadena), asthma severity (moderate and severe *vs* mild), family income (greater *vs* less than $25,000/year), gender, and use of anti-inflammatory medication. We also examined whether there were any differential effects among families who had less than average information about the medical management of asthma or among parents who typically did not consult a physician about their children's asthma outside of the acute care or emergency room setting. Knowledge about asthma medical management was assessed with questions on whether the parents or guardians (1) had received information from a nurse or doctor about asthma medications, when to restrict their child's activity, and how to reduce their child's likelihood of having an asthma attack; (2) could identify the child's asthma triggers; and (3) had received a written plan for managing their child's asthma, particularly during an exacerbation of symptoms.

Use of extra medication (*ie* medication above each person's defined baseline) was analyzed using logistic regression, following a model-building approach similar to that described above.

Results

Descriptive Analysis

During recruitment, 153 eligible subjects were enrolled in the study. Five subjects who provided baseline data never provided any daily diary information. In addition, data from 10 subjects (representing 8.3% of the person-days) were excluded from the analysis because of evidence that the intake data or diary data were likely to have been inaccurate, or because the diaries were returned more than 2 weeks late. This exclusion left a total of 138 children. Of these, 52 (38%) were recruited from health maintenance organizations, 23 (17%) from the Pasadena schools, 15 (11%) from hospitals (one public and two private), 42 (30%) from group medical practices, and 6 (4%) from asthma camps. Of the subgroup living in the central Los Angeles area (N = 115), approximately 90% resided within 10 miles of the downtown Los Angeles monitoring site. All Pasadena children (N = 23) resided within 5 miles of the monitoring station located there. Daily diary start dates were staggered, but most subjects began within the 1st week of the data collection period. Fifty-nine children (43%) completed diaries for essentially the entire sampling period (13 weeks), while an additional 27 children (20%) completed at least 9 weeks.

Table 1 summarizes the demographics, asthma status and income and insurance levels of the study population. Subjects' ages were distributed fairly evenly, and a substantial number of the families' incomes were relatively low. More than half of the children were rated by their parents as moderate or severe asthmatics, an estimate supported by the data on medication and hospital use.

Statistical analysis focused on the daily reporting of respiratory symptoms (cough, shortness of breath, and wheeze, the initiation of asthma episodes), and the use of extra medication. During the study period, the average daily prevalences of cough, shortness of breath, and wheeze for the Los Angeles participants were 15.1, 7.25, and 17.3%, respectively, while for the Pasadena children, the corresponding figures were 11.5, 8.1, and 17.2%. On average, about 6.7, 3.7, and 7.6% of the subjects experienced a new episode of cough, shortness of breath, or wheeze, respectively, on any given day.

Table 2 summarizes the health, pollution, bioaerosol, and meteorological data. Between Pasadena and Los Angeles, the pollutant concentrations were highly correlated: $r = 0.83$ for O_3 and $r = 0.84$ for PM_{10}. Table 3 summarizes within-site correlations of the covariates in Los Angeles. Particles and O_3 were only moderately correlated, while the correlation between $PM_{2.5}$ and PM_{10} (both measured at downtown Los Angeles) was 0.61. Levels of pollens and molds exhibited distinct peaks in October and were moderately correlated with PM_{10}. For example, the correlation between PM_{10} and *Alternaria* was 0.48 in Los Angeles, and 0.33 in Pasadena. Ozone was inversely correlated with *Alternaria* at both sites with $r = -0.16$ in Los Angeles and $r = -0.28$ in Pasadena.

Analysis of Symptoms

A total of 10,022 person-days of symptom data were reported, of which we used 9,126 in the analysis after the health data of questionable validity were excluded. The basic regression model for each symptom included 1-day lags of temperature and humidity, age, income, an indicator variable for city of residence (Los Angeles or Pasadena), day of study, and the pollutant. Five different daily pollutant measures—24-hour average PM_{10}, 1-hour maximum PM_{10}, $PM_{2.5}$, 1-hour maximum O_3, and 1-hour maximum NO_2—were examined in relation to each

TABLE 1. Descriptive Statistics for Children who Completed Diaries for the Full Study

Characteristics	Full Sample (N = 138)	Los Angeles Area (N = 115)	Pasadena (N = 23)
Age (years)			
6	1 (0.7)	1 (0.9)	0 (0)
7–8	26 (18.8)	20 (17.4)	6 (26.1)
9–10	44 (31.9)	39 (33.9)	5 (21.7)
11–12	48 (34.8)	39 (33.9)	9 (39.1)
13	18 (13.0)	15 (13.0)	3 (13.0)
Missing	1 (0.7)	1 (0.9)	0 (0)
Sex			
Percentage male	61	65	44
Income (× $1,000)			
<10	36 (26.1)	31 (30.0)	5 (21.7)
10–25	14 (10.1)	10 (8.7)	4 (17.4)
25–40	38 (27.5)	33 (28.7)	5 (21.7)
40–70	29 (21.0)	23 (20.0)	6 (26.1)
>70	11 (7.9)	9 (7.8)	2 (8.7)
Missing	10 (7.2)	9 (7.8)	1 (4.3)
Insured	133/138 (96.4)	112/115 (97.4)	21/23 (91.3)
Receiving Medi-Cal (government-subsidized medical coverage)	30/133 (22.6)	23/112 (20.5)	7/21 (33.3)
Asthma severity			
Mild	61 (44.2)	54 (47)	10 (43.5)
Moderate	57 (41.3)	46 (40)	11 (47.8)
Severe	20 (14.5)	15 (13)	2 (6.7)
Use oral corticosteroids	51/138 (37.0)	46/115 (40.0)	5/23 (21.7)
Use anti-inflammatory medications	67/138 (48.6)	60/115 (52.2)	7/23 (30.4)
Ever hospitalized for asthma	47/138 (34.1)	42/115 (36.5)	5/23 (21.7)
Smokers in home	53/137 (38.7)	39/114 (34.2)	14/23 (60.9)
Exposed to tobacco smoke elsewhere	72/137 (52.6)	58/114 (50.4)	14/23 (60.9)

Percentage in parentheses.

symptom, as were total pollens and two molds, *Alternaria* and *Cladosporium*.

Using the GEE model, several measures of particulate matter, including PM_{10} (both 24-hour average and 1-hour maximum) and $PM_{2.5}$, demonstrated positive associations with daily probability of shortness of breath, wheeze, and cough. For these pollutant metrics, lags of two or three days, as well as moving averages of four days, showed strong associations with symptoms, while shorter lags did not. For example, as summarized in Table 4, a 3-day lag in PM_{10} (using an interquartile change in $PM_{10} \approx 17\ \mu g/m^3$) was associated with shortness of breath (OR = 1.14; 95% CI = 1.04–1.24) and cough (OR = 1.10; 95% CI = 1.04–1.16), and less so with wheeze (OR = 1.04; 95% CI = 0.98–1.10). Likewise, both 1-hour maximum PM_{10} and 12-hour average $PM_{2.5}$ were associated with the likelihood of reporting asthma symptoms. Slightly stronger associations were found using the complete $PM_{2.5}$ dataset as opposed to the restricted dataset. For example, for shortness of breath,

TABLE 2. Descriptive Statistics for Meteorological Conditions, Air Pollution, Pollens, and Molds in Los Angeles (LA) and Pasadena, August to November, 1993

Variable	Mean (No. days)	SD	Range
O_3, LA (1-h maximum, pphm)	5.95 (91)	3.14	1.00–13.00
O_3, LA (8-h average, pphm)	3.89 (90)	2.22	0.5–9.63
O_3, Pasadena (1-h maximum, pphm)	9.58 (90)	4.90	1–22
O_3, Pasadena (8-h average, pphm)	6.19 (88)	3.11	1.38–13.38
PM_{10}, LA (24-h average, $\mu g/m^3$)	51.81 (91)	16.61	21.29–119.22
PM_{10}, LA (1-h maximum, $\mu g/m^3$)	102.02 (91)	56.60	47–360
PM_{10}, Pasadena (24-h average, $\mu g/m^3$)	42.65 (90)	12.98	11.04–94.96
PM_{10}, Pasadena (1-h maximum, $\mu g/m^3$)	79.25 (90)	59.15	17–598
$PM_{2.5}$ (12-h average, $\mu g/m^3$)*	40.82 (77)	32.47	4.5–208.7
NO_2, LA (1-h maximum, pphm)	7.95 (91)	4.36	2.00–22.00
NO_2, Pasadena (1-h maximum, pphm)	6.81 (89)	3.13	3–17
Maximum temperature (°F)	75.8 (91)	4.1	70.00–90.00
Relative humidity (1-h maximum, %)	93.7	5.6	66–100
Fungi (spores/m^3)	1,252.7 (60)	2,104.4	48–15,427
Alternaria (spores/m^3)	37.0 (52)	39.7	3–237
Cladosporium (spores/m^3)	858.6 (59)	1,912.1	32–14,364
Pollens (grains/m^3)	20 (60)	8.17	1–75
Trees (grains/m^3)	12.97 (60)	10.25	1–47
Grasses (grains/m^3)	0.45 (60)	0.87	0–4
Weeds (grains/m^3)	6.63 (60)	8.17	0–38

* Collected at downtown Los Angeles site only. Some of the 12-hour measures contained missing values, reducing the number of observations.

TABLE 3. Correlations of Pollutants, Molds, Pollen, and Meteorological Variables* in Los Angeles

	PM_{10}	PM_{10} m	$PM_{2.5}$	O_3	NO_2	Maxtemp	MaxRH	Clado	Alter
PM_{10} m	0.68								
$PM_{2.5}$	0.61	0.37							
O_3	0.35	0.09	0.01						
NO_2	0.63	0.38	0.34	0.48					
Maxtemp	0.48	0.42	0.14	0.25	0.33				
MaxRH	0.21	−0.05	−0.01	0.57	0.49	0.07			
Clado	0.31	0.23	0.26	−0.19	0.13	0.26	0.05		
Alter	0.48	0.40	0.48	−0.16	0.28	0.44	−0.02	0.82	
Pollen	0.24	0.20	0.18	0.17	0.39	0.31	0.23	0.29	0.44

* PM_{10} m = 1-hour maximum PM_{10}; O_3 = 1-hour maximum in Los Angeles; Maxtemp = maximum daily temperature; MaxRH = maximum daily relative humidity; Alter = *alternaria*; Clado = *cladosporium*; Pollen = sum of tree, weed, and grass pollens.

the full dataset generated an OR of 1.08 (1.00–1.17) *vs* 1.06 (0.97–1.17) using the restricted dataset, assessed for an IQR of 30 $\mu g/m^3$ $PM_{2.5}$. Nitrogen dioxide was associated with wheeze, with weaker associations with shortness of breath and cough. There was little evidence of association between O_3 and symptoms. Of the bioaerosols, *Cladosporium* was associated with both wheeze and cough, while *Alternaria* was strongly associated with cough. In contrast, there was no evidence of an association of total pollens with symptoms. Inclusion of the health data that were judged *a priori* to be of questionable validity did not alter these results. The associations of air pollution and bioaerosols with the onset of symptom episodes of shortness of breath, cough, and wheeze are summarized in Table 5. PM_{10} demonstrated the strongest effect, particularly for lags of 2 or 3 days. More modest associations were found between symptom episodes and the other PM metrics and NO_2. In this case, the associations using the complete $PM_{2.5}$ dataset as opposed to the restricted dataset were similar. There was no evidence of associations between O_3 and any symptom episodes. Both *Alternaria* and *Cladosporium* counts were associated with all three types of symptom episodes.

We stratified the sample by asthma severity, income, gender, and location to examine factors that might influence susceptibility to 24-hour average PM_{10} and *Alternaria*, which were both associated with most adverse health outcomes. The results are summarized in Tables 6 and 7. Asthma severity, income, and use of anti-inflammatory medication did not markedly affect the associations of PM_{10} with either the daily probability of symptoms or the onset of episodes. Among females and residents of Pasadena, however, we observed slightly stronger relations for several outcomes. Among residents of Pasadena, relatively large associations were observed between PM_{10} and daily cough as well as new episodes of

TABLE 4. Effects of Air Pollutants on Probability of a Day with Symptoms Using Generalized Estimating Equations*

Pollutant (Interquartile Range)	Shortness of Breath		Wheeze		Cough	
	OR	95% CI	OR	95% CI	OR	95% CI
PM_{10} (17 $\mu g/m^3$, 24-h avg)	1.14	1.04–1.24	1.04	0.98–1.10	1.10	1.04–1.16
PM_{10} (31 $\mu g/m^3$, 1-h max)	1.06	1.02–1.10	1.03	1.01–1.06	1.03	1.00–1.05
$PM_{2.5}$ (30 $\mu g/m^3$, 12-h avg)	1.08	1.00–1.17	1.06	1.01–1.11	1.03	0.98–1.07
O_3 (4 pphm, 1-h max)	1.01	0.92–1.10	0.94	0.88–1.00	0.93	0.87–0.99
NO_2 (5 pphm, 1-h max)	1.08	0.99–1.18	1.08	1.02–1.15	1.03	0.97–1.09
Cladosporium (444 spores/m^3)	1.01	0.99–1.04	1.01	1.00–1.03	1.02	1.00–1.04
Alternaria (20 spores/m^3)	1.01	0.95–1.08	1.02	0.98–1.07	1.23	1.18–1.27
Pollen (13 grains/m^3)	1.26	0.55–2.93	0.97	0.93–1.03	0.94	0.90–0.99

* Models include day of study, age, income, residence, and 1-day lags of temperature and humidity as explanatory variables. All exposures are lagged 3 days. Odds ratios are calculated for the specified interquartile ranges.

TABLE 5. Associations of Air Pollutants and Bioaerosols with Onset of Symptom Episodes*

Exposure (Interquartile Range)	Shortness of Breath		Wheeze		Cough	
	OR	95% CI	OR	95% CI	OR	95% CI
PM_{10} (17 $\mu g/m^3$, 24-h avg)	1.20	1.06–1.37	1.12	1.01–1.23	1.25	1.12–1.39
PM_{10} (31 $\mu g/m^3$, 1-h max)	1.06	1.00–1.12	1.02	0.99–1.06	1.07	1.02–1.11
$PM_{2.5}$ (30 $\mu g/m^3$, 12-h avg)	1.10	1.00–1.20	1.08	1.01–1.14	1.10	1.03–1.18
O_3 (4 pphm, 1-h max)	1.00	0.87–1.16	0.95	0.86–1.04	0.88	0.78–0.98
NO_2 (5 pphm, 1-h max)	1.14	0.99–1.31	1.13	1.04–1.24	1.12	1.00–1.24
Cladosporium (444 spores/m^3, 24-h avg)	1.03	1.00–1.05	1.03	1.01–1.05	1.04	1.02–1.06
Alternaria (20 spores/m^3, 24-h avg)	1.11	1.05–1.18	1.08	1.03–1.13	1.11	1.06–1.17
Pollens (13 grains/m^3)	1.11	0.90–1.38	0.94	0.77–1.14	1.01	0.82–1.24

* Models include day of study, age, income, residence, and 1-day lags of temperature and humidity as explanatory variables. All exposures are lagged 3 days. Odds ratios are calculated for the interquartile ranges.

TABLE 6. Sensitivity Analysis of Daily Symptoms for Selected Subgroups*

	Shortness of Breath		Wheeze		Cough	
Pollutant/Subgroup	OR	95% CI	OR	95% CI	OR	95% CI
PM_{10} (24-hour average)						
Moderate/severe asthma	1.16	1.04–1.30	1.08	1.01–1.16	1.11	1.02–1.20
Mild asthma	1.10	0.94–1.28	1.11	1.01–1.22	1.09	1.00–1.18
Females	1.22	1.07–1.40	1.07	0.99–1.17	1.20	1.09–1.32
Males	1.07	0.95–1.20	1.11	1.03–1.20	1.03	0.95–1.11
Low income	1.10	0.98–1.22	1.09	1.00–1.20	1.14	1.04–1.26
High income	1.17	1.02–1.36	1.09	1.01–1.18	1.07	1.00–1.15
Los Angeles	1.12	1.02–1.23	1.10	1.04–1.17	1.06	1.00–1.12
Pasadena	1.15	0.88–1.50	1.07	0.89–1.29	1.43	1.12–1.81
Anti-inflammatory	1.13	1.01–1.27	1.10	1.01–1.19	1.11	1.04–1.19
No anti-inflammatory	1.10	0.94–1.28	1.10	1.00–1.20	1.09	0.99–1.20
Alternaria						
Moderate/severe asthma	1.10	1.04–1.16	1.06	1.02–1.11	1.04	1.00–1.09
Mild asthma	0.98	0.91–1.07	1.03	0.97–1.08	1.02	0.97–1.07
Females	1.07	1.00–1.14	1.04	0.99–1.10	1.07	1.02–1.13
Males	1.04	0.98–1.11	1.05	1.01–1.10	1.00	0.95–1.05
Low income	1.01	0.95–1.07	1.03	0.99–1.09	1.04	0.99–1.10
High income	1.10	1.03–1.17	1.06	1.02–1.11	1.03	0.99–1.07
Los Angeles	1.08	1.03–1.13	1.06	1.02–1.09	1.02	0.99–1.06
Pasadena	0.99	0.88–1.11	1.01	0.93–1.11	1.08	0.98–1.18
Anti-inflammatory	1.09	1.02–1.16	1.05	1.00–1.09	1.07	1.03–1.12
No anti-inflammatory	1.02	0.95–1.09	1.05	1.01–1.11	0.98	0.93–1.04

* Models include day of study, age, income, residence, and 1-day lags of temperature and humidity as explanatory variables. PM_{10} and *Alternaria* exposures are lagged 3 days. Odds ratios are calculated for the interquartile ranges noted in Tables 4 and 5.

cough and shortness of breath. Among those with moderate or severe asthma, we detected stronger associations of *Alternaria* counts with several endpoints. Most other factors did not appear to make much of a difference. Stratification based on information about asthma management and whether families primarily used urgent care facilities also did not affect any associations of symptoms with air pollutants or aeroallergens.

Analysis of Extra Medication Use

In an attempt to model the use of extra medication, we included covariates similar to those used in the analysis of symptoms as explanatory variables. Accordingly, our basic model included the pollutant, day of the study, age, income, 1-day lags of maximum temperature and humidity, and a binary variable for residence. Lags of 0 to 3 days as well as moving averages of pollution were considered. With these models, none of the pollutants, pollens, or molds was associated with the use of extra medication among the full population. These null results were robust to model specification. The data were also stratified on reported asthma severity (moderate and severe *vs* mild) and residence. For moderate and severe asthmatics, a 2-day moving average of 1-hour maximum

TABLE 7. Sensitivity Analysis of Episodes for Selected Subgroups*

	Shortness of Breath		Wheeze		Cough	
Pollutant/Subgroup	OR	95% CI	OR	95% CI	OR	95% CI
PM_{10} (24-hour average)						
Moderate/severe asthma	1.20	1.02–1.41	1.10	0.98–1.24	1.24	1.08–1.43
Mild asthma	1.22	0.98–1.52	1.17	1.03–1.32	1.26	1.08–1.47
Females	1.30	1.08–1.56	1.12	0.99–1.27	1.34	1.15–1.57
Males	1.11	0.93–1.33	1.13	1.00–1.27	1.18	1.02–1.35
Low income	1.11	0.91–1.35	1.08	0.94–1.24	1.28	1.08–1.51
High income	1.27	1.07–1.52	1.15	1.03–1.28	1.22	1.07–1.38
Los Angeles	1.17	1.01–1.35	1.14	1.04–1.25	1.21	1.09–1.36
Pasadena	1.39	0.99–1.95	1.09	0.84–1.42	1.49	1.11–2.01
Anti-inflammatory	1.12	0.93–1.36	1.11	0.98–1.25	1.30	1.12–1.51
No anti-inflammatory	1.26	1.05–1.51	1.14	1.01–1.30	1.20	1.04–1.38
Alternaria						
Moderate/severe asthma	1.13	1.05–1.21	1.11	1.04–1.18	1.11	1.04–1.19
Mild asthma	1.07	0.96–1.20	1.05	0.96–1.14	1.11	1.04–1.20
Females	1.10	1.01–1.20	1.07	0.99–1.15	1.13	1.05–1.22
Males	1.11	1.03–1.20	1.09	1.02–1.16	1.10	1.02–1.19
Low income	1.05	0.96–1.15	1.05	0.97–1.14	1.10	1.02–1.19
High income	1.15	1.07–1.23	1.10	1.04–1.18	1.11	1.05–1.18
Los Angeles	1.13	1.06–1.21	1.09	1.03–1.15	1.10	1.04–1.16
Pasadena	1.02	0.89–1.18	1.05	0.93–1.19	1.17	1.04–1.31
Anti-inflammatory	1.14	1.05–1.23	1.06	0.98–1.14	1.19	1.11–1.27
No anti-inflammatory	1.07	0.99–1.17	1.10	1.03–1.17	1.05	0.97–1.13

* Models include, day of study, age, income, residence, and 1-day lags of temperature and humidity as explanatory variables. PM_{10} and *Alternaria* exposures are lagged 3 days. Odds ratios are calculated for the interquartile ranges noted in Tables 4 and 5.

PM_{10} (OR = 1.18; 95% CI = 1.03–1.34) for the interquartile change of 31 $\mu g/m^3$ as well as a 1-day lag of O_3 (OR = 1.15; 95% CI = 1.12–1.19 for an interquartile change of 4 pphm) were associated with the use of extra medication. Ozone (unlagged) was also associated with extra medication use among the children living in Los Angeles (OR = 1.10; 95% CI = 1.03–1.19). There was little evidence of an association between extra medication use and any of the other pollutants or bioaerosols.

Discussion

In this study of the impact of ambient air pollution on African-American children with asthma, we found that several measures of disease exacerbation were associated with particulate matter and mold counts. These results extend the findings of our pilot study of a similar but smaller population, in which we reported that both PM_{10} and O_3 in central and south-central Los Angeles were associated with increased daily reporting of shortness of breath.[15]

Our results suggest that 24-hour average PM_{10} is associated with both daily probabilities and the incidence of episodes of shortness of breath, cough, and wheeze. One-hour maximum PM_{10} was also associated with these endpoints, but with smaller effect sizes. Nitrogen dioxide (1-hour average) was also associated with the daily probability of wheeze and with episodes of wheeze and cough. Unlike the results of our pilot study, there was little evidence of an association between O_3 and any of the symptom measures. Since O_3 and particulate matter were only moderately correlated, we were able to distinguish the effects of these two pollutants.

Our findings in the present study are generally consistent with other epidemiologic studies that suggest that acute exposure to ambient particulate matter is associated with exacerbation of respiratory symptoms in asthmatics,[5–9,17] and that such exposure may result in increases in hospital admissions or emergency room visits.[10–14] Recently, McConnell *et al*[18] found that longer-term (1-year) exposures to PM_{10} were associated with increases in bronchitis, phlegm, and cough among a cohort of asthmatics. McConnell *et al*[18] and Gielen *et al*[19] also reported relatively greater effects on asthmatics from exposure to PM_{10} than from exposure to O_3. In contrast, Thurston *et al*[20] and Romieu *et al*[6] reported consistent effects of O_3 among asthmatic children. In these latter two studies, however, O_3 concentrations were either very high compared with those of the present study (mean 1-hour average of 19.6 pphm in Mexico City[6] *vs* 6 pphm in Los Angeles and 9.6 in Pasadena), or they were more strongly correlated with PM_{10} or sulfates than they were in our study ($r = 0.74$ with sulfates in the summer camp study[20] *vs* 0.35). In our pilot study,[15] we reported associations between asthma symptoms and both PM_{10} and O_3. In that study, the O_3 concentrations were 33% higher (1-hour average of 8 pphm *vs* 6 pphm for the current study in Los Angeles, where most of the cohort resided) and more strongly correlated with PM_{10} (0.50 in the pilot *vs* 0.35 in the current study). Although we did not detect O_3-symptom relationships in the current study, we did identify associations with extra medication use, another measure of asthma exacerbation.

In general, lags of 2 or 3 days of PM_{10} exposure were more strongly associated with asthma symptoms than were contemporaneous exposures. Similar findings for asthmatics were reported by Pope and Dockery[7] and Gielen *et al*.[19] The delayed manifestation of symptoms suggests that pollutant-induced inflammation may have played a role in these relations. That O_3 appeared to have had a lesser impact on respiratory symptoms than PM_{10} may reflect in part the attenuation of response that occurs with repeated O_3 exposure in some asthmatics as well as in nonasthmatics.[21]

We also examined relations between fine particles and these outcomes, although this analysis was limited by the number of sampling days and by differences in instrumentation for PM_{10} and $PM_{2.5}$. Bearing these limitations in mind, $PM_{2.5}$ was found to be associated with shortness of breath and wheeze, and with the onset of episodes of shortness of breath, wheeze, and cough. Evaluated over the IQR, the effects of $PM_{2.5}$ appeared to be of lesser magnitude than those of PM_{10}.

We further stratified the study population in an attempt to determine the existence of different susceptibilities to PM_{10} and molds based on asthma severity, household income, gender, residential location, and use of anti-inflammatory medication. Children with moderate to severe asthma demonstrated a greater response to *Alternaria* but not to PM_{10}. Subgroups among whom we observed stronger associations between ambient PM_{10} and symptoms included Pasadena residents and girls from both geographic areas. While there was little differential impact of PM_{10} based on use of anti-inflammatory medication, *Alternaria* concentrations were more strongly related to several symptoms among children taking anti-inflammatory medications at baseline. This finding suggests that the members of this subgroup may have been sensitized against *Alternaria*, that they may not have been consistently taking their prescribed medications, or that their asthma severity may have rendered them more susceptible to the effects of *Alternaria* exposure despite their medical regimens.

Alternaria and *Cladosporium* spore counts were associated with several measures of asthma exacerbation. Little association was found, however, between total pollens and either daily symptoms or the onset of episodes. The literature relating airborne mold concentrations with effects in asthmatics is sparse. Nevertheless, the inflammatory and immunological responses to inhaled mold spores that have been linked with early and late asthmatic reactions are similar to those induced by other aeroallergens.[22] In our data, total mold spore counts were dominated by *Cladosporium*, while *Alternaria* counts were often much lower. As the Roto-Rod device used in this study tends to be reasonably accurate for pollen counts but generally undercounts mold spores, it is possible that the odds ratios reported here for *Alternaria* or *Cladosporium* may be systematically overestimated. Although *Al-*

ternaria is not generally found at high concentrations in ambient air, sensitization to this mold and to *Cladosporium* is common in asthmatic children.[22] Other reports have linked episodes of respiratory arrest with *Alternaria alternata*, and asthma mortality with total airborne mold counts.[23,24] In recent studies, Delfino *et al* reported associations between outdoor fungal spores and asthma symptoms, peak flow, and medication use.[17,25] As in the present study, Delfino *et al* found that total mold spore counts were dominated by *Cladosporium*.[17] The same studies did not find an association between asthma-related outcomes and pollen counts, which were at low concentrations.

In general, the impact of air pollution on this population of African-American children with asthma in Los Angeles may be clinically meaningful. For an interquartile change in PM_{10} (17 $\mu g/m^3$), there were 14 and 10% increases, respectively, in the likelihood of daily shortness of breath and cough. In our pilot study, a similar change in PM_{10} was associated with a 15% change in the daily occurrence of shortness of breath.[15] In the present study, an interquartile increase in PM_{10} was also associated with increases in the probability of new episodes of shortness of breath, wheeze, and cough of approximately 20, 12, and 25%, respectively.

The symptom increases observed in this sample of African-American children were larger than those reported in most other studies of asthmatics. It is not clear, however, whether this difference may be due to some inherent susceptibility or simply to differences in study design. Based on a change in PM_{10} (24-hour average) of 10 $\mu g/m^3$, our results suggest a 7 to 18% increase in the onset of asthma symptoms. In studies of lower respiratory symptoms among children diagnosed with asthma, a 10-$\mu g/m^3$ change in PM_{10} was associated with a 4 to 5% increase among cohorts in Utah and Holland.[7,26,27] Studies of emergency room visits and hospital admissions for asthma suggest a 2 to 6% increase in relative risk per 10 $\mu g/m^3$.[10,14,28]

Previous studies have reported associations between PM_{10} and extra medication use in asthmatic children.[5,7] We were unable to reproduce this result after careful consideration of what would constitute *extra* medication for each individual in the study. It is possible, however, that any association may have been obscured by measurement error, as some subjects may have had difficulty recognizing exactly what constituted extra medication. Some evidence for this may be provided by the low correlation between the use of extra medication and symptom reporting. Nevertheless, among children in Los Angeles we did detect associations between extra medication use and O_3 concentrations, as noted above.

We also hypothesized that families who had less information about asthma management or who typically did not consult a physician for their children's asthma outside of the acute care or emergency room setting would be more responsive to air pollution and bioaerosols. When we stratified by these factors, there was little evidence of an association. This result may have been affected by the small numbers within subgroups, the imprecise allocation of the individuals into the groups based on their response to our intake questionnaire, or by a true lack of an association for these subgroups. We also hypothesized that there might be different responsiveness to pollution and bioaerosols among families based on their knowledge about their child's asthma or asthma in general. Although an occasional association was found, no consistent pattern emerged. While there may indeed have been no relation, these results may also have been due to misclassification of the families' asthma knowledge, or to confounding due to correlations between behaviors and asthma knowledge. For example, more severe asthmatics could be expected to have received an asthma management plan or information about their asthma triggers and would also be more likely to use anti-inflammatory medications.

Medication compliance and peak flow meter usage increased during the study. If children were more aware of their symptoms and medication use during the 3 months of study, particularly with respect to the routine administration of inhaled corticosteroids or cromolyn sodium among those with moderate and severe asthma, then the overall morbidity associated with their asthma may well have been reduced during that time. Examination of the proportions of the sample who reported respiratory symptoms on a given day showed inverse, but nonmonotonic, associations with day of the study, thereby providing circumstantial evidence of a Hawthorne effect. Consequently, the actual relations between air pollution and asthma exacerbation may be greater than those observed in our study.

Most previous panel studies of asthmatics have either involved adults or children living in suburban or middle-class environments.[7,8,26] The summer camp study of Thurston *et al*[20] included whites and non-whites, but no stratified analysis was presented. Our study is among the first panel designs to focus on the impact of air pollution on inner-city African-American children, and it indicates that particulate matter air pollution is associated with several measures of asthma exacerbation. The magnitudes of the effects observed in the present study relative to those reported in other panels suggests the possibility of enhanced susceptibility to particulate matter toxicity in this population.

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