
Relationship of outdoor air quality to pediatric asthma exacerbations

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Background: Although exposure to outdoor air pollutants has been shown to be associated with exacerbations of asthma, there are relatively few admissions for asthma to Cincinnati Children's Hospital, Cincinnati, OH during the summer months when air quality tends to be worst.

Objective: The objective of this study was to determine the relationship of outdoor air quality parameters to asthma exacerbations in children.

Methods: The number of emergency room visits and hospitalizations for asthma were determined by review of emergency department logs and the hospital computer database. Outdoor air concentrations of ozone, particulates of $<10\ \mu\text{m}$ diameter (PM-10), pollens, and fungal spores were obtained from the Hamilton County Department of Environmental Services. Multiple regression analysis was performed, looking for relationships between the daily number of asthma visits and the air quality data for the same day and for 1 through 5 days before the visits.

Results: A significant association was found between the number of asthma visits and the daily pollen count ($P = 0.014$, $SE = 0.001$). The effect was stronger for visits 1, 2, and 3 days after the pollen count ($P < 0.001$ for pollen count lagged 3 days). High PM-10 counts were synergistic with the pollen count as a predictor of asthma visits. There was no association between asthma visits and the ozone concentration or fungal spore count.

Conclusions: Exacerbations of asthma severe enough to require visits to the hospital were associated with elevated concentrations of airborne pollens and particulates, with a significant delayed effect. Ozone, in the concentrations measured here, was not a risk factor for severe asthma exacerbations in children.

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INTRODUCTION

Airborne pollutants such as ozone and small particulates have been shown to have detrimental effects on respiratory health. Prolonged exposure of healthy individuals to ozone during exercise can cause decreases in lung function, a neutrophilic infiltrate of the airway submucosa, and symptoms of chest discomfort and cough.¹ In asthmatic patients, experimental inhalation of ozone in concentrations between 0.2 and 0.4 parts per million (ppm) causes increases in airway resistance and airway hyperresponsiveness.^{2–4} Several studies have shown increased rates of emergency room visits and hospitalizations for respiratory illness during periods of elevated ozone concentration.^{5–7} Increased concentrations of airborne particulates $<10\ \mu\text{m}$ diameter (PM-10) have been found to be related to increases in respiratory symptoms⁸ and transiently decreased pulmonary function^{9,10} in normal children. Increases in hospitalizations for respiratory illness^{11,12} and in medication usage by patients with asthma^{13,14} have also been correlated with elevations in the ambient PM-10 concentration.

In 1998, the Environmental Protection Agency proposed a revision of the national ambient air quality standards for ozone which would lower the allowable ozone concentration

from a 1-hour maximum of 0.12 ppm to an 8-hour concentration of 0.08 ppm. Although our area had only occasionally exceeded the existing air quality standards for ozone, under the proposed new standards we would frequently exceed them. Ambient ozone concentrations are highest during the summer months, as ozone is formed by the reaction of sunlight with nitrogen oxides and volatile organic compounds. In the Cincinnati, OH area, greater accumulations of airborne particulates also tend to occur during the summer and early fall months, because of weather patterns including air inversions over the Ohio River valley. However, the number of pediatric hospitalizations and emergency room visits at Cincinnati Children's Hospital for acute asthma episodes is consistently lowest during the summer months. This led us to wonder whether exposure to ozone, particulates, or airborne allergens in the concentrations measured in downtown Cincinnati leads to asthma exacerbations severe enough to require hospital treatment.

The goal of this study was to examine the relationship between the daily number of hospital visits for treatment of acute pediatric asthma attacks and air quality parameters including ozone, PM-10, pollen counts, and fungal spore counts.

METHODS

The setting for the study was Cincinnati Children's Hospital, which provides virtually all the emergency room and inpatient care for pediatric asthma patients residing in the urban Cincinnati area, as well as the majority of inpatient asthma care for children living in the surrounding suburban and rural

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areas. An "asthma visit" was defined as either an emergency room visit or an inpatient hospitalization for treatment of acute asthma. The number of asthma hospital admissions per day was obtained by means of a hospital computer search for all admissions with a primary diagnosis code of 493.91 (status asthmaticus). Because the diagnostic coding for emergency room visits was not well standardized, the handwritten emergency room daily logbooks were reviewed, and patients given a diagnosis of asthma or reactive airway disease were counted as asthma visits. The emergency room and hospital data were cross-referenced to ensure that a patient initially seen in the emergency room and then admitted to the hospital for further treatment would be counted as only one visit. The number of emergency room visits and hospital admissions for asthma were then added, and this number was recorded as the number of asthma visits per day.

Air quality data were obtained from the Hamilton County Environmental Services for the most centrally located Cincinnati monitoring station. This is the only air quality monitoring station in the area that also performs pollen and fungal spore counts. Ozone concentrations were continuously monitored, and data were provided as the daily average, as well as the highest 1-hour average concentration for each day (ozone max). PM-10 counts were obtained using a volumetric air sampler with a size-selective inlet (GMW-1200, General Metal Works, Cleves, OH) and data were provided as the 24-hour average. The pollen and fungal counts were obtained using a Rotorod sampler (Sampling Technologies, St. Louis Park, MN), located on the unobstructed rooftop of a four-story building in an urban neighborhood. Some of the surrounding streets are lined with sycamore trees or ornamental fruit trees; there are several small grassy areas but no open fields or weedy lots nearby. The Rotorod sampling arms were coated with silicone grease and rotated at 2,400 rpm. Intermittent sampling was performed for 1 minute of every 10, so the sample time was 144 minutes per 24 hours and the volume of air sampled was 3.12 cubic meters. The samples were stained with Calberla solution and the pollen counts were obtained by counting the pollen grains on the entire collecting surface at $\times 400$ magnification. Spores were counted at $\times 400$ magnification on a horizontal strip along the long axis of the sampling surface. The count for this strip was multiplied by the width of the collecting surface $\div$ the diameter of the high power field, to obtain an estimate of the total spore count of the sample. The concentration of the pollen

and spores in particles per cubic meter of air was calculated as (particles per sample) $\div$ 3.12 cubic meters, to give the number of particles per cubic meter. Rotorod samples were collected over a 24-hour period, ending at 10 AM. Thus the pollen and spore counts reported on a given day were collected during the preceding day and night, and the morning of the report day. The pollen, spore and ozone counts are obtained only for the months of April through October, so this study included the months of April through October of 1996 and 1997. The emergency room log for the month of August 1996 was lost, therefore this month was excluded from the study.

Data Analysis

The objective of the data analysis was to identify factors that are related to changes in the number of daily asthma visits. To obtain a clearer picture of the nature of both the asthma visit data and the various environmental exposure measures, descriptive statistics were computed. To examine seasonal variation in exposure data, monthly means were plotted (Table 1), averaged over the 7 months during which data were collected.

After preliminary analyses were completed, multiple regression models were developed to examine all potential exposure measures as predictors of the number of daily asthma visits.

The independent variables considered in the multiple regression model included pollen counts, fungal counts, particulates $<10 \mu\text{m}$ (PM-10) provided as a daily average, and ozone concentrations as a daily average and as a maximum during each day. Variables were allowed to enter the model both in a stepwise fashion and also by examining specific combinations of variables thought to have a potential impact on asthma conditions.

We used Poisson regression to model the daily number of asthma visits as a function of air quality data and temporal variables. This method is appropriate for counts of relatively rare events occurring randomly over time. Poisson regression assumes that, after removing the effects of any explanatory variables, the counts follow a Poisson distribution as opposed to a normal distribution as required in ordinary least squares regression.

An additional complexity encountered when modeling events occurring over time is serial correlation of the outcome variable, ie, the daily counts may be nonindependent, even after conditioning on the important explanatory variables. To account for serial correlation, we used a generalized estimating equation approach¹⁵ with an autocorrelation structure for

Table 1. Monthly Means ($\pm$ Standard Deviation)

Variable	April	May	June	July	August	September	October
ER visits/day	9.3 (3.6)	12.3 (5.1)	9.6 (4.3)	5.5 (2.7)	11.0 (5.4)	16.8 (7.9)	17.2 (4.6)
Pollen (grains/m ³)	86.3 (148.2)	189.3 (217.6)	42.7 (51.6)	8.7 (6.4)	54.1 (73.0)	66.8 (55.1)	8.1 (7.2)
Fungal (spores/m ³)	319.2 (291.4)	1251.1 (1169.0)	2408.1 (1321.3)	3206.4 (1611.3)	3161.4 (1504.2)	3157.1 (1492.8)	1978.2 (1627.0)
Ozone (ppm)	0.025 (0.007)	0.026 (0.009)	0.028 (0.011)	0.033 (0.008)	0.028 (0.009)	0.020 (0.007)	0.014 (0.008)
Ozone (max)	0.045 (0.009)	0.049 (0.014)	0.060 (0.023)	0.068 (0.018)	0.061 (0.017)	0.046 (0.017)	0.035 (0.016)
PM-10 (daily) ($\mu\text{g}/\text{m}^3$)	29.1 (8.1)	28.8 (8.2)	35.1 (10.0)	36.9 (11.2)	42.2 (13.5)	36.7 (12.0)	33.0 (12.5)

ER, emergency room; PM-10, particulate matter $<10 \mu\text{m}$.

Table 2. Poisson Regression Models: Relative Risks (Rate Ratios) for Asthma Visits Associated with Pollen Counts, Season, and Particulates

	Variable	Rate ratio	P value	95% Confidence limits
Model 1	ln (pollen) 3 day lag	1.089†	0.004	1.027–1.155
	April	1.44	0.002	1.19–1.75
	May	1.74	<0.001	1.38–2.19
	June	1.45	<0.001	1.20–1.74
	July*	1.00	–	–
	August	1.83	<0.001	1.39–2.41
	September	2.42	<0.001	1.86–3.24
	October	3.06	<0.001	2.55–3.56
Model 2	ln (pollen) 3 day lag	1.090†	0.001	1.036–1.147
	Fall vs spring & summer	1.84	<0.001	1.57–2.15
Model 3	ln (pollen) spring & summer	1.145†	<0.001	1.076–1.217
	ln (pollen) fall	0.960†	0.898	0.658–1.404
	Fall vs spring & summer	3.35	<0.001	2.46–4.55
	Particulates (>33 vs 0–33)	0.824	0.165	0.627–1.083
	ln (pollen) particulates >33	1.251†	<0.001	1.153–1.358
	ln (pollen) particulates <33	1.145†	<0.001	1.076–1.217

* Used as referent month.

† Increase (decrease) in rate ratio per unit increase in ln (pollen).

the variance-covariance matrix similar to analyses reported in Schwartz et al.¹⁶ The autocorrection structure appeared to have a periodicity of approximately 1 week; therefore, the autoregressive structure was set up in clusters of 7-day intervals. Overdispersion (greater than Poisson variation) was handled by scaling standard errors up by the magnitude of the overdispersion factor.¹⁷

As the effects of poor air quality may not always result in an immediate asthma visit, we lagged all air quality measures from zero to 5 days before the asthma visit date to account for any delayed visit effects. We also recognized a possible seasonal trend in asthma visits. Accordingly, we stratified the analysis by season to address changes in asthma attacks because of weather conditions or temporal patterns in infectious diseases.

RESULTS

Table 1 provides the means and standard deviations for the variables examined in the regression models on a monthly basis averaged more than 1996 and 1997. Examination of the table shows seasonal trends for emergency room visits, pollen counts, and ozone concentrations.

A series of Poisson regression models was run to identify predictors of changes in the number of asthma visits. Initial results indicated that the log of pollen counts and month of the year (April to October) were significant predictors of the number of daily asthma visits. The number of asthma visits per day was associated with the pollen count reported for the same day ($P = 0.014$), but the effect became increasingly strong for the pollen counts recorded for 1, 2 and 3 days before the visit. Thus the log of pollen count, lagged 3 days, was the most significant predictor of asthma visits and was used in the regression models. Fungal spore counts were not a significant predictor of asthma visits, either on the same day nor lagged 1 to 3 days.

The average ozone concentration was also a significant predictor but with an inverse relationship, ie, the higher ozone levels predicted lower numbers of asthma visits. However, when month of the year was added to the model, the effect of ozone was no longer a significant factor. Because the ozone effect was inversely related to asthma visits and obviously highly correlated with season, this term was dropped from the model.

After this model was developed, we decided to examine a model stratified by season of the year (spring, summer, and fall). This model indicated a highly significant effect attributed to season with the primary differences attributable to fall versus summer and spring.

After identifying the two most important main effects, we examined effect modification by introducing interaction terms involving pollen counts, season, and other air pollution measures. We found significant interactions between season and pollen count and between pollen count and measured particulate level. Specifically, the exposure-response between asthma visits and log of pollen (lagged 3 days) was very strong in spring and summer. In the fall, both asthma visits and pollen counts were high so there was a significant general correlation, but the day-to-day variations in pollen count did not account for the variations in daily asthma visits the way it did in the other seasons.

We divided continuous measure of particulate levels at the median ($33 \mu\text{g}/\text{m}^3$) and fit separate exposure response curves to high and low levels of particulates. This analysis indicated a synergistic effect between the two air pollutants, ie, the exposure-response for pollen was moderately high for days when particulate levels were low, but significantly higher still for days when particulate levels were higher than 33 units (Fig 1).

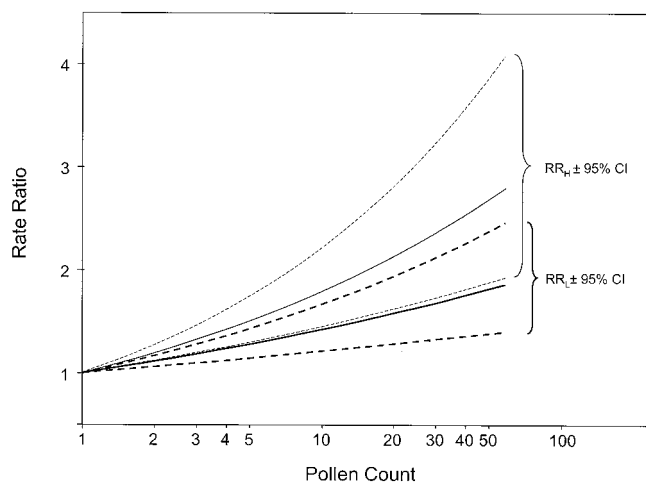


Figure 1. Asthma visit rates as a function of pollen counts, relative to asthma visit rates at low pollen counts; estimated separately for low particulate concentrations ($\text{PM}_{10} < 33 \mu\text{g}/\text{m}^3$; RR_L) and high particulate concentrations ($\text{PM}_{10} > 33 \mu\text{g}/\text{m}^3$; RR_H).

DISCUSSION

This study shows a strong association between acute asthma exacerbations and airborne concentrations of pollens and small particulates. This association does not necessarily reflect a cause and effect relationship. It is possible that coexisting factors such as respiratory infections or other air pollutants are primarily responsible for the asthma attacks. However, there is considerable supportive evidence for the roles of pollens and particulates as exacerbators of allergic disease. Other investigators^{18,19} have demonstrated an association between particulate exposure and emergency room or hospital visits, and several studies^{20–24} have shown correlation of asthma symptoms with pollen counts. Some studies^{22–25} showed a lag effect between pollen counts and allergy symptoms, similar to our findings. The potential interaction between pollen and pollutant exposure has been a source of interest. It has been suggested, based on epidemiologic and air pollution data, that exposure to modern industrial air pollutants is responsible for the increase in allergic disease seen in west Germans versus east Germans,²⁶ and in Inuits who have moved to urban areas compared with those who stay in a rural setting.²⁷ Our study demonstrates the additive clinical effects of elevated pollen and particulate concentrations. Several mechanisms have been proposed to explain this interaction. Although exposure to airborne particles, SO_2 ,²⁸ and ozone²⁹ cause increased release of allergen from grass pollens, allergen release from birch tree pollen was not affected by exposure to heavy metal particles and SO_2 .³⁰ The synergistic effect might be partially related to the binding of pollen allergens to diesel exhaust particles,³¹ which could increase delivery of allergens to the lower respiratory tract. Diesel exhaust particles have also been shown to increase eosinophil adhesion to human nasal epithelial cells and enhance eosinophil degranulation.³² If these proinflammatory

effects also occur in the bronchial mucosa, they could contribute to increased severity of asthma symptoms. Several studies have demonstrated a synergistic interaction between particulate and pollen exposures in enhancing airway immunoglobulin (Ig)E and cytokine production.^{33–35} Diesel exhaust particles contain polyaromatic hydrocarbons which diffuse into cells, bind to cytosolic receptors, and alter ongoing transcriptional programs, enhancing the production of allergen-specific IgE as well as various cytokines.³⁶

Diaz-Sanchez et al³³ performed nasal challenges with ragweed allergen alone, versus ragweed plus diesel exhaust particles, in ragweed-allergic individuals. The concentration of ragweed-specific IgE in the nasal lavage fluid was significantly higher after the combined (ragweed plus diesel exhaust particles) challenge: there was a fourfold difference 1 day postchallenge, and a 16-fold difference 4 days postchallenge. These findings may in part explain the lag effect noted in the present study, with increasingly stronger correlations of asthma visits with pollen and PM_{10} levels measured from 1 to 4 days before the visit. In addition to the effect on enhanced IgE production, the lag effect may also be related to late-phase inflammatory reactions in the bronchial mucosa, leading to increasing symptoms and airway hyperreactivity over the several days after allergen and irritant exposure.

The inflammatory response of the nose and lungs to allergens can also be upregulated by preceding exposure to ozone.^{37–39} Our study, however, found no significant positive association between asthma visits and any combination of ozone concentration with pollen or fungal counts or particulates. To the contrary, a strong negative correlation was found between asthma visits and ozone concentrations. Other studies^{40,41} have noted similar inverse correlations between acute asthma visits and ambient ozone concentrations. During the summer months when ozone levels are highest, acute asthma attacks are relatively rare, presumably because of other factors such as low community rates of respiratory infections and relatively low pollen counts. Day-to-day analysis within this time frame showed no increase in asthma visits on the days of higher ozone counts, nor for the 3 subsequent days. One can conclude from these results that ozone concentrations, in the moderate levels measured during this study, are not associated with pediatric asthma attacks severe enough to require hospital treatment. Similar findings were reported by White et al,⁷ who found that although peak ozone concentrations greater than 0.11 ppm correlated with asthma visits to emergency rooms, there was no such correlation at peak ozone concentrations below 0.11, which was the highest concentration recorded during our study.

The fact that a model including stratification by month provided the best fit for the data are probably related to seasonal changes in the incidence of infectious diseases as well as possibly other air pollutants not measured in this study. Jamason et al⁴² examined the relationship of various weather patterns, air pollutants, and pollen counts to hospitalization rates for asthma. They found a strong association between asthma admissions and the higher concentrations of

various pollutants during the spring and summer months, but not during the fall and winter. During the fall and winter seasons, they found that certain weather patterns correlated with increased rates of asthma admissions, whereas this was less evident in the spring and summer. Similarly, our study showed a strong association of asthma admissions with pollen counts in the spring and summer but not in the fall, although both pollen counts and asthma admissions were high in the fall. It is possible that weather variables and the high incidence of respiratory infections triggering asthma attacks during the fall and winter obscure the effect of the airborne precipitants during these seasons. It is also possible that the method of sample collection affected the results. As only a single rooftop Rotorod was the source of the pollen counts for the study, the pollen counts give only a rough approximation of the actual pollen exposure of individuals on the ground level. It is possible that the fall weed pollens are more variable in their regional concentrations than the tree pollens, which are more thoroughly dispersed because of their higher altitude and the grass pollens, which are more ubiquitous.

In this study, fungal spore concentrations were not found to correlate with asthma visits. However, the Rotorod is not the optimal method for measuring airborne spores, as the smaller spores tend to flow around the rod rather than impacting on it. Because only total spore counts are available, this study also does not rule out the possibility that high concentrations of individual allergenic fungal species could be associated with asthma exacerbations, as has been suggested for *Alternaria*.⁴³

CONCLUSION

Ambient concentrations of pollens and small particulates are strongly associated with emergency visits for pediatric asthma in Cincinnati. The concentrations of ozone in the Cincinnati environment are moderate and are not associated with pediatric asthma exacerbations.

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