Asthmatic Responses to Airborne Acid Aerosols

ABSTRACT

Background: Controlled exposure studies suggest that asthmatics may be more sensitive to the respiratory effects of acidic aerosols than individuals without asthma. This study investigates whether acidic aerosols and other air pollutants are associated with respiratory symptoms in free-living asthmatics.

Methods: Daily concentrations of hydrogen ion (H^+), nitric acid, fine particulates, sulfates and nitrates were obtained during an intensive air monitoring effort in Denver, Colorado, in the winter of 1987–88. A panel of 207 asthmatics recorded respiratory symptoms, frequency of medication use, and related information in daily diaries. We used a multiple regression time-series model to analyze which air pollutants, if any, were associated with health outcomes reported by study participants.

Results: Airborne H^+ was found to be significantly associated with several indicators of asthma status, including moderate or severe cough and shortness of breath. Cough was also associated with fine particulates, and shortness of breath with sulfates. Incorporating the participants' time spent outside and exercise intensity into the daily measure of exposure strengthened the association between these pollutants and asthmatic symptoms. Nitric acid and nitrates were not significantly associated with any respiratory symptom analyzed.

Conclusions: In this population of asthmatics, several outdoor air pollutants, particularly airborne acidity, were associated with daily respiratory symptoms. (*Am J Public Health.* 1991;81:694–702)

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Introduction

Exposure to acidic aerosols and sulfates has been associated with increased mortality and respiratory morbidity in a variety of settings.[1–5] Controlled exposure chamber studies suggest that individuals with asthma are more sensitive to the bronchoconstrictive effects of acidic sulfates than individuals without known pulmonary disease.[6–9] While the effects of exposure to ambient particulates (which may include acid aerosols) on asthmatic symptoms have been studied epidemiologically, previously published investigations have not included concurrent daily measurements of ambient airborne acidity.[4,5,10–12] Since the US Environmental Protection Agency has recently begun to consider whether to promulgate a national ambient air quality standard (NAAQS) for acid aerosols, it is important to assess the effects of relatively low levels of exposure on individuals in typical, free-living conditions. Thus, the need to extrapolate from studies of animals or of volunteers in controlled human clinical studies is obviated. In this study we report the results of an analysis of the association between ambient airborne acidity and daily respiratory symptoms recorded by a panel of asthmatics in Denver, Colorado during the winter of 1987–88.

Particulate air pollution has been associated with increased asthmatic symptoms and respiratory hospital admissions.[4,5,10–12] In an analysis of daily diaries of 454 asthmatics in the Los Angeles area, Whittemore and Korn[10] reported increased probabilities of attacks on days with high oxidant and total suspended particulate (TSP) pollution. Interpretation of this study is limited, however, by (among other things) the inadequacy of TSP as a measure of respirable particulate exposure and by significant covariation of TSP and ozone. Using a modification of the analytic model developed by Whittemore and Korn,[10,11] Perry, *et al,*[12] investigated the effects of fine (<2.5 microns in aerodynamic diameter) and coarse (>2.5 and <15 microns) particulates on respiratory symptoms, peak flows, and bronchodilator usage in 24 asthmatics in Denver in winter 1979. Fine nitrates were associated with increased symptoms and bronchodilator usage, while fine sulfates were associated with increased bronchodilator usage. The implications of this analysis are unclear because of the small sample size, the relatively low levels of particulate pollution, and the absence of acid aerosol measurements. In an ongoing study in Ontario, Canada, summer hospital admissions for asthma have been associated with exposure to ozone, sulfates, and sulfur dioxide.[4,5] These constituents of the "acid summer haze" were highly correlated; however, recent evidence[5] suggests that ozone may be less important than sulfates since there was a low correlation between respiratory admissions and ozone during one month of particularly high ozone concentrations. Again, acid aerosols were not measured.

The respiratory effects of airborne particulates on asthmatics and others have been attributed to the irritant, acidic frac-

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tion of this heterogeneous mixture of pollutants.[13–15] In controlled chamber studies of healthy individuals and asthmatics, acidic sulfates (H_2SO_4 and NH_4HSO_4) have been associated with bronchoconstriction and increased bronchial reactivity.[6–9] In a study involving short exposures (30 minutes at rest followed by 10 minutes of exercise), Koenig, *et al*,[6] reported significant changes in flow rates and pulmonary resistance in adolescent asthmatics exposed to 100 $\mu g/m^3$ H_2SO_4. Some studies showed effects only at higher levels of exposure which exceed typical urban peak sulfate levels,[7–9] and some showed no effects.[16] Nitrates and nitric acid have been studied less than acidic sulfates. Overall, the results of chamber studies suggest that asthmatics may be an appropriate "sensitive population" to study epidemiologically in relation to airborne acidity.

An intensive daily air monitoring program in the metropolitan Denver area was conducted from November 1987 to February 1988 to investigate the chemical composition and particle size distribution of the winter "brown cloud." The Integrated Environmental Management Program of Region VIII of the US Environmental Protection Agency (EPA) conducted a complementary air monitoring program from November 1987 to March 1988. The joint monitoring effort included twice-daily measurements of particulates (sulfates, nitrates, and all particles less than 2.5 microns in diameter or PM2.5), airborne acidity, and sulfur dioxide at two sites. Aerosol acidity was measured using annular denuder instrumentation[17] and included nitric acid vapor and nanoequivalents of hydrogen ion (H^+) in particulate form, which was not further speciated (into H_2SO_4 or NH_4HSO_4). Meteorologic data were collected by the State of Colorado and by Stapleton Airport in Denver. This period of intense air monitoring provided an occasion to investigate whether exposure to fine acidic particulates is associated with respiratory effects in asthmatic individuals. No previously published epidemiologic studies have correlated concurrently measured airborne acidity with asthmatic symptoms and behavior.

Data and Methods

Study Population

Study participants were recruited from patients attending the clinic of one co-author (JCS). Diagnosis of asthma was made in each case by history and signs of airway obstruction on physical examination, confirmed by spirometric demonstration of obstruction reversible with a β-agonist bronchodilator (>15 percent change in FEV_1). Asthmatic patients were identified by clinic staff and were recruited for participation either during an office visit or by telephone and postcard contact. Denver residents between ages 18 and 70 were eligible to participate in the study if they had asthma currently managed with medication. Individuals with any other chronic medical condition that would restrict their activity were excluded.

This panel of asthmatics was asked to record, on a daily basis for several months, information about symptoms, medication use, utilization of medical services, indoor exposures, and other variables described below. In the context of the air monitoring efforts noted previously, a panel study has several advantages over other investigative designs. First, it provides a large number of observations, increasing the degrees of freedom and the stability of any estimates. Second, problems of confounding, omitted variables, and exposure assessment, while always present, are substantially reduced since individuals serve as their own controls over time. Thus, the impact of factors that vary daily, such as air pollution, can be isolated while other factors are held constant. Third, the consideration of a given sample in one metropolitan location over time eliminates the potential for any intercity confounding.

Health Measurements and Covariates

After giving informed consent, participants were required to fill out an intake questionnaire providing background data on demographics (age, sex, race, level of education, employment status, residential history), asthma severity and characteristic triggers and symptoms, medical history including medication use, smoking history, and previous environmental exposures. A diary instrument was designed to provide daily information on asthma symptoms, including the presence and severity on a scale of 0 to 4 (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = incapacitating) of cough, wheeze, shortness of breath, chest tightness, and sputum production, as well as physician and emergency room visits. In addition, information was obtained on frequency of medication use, time spent outdoors, levels of exercise intensity and whether exercise occurred indoors or outside, indoor exposure to respiratory irritants (such as gas stoves, fireplaces, and environmental tobacco smoke), and occupational exposures. Participants were told that this was an investigation of environmental factors affecting asthma, but not that the principal variables of interest were air pollutants.

There were 330 intake questionnaires distributed (93 during office visits and 237 by mail) from November 15 to December 16, 1987. Of the initial group recruited, 256 returned the intake questionnaires. Study subjects were contacted by clinic staff intermittently throughout the study period (December 1987 through February 1988) to enhance compliance and continued participation. Two hundred and seven patients returned their daily diaries. There were similar distributions of demographic variables and asthma severity in the initial study population and those who returned the daily diaries (Table 1). The group un-

TABLE 1—Characteristics of Patient Population Participating in the Denver Asthma Study

Characteristics	Total Study Population (n = 256)	Diary Participants (n = 207)
Mean age	44.3	45.6
% Male	34	34
Race (% White/Black/other)	94.6/2.3/3.1	96.5/1.5/2
Education (%)		
College	62	62
High school	37	37
Less than high school	1	1
Employment status (% employed outside home/homemaker/retired/other)	71/10/15/4	70/10.5/13.5/6
Mean subjective asthma severity rating (0 = none, 4 = incapacitating)	1.78	1.74
% Daily Theophylline	56.4	58.0
% Daily oral steroids	21.6	18.9
% Current smokers	3.1	3.0

TABLE 2—Descriptive Statistics of Pollutant, Meteorological, and Health Variables

	N	Mean	Std Dev	Minimum	Maximum
Sulfates ($\mu g/m^3$)	74	2.11	2.47	0.12	12.65
Nitrates ($\mu g/m^3$)	54	6.83	17.56	0.01	24.5
PM2.5 ($\mu g/m^3$)	47	21.97	20.40	0.51	73.08
Sulfur dioxide ($\mu g/m^3$)	78	14.14	12.82	0.80	59.8
Nitric Acid ($\mu g/m^3$)	64	1.81	2.25	0.06	13.54
H^+ (neq/m^3)	27	10.07	9.52	2.00	41.31
$SH+$ (neq/m^3)	74	8.15	8.29	0.59	44.25
Minimum temp. (F)	105	17.71	11.97	−11.00	39.00
Asthma	105	16.33	3.84	7.41	30.56
Cough	105	15.08	4.26	7.41	32.00

SH^+ = Hydrogen ion readings including substitutions for missing values.
Asthma = Group probability (×100) of reporting a moderate or worse overall asthma condition on each day.
Cough = Group probability (×100) of reporting a moderate or worse cough on each day.
All pollutants are measured as the average from 9:00 am to 4:00 pm

TABLE 3—Correlation Coefficients for Pollution and Meteorological Variables

	SULF	SO_2	NITR	PM2.5	HNO_3	H^+	SH^+	Mintemp
SO_2	.51							
NITR	.20	.18						
PM2.5	.88	.64	.40					
HNO_3	.22	.37	.78	.68				
H^+	.66	.35	.40	NA	−.11			
SH^+	.86	.44	.15	.56	.23	1.0		
MINTEMP	−.45	.26	−.08	−.34	−.07	−.57	−.43	
RH	.35	.12	.15	.40	.17	.32	.34	−.34

SULF = Sulfates
SO_2 = Sulfur dioxide
NITR = Nitrates
PM2.5 = Particulate matter less than 2.5 microns in diameter
HNO_3 = Nitric acid
H^+ = Hydrogen ion
SH^+ = Hydrogen ion with substitution for missing values (see text)
Mintemp = Minimum daily temperature
RH = Relative humidity
NA = Not available

der study was predominantly White, female, employed, and well educated, with an average age of approximately 46. The mean subjective asthma rating of moderate to severe is supported by the relatively large proportion of individuals taking daily oral theophylline and steroid preparations.

Exposure Measurement

The ambient air pollutants incorporated in the analysis were daily measures of sulfates, nitrates, PM2.5, nitric acid, hydrogen ion (H^+), and sulfur dioxide. Two different pollutant averaging times were considered initially: the 24-hour average (ending at 4:00 pm on the reporting day) of pollutant readings from the monitor in downtown Denver, located about two miles from the clinic; and the daytime average (9:00 am to 4:00 pm) from the same monitor. Since these averaging times were highly correlated (usually $r > .90$), only the daytime average was used in subsequent analysis. A second monitor, located about seven miles away in the northwestern suburb of Arvada, also provided measurements of these pollutants. Table 2 provides descriptive statistics for the pollutant, meteorologic and health variables. We found no statistically significant relationship between any pollutant and either the number of the day of the survey period or whether the reading was on a weekday or weekend and no significant time trend for either daily minimum temperature or daily humidity.

There was substantial covariation among some of the pollutants; the highest correlations were observed between PM2.5 and sulfates ($r = .88$), and between nitrates and nitric acid ($r = .78$). Sulfates and H^+ were both negatively correlated with maximum daily temperature (Table 3). Of the pollutants measured on a daily basis, sulfates had the most complete data. Values for missing days of PM2.5 and nitrates were derived from stepwise regressions using all other pollutants. PM2.5 could be predicted well by concurrent values of sulfates and nitrates ($r = .97$), and nitrates could be predicted by nighttime (4:00 pm to 9:00 am the following day) PM2.5 readings ($r = .86$).

The data on H^+ required additional attention. Because of problems in sample processing, the H^+ data were available only for half of the study period. The first seven days of H^+ readings were extremely high, with a mean of 288 nanoequivalents per cubic meter (neq/m^3), versus a mean of 10.1 for the following 28 days. The hydrogen ion concentrations during the first seven days were also unrelated to any other pollutant or meteorologic variables, while during the next 28 days there was a correlation, as expected, between H^+ and sulfates ($r = .66$). Consequently, the first seven days were dropped from the subsequent analysis. For H^+, missing values for the entire survey period were predicted using regression results with concurrent sulfate as the explanatory variable. With these substitutions, the daytime mean of H^+ was 8.15 neq/m^3 or approximately 0.4 $\mu g/m^3$ measured as sulfuric acid, with the highest daily average of 44 neq/m^3. All subsequent analysis for H^+ combined actual and imputed values. The one-hour peak may be three to four times higher than this longer-term average. These levels are typical of urban areas.[18] Analysis of the two monitors recording H^+ indicated that the concentrations of airborne acidity were fairly evenly distributed throughout the Denver area; the daily correlation of the readings was 0.88. Thus, the one downtown monitor was used to represent daily levels of H^+. Ozone concentrations, which frequently are highly correlated with sulfates and acids in the summer, were essentially at background levels through the winter in Denver (i.e. the maximum one-hour concentration was 0.042 ppm) and do not correlate with H^+ concentrations.

Previous research[19,20] suggests that incorporating information on exercise and time spent outdoors will improve the estimate of exposure. Therefore, we developed a measure of exposure that involved the product of the ambient pollution level, the duration of exposure, the time spent indoors and outdoors, and the ventilation

rates based on exercise level (i.e. ventilation rates of 7, 10, 25, and 40 liters per minute for resting, mild, moderate, or strenuous exercise, respectively). Since the actual time and duration of exercise was not recorded in the diary, it was assumed to occur during the day and to last for one hour. Hours outdoors and exercise levels were taken directly from the daily diary, while the penetration ratio of indoor to outdoor levels of H^+ of 0.3 was derived from the published literature.[21] This adjustment for exposure was crude but represents an improvement over simply using outdoor levels of air pollution. The extent of the reduction in measurement error (and improvement in exposure assessment) is specifically tested in the subsequent analysis.

All data from questionnaires, daily diaries, air quality, and meteorologic monitoring were coded and edited in a SAS format for analysis.

Statistical Methods

For this analysis, two different health outcomes were used as dependent variables in the multiple regressions: the probability of a respondent reporting on a given day a moderate (or worse) cough and the probability of reporting a moderate (or worse) rating of overall asthma status. The daily diary question regarding asthma status follows queries about the severity of wheezing, shortness of breath, chest tightness, and sputum production and should, therefore, reflect the respondents' subjective overall ratings of their individual asthma symptoms. As a daily average, 16.33 percent of the respondents (range 7.4 to 30.6 percent) reported a moderate or worse asthma day and 15.1 percent (range of 7.4 to 32 percent) reported a moderate or worse cough (see Table 2).

We estimated effects on each health outcome using ordinary least squares regression models. Variables included in each regression were minimum daily temperature, and binary variables indicating daily use of a gas stove and if the response occurred on a weekend. Since reporting of symptoms decreased during the course of the study, we also included the time since the start of the study. The probability of a symptom on the previous day was included as an explanatory variable in light of previous reports.[10,11] Daily relative humidity was examined and eliminated from the model after it was consistently found to be unrelated to any of the health outcomes, as were several time-invariant variables such as sex and education. Each pollutant's effect on health was estimated by entering it separately into the regression equation.

We also fitted a linear model of outcome using the logarithm of the pollutant, and a logistic model. There was little difference in model fit across the functional forms, but the log value of pollution provided the greatest association with the health outcomes. Thus, ordinary least squares with a log pollution term was used throughout the analysis. The similarity of results between ordinary least squares and logistic models probably was due to the relatively high rates of symptom incidence.

Significant autocorrelation was present, leading to biased estimates of the standard error of the estimated coefficients, and incorrect tests of significance.[22] The standard correction for autocorrelation involves estimation of a parameter (ρ) relating the regression residual at time t, r_t, to the residual for the previous time interval, r_{t-1}. When this feature is added to the estimation, the new model will have adjusted residuals which are uncorrelated. However, in this case, the procedure is biased and inconsistent because a lagged dependent variable (probability of symptom of the previous day) is included as an explanatory variable, and is correlated with the error term. Thus, the two-step procedure suggested by Fuller[23] was used. First, a predictive model was developed for the lagged value of the health effect (y_{t-1}) by regressing it on several independent variables, including time since start of the survey, specific air pollutants, minimum daily temperature, and humidity. Then the predicted value of y_{t-1} was used as an instrumental variable along with the other explanatory variables in the regression equation for y_t. Since the predicted value of the lagged dependent variable is uncorrelated with the adjusted residuals, the estimates are consistent. The estimation was performed using Proc Autoreg in SAS[24] with a maximum likelihood procedure that estimates both the regression coefficient and the autoregressive term.

Additional sensitivity analysis was conducted on the data, including a test for the influence of extreme observations, examination of other respiratory symptoms, and utilization of the exposure-adjusted measure of air pollution described above.

TABLE 4—Regression Coefficients Relating Ambient Air Pollution and Exposure-adjusted Air Pollution to Moderate Asthma Symptoms, Corrected for Autocorrelation (standard error in parentheses)

Independent Variables	Cough	Asthma Rating	Cough	Asthma Rating
Constant	5.9	0.026	−0.15	−7.9
Symptom on previous day	74.8[a]	83.0[a]	76.6[a]	97.1[a]
	(14.5)	(8.1)	(15.6)	(8.3)
Log (H^+)	0.76[b]	0.31		
	(0.38)	(0.42)	—	—
Exposure-adjusted log (H^+)	—	—	1.09[b]	1.00[c]
			(0.51)	(0.57)
Day of Survey	−0.067[c]	0.005	−0.76[c]	0.014
	(0.038)	(0.035)	(0.041)	(0.036)
Weekend	−0.85[c]	−0.04	−1.5[b]	−0.39
	(0.66)	(0.79)	(0.71)	(0.82)
Gas stove	6.53[a]	6.97[a]	8.25[a]	6.69[a]
	(1.75)	(1.88)	(1.94)	(2.03)
Minimum temperature	0.012	0.003	0.055	0.029
	(0.039)	(0.044)	(0.044)	(0.050)
R^2	.44	.37	.46	.37
# of observations	7417	7420	6364	6365
(# of people)	(168)	(168)	(163)	(165)

NOTE: a) significant at $p < .01$; b) significant at $p < .05$; c) significant at $p < .10$. All coefficients are ×100.

Results

Table 4 provides the ordinary least squares regression results for H^+, with the correction for autocorrelation. In the first two models, the dependent variables are the probability (×100) of reporting moderate or severe cough, and the probability of a moderate or worse asthma rating, respectively. The results indicate a statistically significant relationship between H^+ concentration and cough ($p < .01$) but not with overall asthma rating. Approximately 40 percent of the variation in the

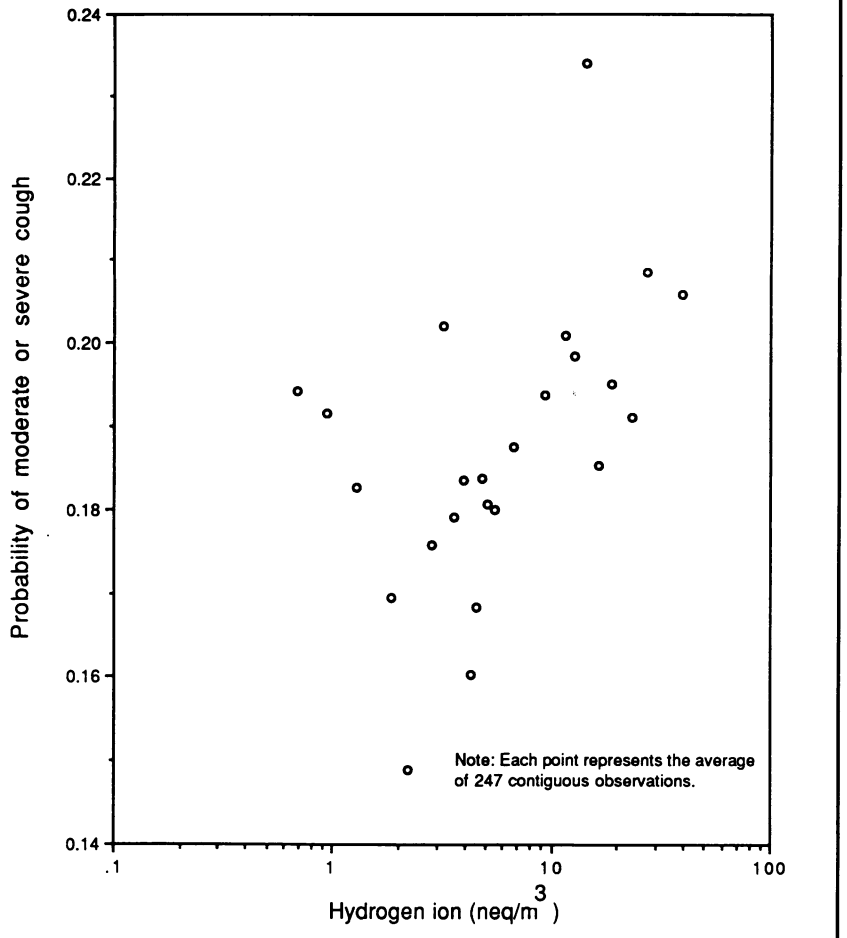

FIGURE 1—Association of Moderate or Severe Cough with Hydrogen Ion

probability of reporting these symptoms was explained by the regression. For both cough and asthma status, reporting that symptom on the previous day was significantly related ($p < .0001$) with reporting a moderate or worse symptom. For cough, the day of the survey, responding on a weekend, and using a gas stove were statistically significant. Using overall asthma rating as the dependent variable, the only other significant risk factor (besides symptom on previous day) was usage of a gas stove ($p < .001$). For both cough and asthma status, autocorrelation corrections were appropriate and a second-order autocorrelation model was indicated. Figure 1 displays a plot of the relationship between hydrogen ion and moderate or severe cough.

Next, models with exposure-adjusted measure of H^+ were examined (Table 4). These models adjust outdoor air pollution levels for daily exercise levels and time spent outdoors. The results indicate that the exposure-adjusted measure of H^+ had a statistically significant association with both moderate cough ($p < .05$) and general asthma rating ($p < .10$). Figures 2 and 3 display these relationships.

Additional models correcting for autocorrelation were examined for each of the other pollutants, including sufates, sulfur dioxide, PM2.5, PM2.5 with substitutions for missing values, nitrates, and nitric acid. Each pollutant was considered individually and regressed first on cough and then on asthma rating and on shortness of breath. The other explanatory variables used in the multiple regression were those used above. Thus, Table 5 gives the results of these 18 separate regressions, each with one pollutant included in the equation. For comparison, the previous results for H^+ and exposure-adjusted H^+ are also included in the table.

The results suggest that H^+, besides being associated with cough and overall subjective asthma rating, is also related to the reporting of moderate or worse shortness of breath. Besides H^+, the only other associations between individual air pollutants and these symptoms include: 1) sulfates and the probability of reporting moderate or worse shortness of breath ($p < .05$); and 2) PM2.5 and asthma rating ($p < .10$), after substitutions for missing values of PM2.5 were made, increasing the study duration from 46 to 75 days. Sulfur dioxide, nitrates, and nitric acid were not associated with moderate cough, asthma, or shortness of breath. The results for pollutants other than H^+ did not change when exposure-adjusted measures were used.

Additional analyses of the relationship of H^+ and asthmatic symptoms were conducted. The sensitivity of the models to the influence of extreme observations was tested using statistics proposed by Belsley, *et al.*[25] The test indicated that only the data from day = 2 had a relatively large influence on the regression results. The autoregressive model was rerun with that observation deleted, resulting in estimated regression coefficients that were essentially unchanged. Next, one- and two-day lags in H^+ were examined, indicating that contemporaneous measures of pollution provided the best association with asthma status. Finally, several time-invariant factors including education, sex, and whether an individual was recruited through office visit or by telephone were individually examined in the regression model. Their inclusion did not alter the estimated pollution effects.

Discussion

This analysis tested for an association between respiratory symptoms and several different air pollutants in a group of generally moderate to severe adult asthmatics. The results indicate a statistically significant association between ambient concentrations of hydrogen ion and the proportion of the subjects reporting moderate or worse cough and shortness of breath, with a lesser association observed in relation to the study subjects' overall asthma rating. Several lines of statistical and biomedical evidence implicate hydrogen ion as the principal pollutant of concern. First, although hydrogen ion was moderately correlated with minimum temperature and humidity (see Table 3), neither of these potentially confounding meteorologic variables was associated with the respiratory effects under investigation. Thus, it is unlikely that the estimated effects of hydrogen ion should be attributed to meteorologic changes over the survey period.

Second, confounding due to exposure to ambient ozone, which may cause

exacerbations of asthma, was not a factor here. In studies linking health effects in asthmatics with resulting from summer haze in Southern Ontario[4] and particulate matter in Los Angeles,[10] ozone was highly correlated with the particle measure used in each study (sulfates and total suspended particulates, respectively), which in turn could be a surrogate for acid aerosol. In the Denver winter of 1987–88, ozone was generally found at background levels, as expected, with a maximum hourly concentration of 0.042 ppm.

Third, sensitivity analysis indicates that the findings were robust to functional form, specification, and influential observations. Linear and logistic functional forms provided similar results, and the estimated effect of air pollution was not affected by the exclusion of influential observations. In addition, the regressions were corrected for autocorrelation. Therefore, the results of the above analysis indicate that the symptoms reported are not likely to be due to a statistical anomaly.

The estimated impact of air pollution is greater when an adjustment for actual exposure is undertaken. For example, as indicated in Table 4, after adjusting exposure for intensity and location of exercise, time spent outdoors, and penetration rate of H^+, the estimated effect of air pollution on cough is 43 percent greater than that obtained from the unadjusted pollution measurements. This suggests that dose-response estimates for H^+ that do not incorporate behavioral factors affecting actual exposures may seriously underestimate the impact of air pollution.

Evidence from controlled exposure studies supports an etiologic role of hydrogen ion exposure in evoking asthmatic symptoms. Increasing sulfate aerosol acidity enhances the bronchoconstrictive effects in asthmatics in rough proportion to the acidity.[7] Exposure to 75 $\mu g/m^3$ of the nonacidic respiratory irritant, ferric sulfate, did not cause adverse effects on pulmonary mechanics or respiratory symptoms in normal or asthmatic subjects.[26] More recently, Fine, *et al,*[27] showed that buffered acid aerosols were significantly more potent bronchoconstrictors than unbuffered acids at the same pH, suggesting that the total available hydrogen ion is a critical determinant of airway responsiveness. The relationship between asthmatic symptoms and pulmonary function changes due to acid exposure is not clear-cut; however, some studies indicate that symptoms (especially cough) precede accompanying changes in respiratory mechanics, although this has not been consistently observed.[27–29]

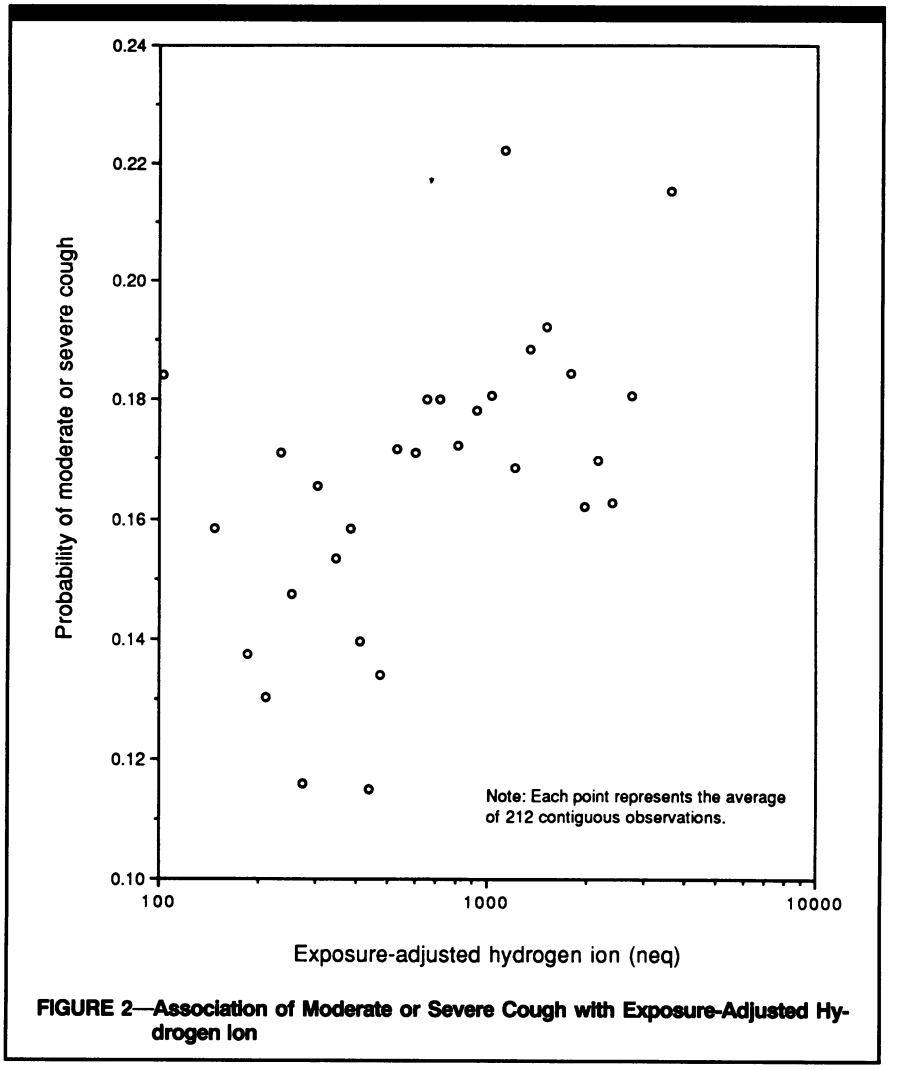

FIGURE 2—Association of Moderate or Severe Cough with Exposure-Adjusted Hydrogen Ion

This study suggests that hydrogen ion is the pollutant of primary concern. Although both sulfates and hydrogen ion were significantly related to the probability of reporting moderate or worse shortness of breath, only exposure-adjusted hydrogen ion was associated with the probability of reporting both a moderate or worse cough and asthma rating. Concentrations of particulate matter less than 2.5 microns were mildly associated with overall asthma ratings, but not with either cough or shortness of breath. Supporting evidence comes from a study of both asthmatics and healthy individuals,[30] in which ambient sulfates were not associated with acute respiratory symptoms, but airborne pH levels were. The importance of hydrogen ion over total sulfates or particle mass has also been suggested by the US EPA.[31] Since sulfate and particle measurements may include both acidic and nonacidic exposures, they incorporate measurement error which would bias downward the estimated regression coefficients and level of significance.

Of additional interest is the lack of association between nitrates or nitric acid and respiratory symptoms. Limited data from controlled chamber studies suggest that brief (10–16 min) exposure to high concentrations (up to 1,000 $\mu g/m^3$) of inorganic nitrate ($NaNo_3$) aerosols do not evoke respiratory symptoms or changes in pulmonary function in mild asthmatics.[32,33] Thus, there is some (admittedly sparse) clinical evidence to support the notion that particulate nitrates *per se* would not be expected to cause the effects reported here.

Our findings ostensibly conflict with those of Perry, *et al,*[12] who reported a mild association between respiratory symptoms and nitrates, but not sulfates, in a sample of 24 asthmatics. There may be at least three reasons for this discrepancy. First, the small sample size limits the generalizability of their findings. Second, the

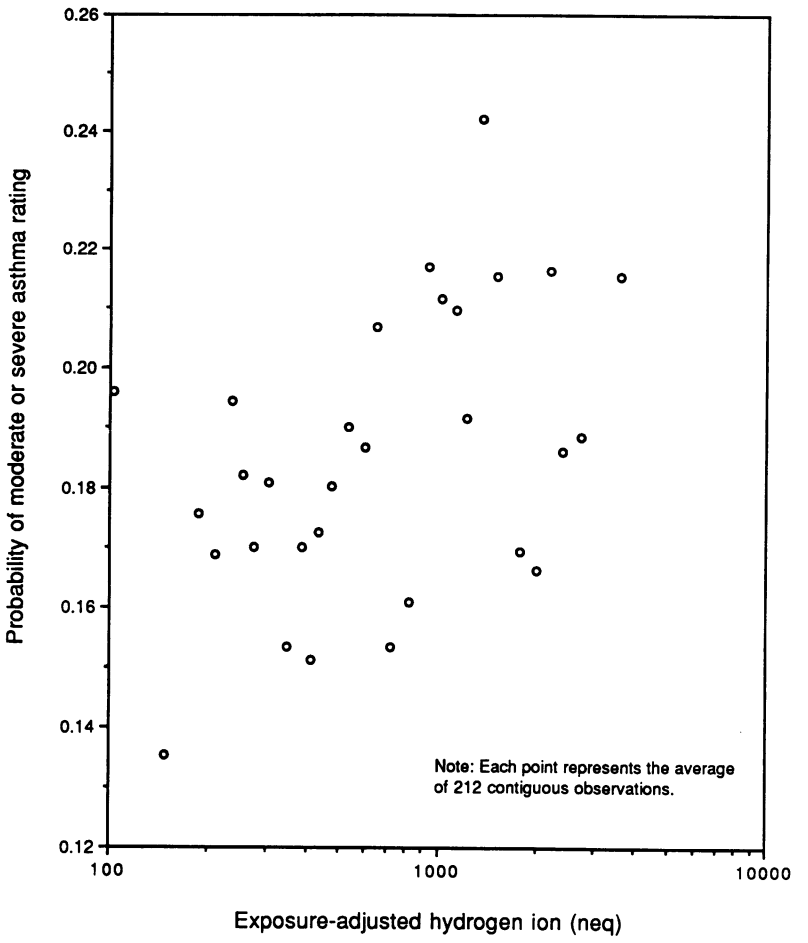

FIGURE 3—Association of Moderate or Severe Asthma Rating with Exposure-Adjusted Hydrogen Ion

rate of respiratory symptom reporting in that investigation was very low relative to ours. Third, there is a difference in pollutants under consideration and their dispersion patterns. Perry, *et al,* measured nitrates, sulfates, sulfur dioxide, and PM2.5 but not acid aerosols. In the Perry study and the present study the correlations among sulfates, sulfur dioxide, PM2.5, and temperature were remarkably similar, but nitrates were less correlated with other pollutants in the present study. This suggests that the sources of nitrates may have been quite different. Prior to the use of nylon back-up filters in the mid-1980s, nitrates were commonly measured inaccurately. Population growth and changes in automobile travel patterns also may have led to a change in exposures. In addition, during the winter of 1987–88, the major electric utilities, as part of a clean air campaign, burned natural gas instead of coal for alternate 15-day periods. These factors may have altered the dispersion pattern of nitrates, relative to sulfates and other pollutants, and the subsequent exposures of residents of the metropolitan area.

Since only about half of the individuals in this study completed their diaries every day, we investigated the potential for bias due to variable daily response rates. We found no relationship between air pollution and the number of people responding on a given day. We also investigated whether health status influenced response rates and found no relationship between overall severity of asthma and the number of days that people filled out the daily diaries. We infer that responses recorded in the daily diaries represent those of the group as a whole.

In this study population, the products of gas consumption appeared to exacerbate asthmatic symptoms. Peak indoor exposures to nitrogen dioxide (NO_2) resulting from gas stove use have been reported to range from 0.2 to 1.7 ppm,[34] which includes concentrations at which effects on symptoms or bronchial reactivity in asthmatics have been reported.[35,36] The concentrations of NO_2 and other constituents of natural gas combustion were not measured, but it is plausible that some symptoms were attributable to such indoor exposures.[37]

The results of this study, while supporting an association between asthmatic symptoms and ambient hydrogen ion exposure, should be interpreted with caution since pollutant measurements from fixed-site monitors cannot accurately represent individual exposures. Further, asthmatics may change their activity or medication use in order to reduce or eliminate symptoms related to air pollution; this would reduce the estimated effect of air pollution. Adjusting the pollution exposures for exercise and time outdoors increased the magnitude and precision of the estimate.

This study has several strengths, including the prospective nature of the investigation, the relatively large sample size, and the screening of the survey participants. Unlike previous large-scale studies of asthmatics, the sample for this study was recruited from one private practice at one location. Medical and personal histories were fully documented. Since the study was conducted as a time-series in one city over a relatively short period of time, geographic confounding factors were minimized, as was potential confounding due to ozone exposure. Relevant airborne acidity data, never previously collected concurrently with asthmatic symptom data, were also available.

This study provides evidence from a free-living population that is qualitatively consistent with the results of several controlled clinical investigations. Furthermore, our analysis indicates that, among moderate to severe asthmatics, respiratory symptoms occur at average hydrogen ion concentrations substantially lower than those at which effects on pulmonary mechanics have been observed in the laboratory.[7,9,28,29] That we were able to detect acute symptoms at the ambient concentrations measured was somewhat surprising. However, the study population was in general more severely afflicted than asthmatics volunteering for chamber studies. Some patients with severe asthma are known to have airway mucus with low pH, which may increase their susceptibility to acidic environmental insults.[38] Furthermore, the Denver winter temperatures and low relative humidity may have potentiated the effects of the airborne acidity (although we did not observe any obvious independent or interactive effects of these factors in the regression analysis). Cold dry air has been reported to enhance

TABLE 5—Estimated Regression Coefficients, Corrected for Autocorrelation, for Pollutants Examined Individually (standard error in parentheses)

Pollutants*	Asthma	Cough	Shortness of Breath
H^+	0.31	0.76[a]	1.05[a]
	(0.42)	(0.38)	(0.42)
Exposure adjusted H^+	1.00[b]	1.09[a]	1.33[a]
	(0.57)	(0.51)	(0.57)
Sulfate	0.24	0.42	0.77[a]
	(0.39)	(0.35)	(0.38)
SO_2	0.26	0.27	0.04
	(0.38)	(0.33)	(0.38)
PM2.5	0.06	0.12	−0.35
	(0.53)	(0.43)	(0.52)
PM2.5(Subs)	0.06[b]	0.14	0.29
	(0.03)	(0.29)	(0.38)
Nitrate	−0.25	−0.21	0.10
	(0.25)	(0.94)	(0.25)
Nitric acid	−0.03	−0.32	−0.10
	(0.35)	(0.34)	(0.34)

a) significant at $p < .05$; b) $= p < .10$
PM2.5(Subs) = substitute for missing values of PM2.5 = 8.67 * sulfate + 1.071 * nitrate
*All pollutants are in log terms. Besides the air pollutant, all equations include day of the survey, symptom on previous day, an indicator for weekend vs. weekday, use of gas stove, and minimum temperature as explanatory variables and are corrected for autocorrelation.
All coefficients are ×100.

bronchoconstriction caused by sulfur dioxide in one of the few experiments investigating interaction between physical and chemical exposures.[39] In other contexts, observational studies have found air pollution effects at concentrations below those at which chamber studies reported positive results.[40] This suggests that factors that are typically not included in chamber studies may play an important role in determining individuals' responses to air pollution. □

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Homeless Mentally Ill Will Benefit from Research Demonstration Projects

A unique collaborative effort to improve housing and services for homeless people who have a severe mental illness was announced recently by Health and Human Services Secretary Louis W. Sullivan, MD. The Department of Housing and Urban Development will join with HHS in supporting six research demonstration projects, each of which will combine housing assistance with mental health services.

The new projects will be carried out in five cities across the country and will be administered by the National Institute of Mental Health.

According to previous NIMH-sponsored research, one third of the homeless population has severe and persistent mental illnesses, including schizophrenia and mood disorders. Yet with adequate housing, treatment and support, most of these individuals can lead productive lives in the community.

NIMH funding for the new projects will be approximately $5.8 million in FY 1991 out of a planned total of $16.8 million over the next three years. HUD will contribute over $10 million in housing assistance. Projects will be located in Boston, Massachusetts; San Diego, California; Baltimore, Maryland; Cincinnati, Ohio; and two in New York City. In *Boston,* the project will evaluate two alternatives to housing homeless mentally ill individuals; consumer-managed group homes and independent living arrangements will be compared to determine which approach results in better housing stability with higher levels of functioning.

In *San Diego,* the research demonstration project will evaluate the effectiveness of linking comprehensive services to independent housing for severely mentally ill homeless persons.

In *Baltimore,* the project will test an "assertive community treatment" program designed to increase the clients' access to housing, as well as general health and mental health services.

The project in *Cincinnati* will compare the benefits of transitional housing and permanent housing.

In *New York City,* one research demonstration project will help individuals on the street obtain housing, such as single-room occupancy units, made available through a city/state agreement, while another project will be directed at mentally ill men who are preparing to leave a homeless shelter.

For further information, contact the Department of Health and Human Services, (301) 436-4536.