

Air Pollution and Bronchitic Symptoms in Southern California Children with Asthma

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The association of air pollution with the prevalence of chronic lower respiratory tract symptoms among children with a history of asthma or related symptoms was examined in a cross-sectional study. Parents of a total of 3,676 fourth, seventh, and tenth graders from classrooms in 12 communities in Southern California completed questionnaires that characterized the children's histories of respiratory illness and associated risk factors. The prevalences of bronchitis, chronic phlegm, and chronic cough were investigated among children with a history of asthma, wheeze without diagnosed asthma, and neither wheeze nor asthma. Average ambient annual exposure to ozone, particulate matter (PM₁₀ and PM_{2.5}; $\leq 10 \mu\text{m}$ and $< 2.5 \mu\text{m}$ in aerodynamic diameter, respectively), acid vapor, and nitrogen dioxide (NO₂) was estimated from monitoring stations in each community. Positive associations between air pollution and bronchitis and phlegm were observed only among children with asthma. As PM₁₀ increased across communities, there was a corresponding increase in the risk per interquartile range of bronchitis [odds ratio (OR) 1.4/19 $\mu\text{g}/\text{m}^3$; 95% confidence interval (CI), 1.1–1.8]. Increased prevalence of phlegm was significantly associated with increasing exposure to all ambient pollutants except ozone. The strongest association was for NO₂, based on relative risk per interquartile range in the 12 communities (OR 2.7/24 ppb; CI, 1.4–5.3). The results suggest that children with a prior diagnosis of asthma are more likely to develop persistent lower respiratory tract symptoms when exposed to air pollution in Southern California. **Key words:** air pollution, asthma, bronchitis, children, respiratory tract. *Environ Health Perspect* 107:757–760 (1999). [Online 5 August 1999] <http://ehpnet1.niehs.nih.gov/docs/1999/107p757-760mcconnell/abstract.html>

The role of air pollution in the exacerbation of existing asthma has been studied and debated (1–3). In ecologic studies, the concentration of ambient particulate matter with aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀), primarily in combination with high sulfur dioxide (SO₂) and sulfate particulate matter, has been associated with increased hospitalization for asthma (4). As air pollutants, especially ozone, increase, emergency room visits for asthma increase, acute symptoms and medication use among asthmatic patients increase, and peak expiratory flow rate decreases (5–8).

There has been little population-based research examining the role of air pollution in causing bronchitis and associated chronic respiratory symptoms—cough and phlegm—in children with asthma or wheeze. One study showed an increase in prevalence of bronchitis associated with particulate pollution among children who had a history of wheezing or asthma (9). The results did not distinguish the effect of pollution in children with asthma from the effect in children who had a history of wheezing but not a diagnosis of asthma, differences that could be important in identifying the most susceptible populations for public health interventions and for further study.

The Children's Health Study is a population-based investigation of respiratory health in school children from 12 communities in Southern California with different mixes of air pollutants (10). We evaluated the effect of ambient pollutants on the prevalence of bronchitis, chronic cough, and phlegm among potentially sensitive children in this study; children were divided into three groups, based on a history of asthma, a history of wheezing but no asthma, and no history of either asthma or wheeze. Historic exposures in Southern California to ambient ozone (O₃), PM₁₀, and nitrogen dioxide (NO₂) have been among the highest in the United States (2,3), making this an ideal region for evaluating health effects. In addition, the mix of pollutants offers the opportunity to examine the impact of high particulate exposure on respiratory morbidity in the absence of the high ambient concentrations of SO₂ and SO₂-derived particulate sulfates characteristic of air pollution in the eastern United States.

Methods

The quasi-factorial, cross-sectional study design, health outcome evaluation, and exposure assessment have been described previously

(10). Briefly, a total of 3,676 children participated (approximately 150 fourth graders, 75 seventh graders, and 75 tenth graders in each of 12 primarily suburban communities). These children were from primarily middle class public school classrooms selected based on historical measurements of air quality, demographic similarities, and a cooperative school district. In early 1993, a parent of each study subject provided written informed consent and completed a written questionnaire that characterized the child's history of respiratory illness and its associated risk factors. Principal outcomes of interest included *a*) one or more episodes of bronchitis (defined by the question "How many times in the past 12 months did your child have bronchitis?") and the following symptoms associated with bronchitis; *b*) chronic cough (defined by a "yes" answer to the question "During the past 12 months, has this child had a cough first thing in the morning that lasted for as long as 3

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months in a row?" or to the question "During the past 12 months, has this child had a cough at other times of the day that lasted for as much as 3 months in a row?"; c) chronic phlegm (defined by a "yes" answer to the question "Other than with colds, does this child usually seem congested in the chest or bring up phlegm?").

The association of air pollution with these symptoms was examined in children with a) asthma (defined by a "yes" answer to the question "Has a doctor ever diagnosed this child as having asthma?"); b) wheeze (defined by a "yes" answer to the question "Has your child's chest ever sounded wheezy or whistling, including times when he or she had a cold?"), exclusive of those children with asthma; and c) no history of asthma or of wheezing.

Children with questionnaire responses of "don't know" to asthma or wheeze or with missing values were excluded from the analysis, leaving 493 children with asthma, 653 with wheeze, and 2,211 with neither. The 12 communities were systematically selected to maximize the range of exposures and to obtain a variety of profiles of mixes of criteria air pollutants measured in Southern California (10). Using 1994 data from air monitoring instruments installed for the study, ambient exposure was estimated in each of the 12 communities for yearly average daily maximum 1-hr ozone concentration (mean 65.6 ppb; range 35.5–97.5 ppb), average 24-hr NO₂ concentration (mean 21.9 ppb; range 2.7–42.6 ppb), average 24-hr PM₁₀ concentrations (mean 34.8 µg/m³; range 13.0–70.7 µg/m³), yearly mean 2-week averaged particulate matter < 2.5 µm in aerodynamic diameter (PM_{2.5}; mean 15.3 µg/m³; range 6.7–31.5 µg/m³), and yearly mean 2-week averaged gaseous acid (nitric and hydrochloric; mean 2.9 ppb; range 1.0–5.0 ppb). Exposures to particulate air pollution, NO₂, and acid were highly correlated (Table 1). In addition, we estimated exposure to ozone and NO₂ for 1992 (the year before the collection of symptom prevalence information) from data collected by the nearest station of the State of California South Coast Air Quality Monitoring District.

Analysis. The relationships between air pollution and the prevalence of bronchitis

and phlegm were examined in each subgroup (children with asthma, wheeze only, and neither wheeze nor asthma) by using a two-stage modeling strategy that has been described in detail (10). Briefly, a logistic regression model was fitted in the first stage for a symptom within each subgroup as a function of community-specific intercepts, α_j , where $j = 1, \dots, 12$, and personal covariates (age, sex, race, school grade, and membership in a health insurance plan). The adjusted community-specific intercepts and prevalence rates are related by $P_j = e^{\alpha_j} / (1 + e^{\alpha_j})$. In the second stage, these intercept terms representing the logit of the community-specific prevalence rates (P_j , $j = 1, \dots, 12$), adjusted for personal covariates, were regressed on each community-specific ambient pollutant level by using a simple linear "ecologic" regression, i.e., $\text{logit } \alpha_j = \alpha + \beta Z_j$, where Z_j denotes the ambient pollution level for community j . Thus, β can be interpreted as the log odds ratio (per interquartile change) for each pollutant, adjusted for personal characteristics. The results from the models are presented as odds ratios (ORs), along with their 95% confidence intervals (CIs). Pictorial depiction of the results are presented using the prevalence scale for ease of interpretation. Additional potential confounders reported on the questionnaire and also considered included mildew, gas stove use or cockroaches in the child's home, current passive exposure to tobacco smoke (anyone who lived and regularly smoked inside the home), carpet in the child's bedroom, one or more pets, low

parent or guardian education (grade 12 or less), and a large household (more than 2 children under 18 years of age in the home). A 10% or greater change in β , due to addition of any one of these variables, was used as a criterion for confounding.

Results

Compared to children with a history of neither wheezing nor asthma, children with wheeze and children with asthma were much more likely to have bronchitis or related symptoms (Table 2). Children with asthma also were more likely to be boys, to have health insurance, and to report mildew or pets in the home, and were less likely to have parents with low educational achievement.

For children with asthma, all pollutants except ozone were positively associated with the risk of bronchitis, although the association was strongest for particulate pollutants (OR = 1.4 per interquartile range for both particle indices) and was statistically significant for PM₁₀ (Table 3). There was a strong positive association between phlegm and ambient particulates and NO₂, and a slightly weaker, but also significant, association with acid pollutants. There was a modest positive, but not significant, association between cough and PM_{2.5}, NO₂, and acid. There was no association between air pollution and prevalence of bronchitis or associated symptoms among children with a history of wheezing (without asthma). Among children with neither wheeze nor asthma, there was a weak inverse association between bronchitis

Table 2. Distribution of bronchitic symptoms, demographic and other characteristics by history of wheeze and asthma.

	Asthma ^a (n = 493)	Wheeze ^a (n = 653)	No wheeze/no asthma ^a (n = 2,211)
Outcomes			
Bronchitis	154 (32.6)	147 (23.3)	117 (5.4)
Phlegm	122 (25.7)	86 (13.8)	93 (4.4)
Cough	83 (16.9)	63 (9.8)	84 (3.9)
Boys	276 (56.0)	305 (46.7)	1,023 (46.3)
Race/ethnicity			
White	324 (68.5)	428 (72.3)	1,336 (64.9)
Black	32 (6.8)	18 (3.0)	108 (5.3)
Asian	17 (3.6)	13 (2.2)	116 (5.6)
Other	88 (18.6)	127 (21.5)	478 (23.2)
Grade			
Fourth	229 (46.6)	335 (51.3)	1,102 (49.8)
Seventh	130 (26.4)	161 (24.7)	580 (26.2)
Tenth	134 (27.2)	157 (24.0)	529 (23.9)
Insurance	435 (90.4)	555 (87.7)	1,766 (82.3)
Low parental education	147 (30.1)	212 (33.0)	806 (37.8)
Age (mean ± SD)	12.4 ± 2.5	12.2 ± 2.5	12.3 ± 2.5
Large household	201 (41.4)	273 (42.6)	988 (45.7)
Bedroom carpet	408 (87.4)	552 (89.6)	1,839 (88.4)
Mildew	177 (37.1)	239 (38.2)	544 (25.9)
Cockroaches	47 (9.5)	75 (11.5)	242 (11.0)
Pets	403 (81.7)	540 (82.7)	1,666 (75.4)
Gas stove	392 (80.0)	522 (81.3)	1,718 (79.2)
Passive smoke	124 (25.7)	157 (24.5)	427 (19.7)

SD, standard deviation. Values shown are number (percent) except where indicated.

^aBased on number responding positively for each variable/total number; variations in total number are due to missing values and "don't know" answers.

Table 1. Correlations of pollutants across 12 communities.

	PM ₁₀	NO ₂	Ozone	Acid	PM _{2.5}
PM ₁₀	1.00				
NO ₂	0.74*	1.00			
Ozone	0.32	0.33	1.00		
Acid	0.54	0.83*	0.69*	1.00	
PM _{2.5}	0.90*	0.83*	0.50	0.71*	1.00

Abbreviations: NO₂, nitrogen dioxide; PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; PM₁₀, particulate matter ≤ 10 µm in aerodynamic diameter.

* $p < 0.01$.

and pollution, which was marginally significant for particulate pollutants.

The strongest associations observed, between PM_{10} exposure and bronchitis and between NO_2 exposure and phlegm in the 12 communities, are presented in Figures 1 and 2 for children with asthma (and for comparison for children with neither asthma nor wheeze). For ease of interpretation, the figures are plotted using prevalence rates. Throughout the range of exposure to PM_{10} and NO_2 across the 12 communities, there was increasing prevalence of bronchitis ($R^2 = 0.44$; $p = 0.02$) and phlegm ($R^2 = 0.54$; $p = 0.006$), respectively. Valid estimates of community-specific pollutant concentrations were available only for NO_2 (11 of 12 communities) and for ozone from existing air monitoring stations for 1992 (the full year most closely corresponding to the reported symptoms). Mean exposure estimates and interquartile ranges for both pollutants and the rank order of communities were very similar to those for 1994, which were used in the results presented above. The associations among children with asthma between these pollutants and bronchitic symptoms were also similar for both years.

There was a small increase in the association of all pollutants with phlegm after adjusting for reported mildew in the houses of children with asthma. Otherwise, the observed pattern of associations among asthmatic children did not change substantially after adjusting for additional potential confounding variables. The risk of chronic phlegm among girls was more than double

the risk for boys for particulates, NO_2 , and acid, but this difference between sexes was not statistically significant. Similar effect modification by sex was not observed for bronchitis and could not be evaluated for chronic cough because there were too few children reporting chronic cough to determine a maximum likelihood estimate in the first stage model.

Discussion

Among children with asthma in this study, increased particulate air pollution was associated with significantly increased prevalence of chronic phlegm production and with bronchitis. There also was a strong association of NO_2 and gaseous acid with increased phlegm prevalence and a modest and nonsignificant association of NO_2 with increased prevalence of bronchitis. No significant associations were found between air pollution and chronic cough, but power to assess this relationship was limited by the small number of children with cough. The increased prevalence of bronchitis observed among children with asthma is consistent with the known overlap between the two conditions (11,12). In the context of this investigation, bronchitis and related chronic symptoms may represent exacerbation of asthma by air pollution rather than conditions that can be separated from asthma. Alternatively, the results may have reflected the persistent respiratory symptoms reported among asthmatic children with viral infections in communities with air pollution, especially NO_2 (13). Because of the high correlation of particulate air pollution, NO_2 ,

and acid (Table 1), it was not possible to distinguish which of these pollutants was more likely to be responsible for the observed effects.

Physician-diagnosed asthma and the outcomes of interest, although relatively imprecise end points with somewhat limited reliability (14), have been widely used in epidemiologic studies of children, and physician-diagnosed asthma has been found to reflect what physicians actually reported to patients, at least in adults (15). In this study, children with reports of physician-diagnosed asthma were uniquely sensitive to air pollution in Southern California. Children with a history of wheezing but without physician-diagnosed asthma are an even more heterogeneous group, which includes children with undiagnosed asthma, with wheezing illness in infancy and early life associated with respiratory infections, or with small airways (16), in addition to a large number of other wheezing conditions that must be excluded before the diagnosis of asthma can be made (12). In this study, although air pollution was not associated with chronic symptoms among children with wheeze, there was no inverse relationship between air pollution and bronchitis, as was observed for children without wheeze (Table 3), an association that may reflect underlying unadjusted confounding by unmeasured covariates in the study communities. It is possible that more accurate

Table 3. Risk of bronchitis, phlegm, and cough by air pollutant concentration^a among children with a history of asthma, wheeze, and neither asthma nor wheeze.

	Asthma		Wheeze/no asthma		No wheeze/no asthma	
	OR	CI	OR	CI	OR	CI
Bronchitis	(n = 154/473) ^b		(n = 147/630) ^b		(n = 117/2,162) ^b	
PM_{10}	1.4	1.1–1.8	0.9	0.7–1.3	0.7	0.4–1.0
$PM_{2.5}$	1.4	0.9–2.3	0.9	0.6–1.4	0.5	0.3–1.0
NO_2	1.3	0.8–2.2	0.9	0.6–1.4	0.8	0.4–1.7
Ozone	1.0	0.6–1.7	1.1	0.7–1.6	0.9	0.4–1.8
Acid	1.1	0.7–1.6	0.9	0.7–1.6	0.9	0.5–1.0
Phlegm	(n = 122/475) ^b		(n = 86/625) ^b		(n = 93/2,092) ^b	
PM_{10}	2.1	1.4–3.3	0.9	0.6–1.4	0.8	0.6–1.3
$PM_{2.5}$	2.6	1.2–5.4	1.0	0.6–1.8	0.8	0.4–1.5
NO_2	2.7	1.4–5.3	1.0	0.6–1.8	1.0	0.5–1.9
Ozone	1.2	0.5–3.1	0.8	0.5–1.4	0.8	0.5–1.5
Acid	1.9	1.0–3.6	0.9	0.6–1.4	1.1	0.7–1.8
Cough	(n = 84/491) ^b		(n = 63/644) ^b		(n = 84/2,180) ^b	
PM_{10}	1.1	0.8–1.7	1.2	0.9–1.8	0.9	0.7–1.2
$PM_{2.5}$	1.3	0.7–2.4	1.1	0.6–1.9	0.9	0.6–1.3
NO_2	1.6	0.9–2.7	1.3	0.7–2.2	0.8	0.5–1.2
Ozone	1.1	0.6–2.0	0.7	0.5–1.1	0.9	0.6–1.3
Acid	1.4	0.9–2.1	1.0	0.6–1.5	0.9	0.7–1.3

Abbreviations: CI, 95% confidence interval; NO_2 , nitrogen dioxide; OR, odds ratio; PM_{10} , particulate matter $\leq 10 \mu m$ in aerodynamic diameter; $PM_{2.5}$, particulate matter $< 2.5 \mu m$ in aerodynamic diameter.

^aPrevalence ORs were calculated per interquartile range of yearly mean exposure for each pollutant [daily peak ozone, 32 ppb; daily average PM_{10} , 19 $\mu g/m^3$; daily average NO_2 , 24 ppb; 2-week average $PM_{2.5}$, 15 $\mu g/m^3$; and acid (1.8 ppb of HCl + HNO_3 , measured on a mole basis)]. All models were adjusted for age, sex, race, school grade, and membership in a health insurance plan. ^bNumber responding positively for each outcome/total in stratum; total varies by outcome because of variable "don't know" responses or missing values (which were excluded).

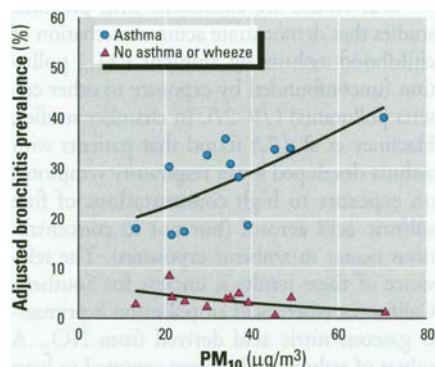


Figure 1. Particulate matter and bronchitis. PM_{10} , particulate matter $\leq 10 \mu m$ in aerodynamic diameter.

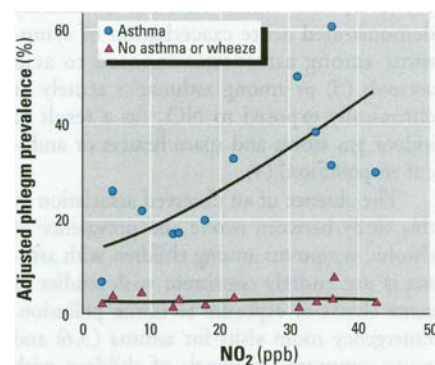


Figure 2. Nitrogen dioxide and phlegm.

classification of individuals based on objective hallmarks of asthma, such as atopy or bronchial hyperreactivity, would strengthen the observed associations. Individuals with greater airway lability, for example, have been found to be more responsive acutely to air pollution, regardless of asthma diagnosis (17).

There have been few other population-based studies of air pollution and prevalence of chronic respiratory symptoms among children with asthma. In the Six Cities Study, Dockery et al. (9) reported an association between exposure to particulate matter < 15 µm in diameter and the prevalence of bronchitis among children with wheeze or asthma. In that study, an association with NO₂ was not reported. Our results differed from those of Dockery et al. (18) in their study of children in 24 North American cities; they reported that an observed positive association of bronchitis prevalence with particle strong acidity in the overall population of children was not significantly different among children with asthma. Their results were heavily influenced by eastern cities. In Southern California ambient particulate matter is relatively low in sulfates, and our results suggest that the increased risk among asthmatic children of lower respiratory symptoms associated with particulate exposures does not depend on the presence of SO₂ and SO₂-derived sulfates, which are characteristic of air pollution in the eastern United States.

Our results are consistent with previous studies that demonstrate acute exacerbation of childhood asthma by ambient PM₁₀ pollution (unconfounded by exposure to other criteria pollutants) (19–21). In chamber studies, Hachney et al. (22) found that patients with asthma developed lower respiratory symptoms on exposure to high concentrations of fine sulfuric acid aerosol (but not to concentrations nearer to ambient exposures). The relevance of these results is unclear for Southern California, where acid air pollution is primarily gaseous nitric acid derived from NO₂. A subset of asthmatics has been reported to have consistent acute decrements in lung function in response to exposures to NO₂ (23). However, other studies have not consistently demonstrated acute exacerbation of symptoms among asthmatics exposed to acid aerosols (3) or among asthmatics acutely or chronically exposed to NO₂ (as a result of indoor gas stoves and space heaters or ambient air pollution) (4).

The absence of an observed association in this study between ozone and prevalence of chronic symptoms among children with asthma is not entirely consistent with studies of acute effects of exposure to ozone pollution. Emergency room visits for asthma (5,6) and acute symptoms in panels of children with asthma (7,8), including children in Southern

California (24,25), have been associated with ozone exposure. However, some experimental chamber studies suggest that asthmatic volunteers, in the absence of intense exercise, may not be more sensitive to ozone than subjects without asthma (4). In addition, acute exacerbation of asthma by ozone does not necessarily mean that chronic bronchitic symptoms must result from chronic exposure. Attenuation by repeated exposure of the acute response to ozone has been observed (3). In the Six Cities Study, no association was observed between ozone and prevalence of bronchitis among children with wheeze (9).

There were several limitations to our study, including the use of 1994 exposure information to evaluate the relationship with symptoms corresponding to the 12 months before the questionnaire was completed in early 1993. However, a comparison of measured exposures in 1994 with estimated exposures in 1992, based on NO₂ and ozone measured at existing monitoring stations, suggests that ambient exposures and effects were very similar in both years. The misclassification of personal exposure based on community monitors is likely to result in underestimation of a true association. Error also is likely in reporting bronchitis and phlegm, but this bias also might be expected to dampen the observed relationship between air pollution and a true effect. Finally, exposure to pollutants could be associated independently with the prevalence of asthma and of bronchitis, producing confounding. However, in these data there was no association between bronchitis and pollution, except in the population with asthma; in previous analyses we have demonstrated that air pollution was not associated with asthma prevalence (10).

The results of this study indicate that children with asthma are especially sensitive to the effects of air pollution in Southern California. Prospective follow-up of this cohort of children, who are being reexamined yearly, will identify the onset of new symptoms indicative of asthma activity in relation to exposure to criteria pollutants. Year-to-year variability in the mix of pollutants associated with symptoms may permit the evaluation of the contribution of individual pollutants.

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