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Respiratory Hospital Admissions and Summertime Haze Air Pollution in Toronto, Ontario: Consideration of the Role of Acid Aerosols

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A study of air pollution and daily hospital admissions for respiratory causes was conducted in Toronto, Ontario. Fine aerosol ($d_a < 2.5$ μm) samples were collected daily at a central city site during July and August 1986, 1987, and 1988 and were subsequently extracted and analyzed for daily particulate phase aerosol strong acidity (H^+) and sulfates ($SO_4^=$). Daily counts of respiratory admissions to 22 acute care hospitals and daily meteorological and environmental data (e.g. ozone [O_3], total suspended particulate matter [TSP], and thoracic particle mass [PM10] were also obtained. Regression analyses indicated that only the O_3, H^+, and $SO_4^=$ associations with respiratory and asthma admissions remained consistently significant after controlling for temperature. Even after excluding days with maximum 1-hr $O_3 > 120$ ppb; O_3 was still strongly significant. In the various model specifications considered, the relative particle metric strengths of association with admissions were generally $H^+ > SO_4^= >$ FP > PM10 > TSP, indicating that particle size and composition are of central importance in defining the adverse human health effects of particulate matter. On average, summertime haze air pollution was associated with 24% of all respiratory admissions (21% with O_3, 3% with H^+). On peak pollution days, however, aerosol acidity yielded the highest relative risk estimates (e.g., RR = 1.5 at 391 nmole/m^3 H^+), and summertime haze was associated with roughly half of all respiratory admissions.

INTRODUCTION

Historically, the acute mortality and morbidity associated with air pollution have been most clearly identified and quantified in episodic situations. For example, during the December 1952 London fog, a classic example of a major air pollution episode, increases were seen in both daily mortality and hospital admissions (MHGB, 1954). The daily respiratory disease admissions to hospitals in greater London peaked at 460 cases, compared to an average of 175 cases per day immediately preceding the fog. Sickness claims also rose during the following week. Although the extent and time lag of each response outcome varied somewhat, the stress caused by such an extreme air pollution episode was coherently reflected not only in mortality, but also in all of the other health effects end points available for study.

The adverse health effects of more routine levels of air pollution are not as readily observable, and quantitative assessments of effects require more compli-

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cated statistical analyses and more extensive periods of study. Although associations between hospital visits/admissions and air pollution have been reported for a number of locations in the past (e.g., by Kenline, 1966 for New Orleans, LA; by Girsh *et al.*, 1967 for Philadelphia, PA: by Pope, 1989, 1991 in Utah; by Cody *et al.*, 1992 for central New Jersey; and by Thurston *et al.*, 1992a for New York City and Buffalo, NY), probably the largest database analyzed to date comes from the series of studies of southern Ontario hospital admissions and air pollution data conducted by Bates and Sizto (1983, 1986, 1987, 1989). The earliest of these analyses (of data collected during July and August in 1974, 1976, 1977, and 1978) reported significant associations of excess respiratory admissions with sulfur dioxide (SO_2), ozone (O_3), and temperature lagged 1 and 2 days (i.e., the preceding 2 days). The second analysis, employing an extended data set (1974 and 1976 to 1983), reported significant associations of lagged sulfate ($SO_4^=$), O_3, SO_2, and temperature with respiratory admissions. Lipfert and Hammerstrom (1992) also reanalyzed these respiratory hospital admissions and pollution data for 1979 through 1985 winters and summers. Although their analytical technique was different, also including subregion analysis and regressions with autoregressive error structure, this work confirmed the $SO_4^=$, SO_2, and O_3 associations with respiratory admissions reported by Bates and Sizto (1983, 1986, 1987, 1989), attributing 20% of summer respiratory admissions to air pollution. Burnett *et al.* (1994) also evaluated the Ontario acute care hospital database, but considered all of Ontario and analyzed the data from each of the 168 hospitals in the province using Poisson regression models. Significant ozone and sulfate associations were confirmed with asthma, chronic obstructive pulmonary disease (COPD), and infections, with ozone being identified as a stronger predictor of admissions than sulfates.

While the various past southern Ontario study results suggested a causal relationship between summertime air pollution and increased hospital admissions, they did not clearly discriminate among these several associated chemical species as to responsibility for the observed health effects, in part because of the serial intercorrelations among the environmental variables considered (Bates and Sizto, 1989). Furthermore, it is possible that some unmeasured environmental factor, also correlated with these pollutants, was responsible for the health effects. In fact, Bates and Sizto speculated as to the possible role of acid aerosols ("acid summer haze") in their latest reports (1987, 1989), although aerosol acidity was not directly measured in Toronto during their study periods.

Toxicological, clinical, and epidemiological studies have all been accumulating suggestive evidence of a causal role by acid aerosols on human health. Indeed, the U.S. Environmental Protection Agency (U.S. EPA) compiled an issue paper reviewing the existing knowledge on this matter, in order to evaluate the potential need to list acid aerosol as a criteria pollutant (U.S. EPA, 1989). On the other hand, some recent mortality and morbidity analyses (e.g., Dockery *et al.*, 1992; Ransom and Pope, 1992) have suggested that the mass of particles less than 10 μm in aerodynamic diameter (PM10) is the most appropriate particulate matter parameter to consider. To aid in the assessment of these various particle metrics' respective associations with health effects, particulate aerosol strong acidity (H^+), as well as $SO_4^=$, PM10 and other particulate matter concentrations were

directly measured at a central site in Toronto, Ontario during the summers (July and August) of 1986, 1987, and 1988. Thus, it is now possible to directly examine the respective roles of both particulate matter acidity and mass in the previously reported associations between hospital admissions and summertime haze air pollution in Toronto, Ontario.

DATA COLLECTION

Hospital Admissions Data

Daily hospital admissions data for July and August, 1986, 1987, and 1988, were obtained from Health and Welfare Canada for the Toronto metropolitan area. The ninth revision of the International Classification of Disease (ICD9) primary admissions diagnosis categories employed here are essentially the same as those analyzed by Bates and Sizto in their past Toronto analyses: (1) total respiratory (ICD9 codes 466, 480, 481, 482, 485, 490, 491, 492, 493); (2) asthma (493); and (3) nonrespiratory control (365, 430, 431, 432, 434, 435, 531, 543, 553.3, 537, 540, 541, 542, 543, 590). Because the pollution data were collected in the metropolitan area of Toronto, the daily admission counts analyzed were totals from the 22 acute care hospitals in the metropolitan area (population, 2.4 million), in contrast to Bates and Sizto's 79 acute care hospitals serving the entire southern Ontario area (5.9 million persons). The means and maxima of these hospital admissions groupings are shown in Table 1. It should be noted that, because of the pollution sampling schedule, the 6-week period analyzed was slightly different for each summer: July

TABLE 1
MEAN/MAXIMUM OF KEY VARIABLES IN TORONTO SUMMER

	1986 (n = 40)	1987 (n = 41)	1988 (n = 42)
$SO_4^=$ (nmole/m^3)[a]	74.4/415.0	38.0/241.5	123.6/507.7
H^+ (nmole/m^3)[a]	21.4/170.0	12.6/67.2	52.3/391.0
Max O_3 (ppb)[a]	49.3/86.0	53.4/111.0	69.7/159.0
FP (μg/m^3)[a]	17.7/66.0	15.8/63.0	22.3/50.7
CP (μg/m^3)[a]	12.7/30.0	13.9/33.0	16.5/31.2
PM10 (μg/m^3)[a]	30.4/86.0	29.5/96.0	38.8/80.1
TSP (μg/m^3)[a]	62.3/121.0	65.9/139.0	87.0/180.0
TSP-PM10 (μg/m^3)[a]	31.8/68.0	35.3/93.6	46.9/115.9
Max SO_2 (pphm)[a]	1.2/7.0	1.4/9.0	2.5/11.0
Max NO_2 (pphm)[a]	5.1/9.0	3.7/8.0	5.4/11.0
Max temp (°C)[b]	26.4/32.5	26.2/33.8	29.5/37.0
Total respiratory admissions/day	14.4/25	12.8/24	14.1/26
Control admissions/day	22.2/34	20.6/34	19.2/32
Total asthma admissions/day	9.0/15	8.3/17	9.5/20

[a] Measured at a downtown site (Breadalbane St.).
[b] Mean of daily maximum hourly measurements at Lawrence–Kennedy site and Pearson International Airport.

2nd through August 10th for 1986; July 12th through August 21st for 1987; and July 7th through August 17th for 1988.

Pollution and Temperature

Aerosol acidity and sulfate ions were measured collaboratively by the New York University Medical Center (NYUMC) and the Robert Wood Johnson Medical Center (RWJMC) during the summers of 1986 and 1987 and by the NYUMC during July and August 1988. As described in more detail by Thurston *et al.* (1994), these pollutants were measured during 1986 and 1987 at three sites: (1) the University of Toronto, Scarborough campus (20 km northeast from downtown Toronto); (2) the Ontario Ministry of Environment and Energy (MOEE) research labs at Resources Road, Etobicoke (15 km northwest of downtown Toronto); and (3) the MOEE Breadalbane Street air-monitoring site (in center city Toronto). Filters were changed twice per day (9 AM and 5 PM). During the summer of 1988, acid aerosols were sampled at the Breadalbane Street site only. Ion chromatography was used for sulfate analyses, and a pH determination was used to assess particulate aerosol strong acidity (H^+) (Koutrakis *et al.*, 1988).

Hourly observations of O_3, nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) data for the Breadalbane site and hourly temperature as measured at the Lawrence–Kennedy site (located between sites 1 and 3) were provided by the Air Resources branch of the MOEE. For O_3, NO_2, and SO_2, daily maximum 1-hr average concentrations between 6 AM and 9 PM were obtained in order to better represent outdoor exposures (i.e., during the time period when people are most likely to be active outdoors). Similarly, the 9 AM–5 PM H^+ and $SO_4^=$ samples were used in this analysis. Daily 24-hr average measurements of particulate matter mass concentrations of fine particles, PM2.5 ($d_a < 2.5$ μm), coarse thoracic particles, CP (2.5 μm $< d_a <$ 10 μm), and total suspended particulate matter (TSP) were also made by the MOEE at the Breadalbane Street site during our study. CP and PM2.5 samples, which were collected via a dichotomous sampler having a PM10 cutpoint inlet, were both weighed and analyzed for trace elements (e.g., Si, S, Pb) by X-ray fluorescence (xrf). In certain cases, the filters were not weighed; therefore, the xrf elemental concentrations for those filters were employed in regression equations, developed from the concentrations on all other days over the three summers, in order to estimate the missing PM2.5 and CP values from the trace element concentrations on those days. PM10 ($d_a < 10$ μm) concentrations were calculated for each day by summing the PM2.5 and CP mass concentrations. The trace element predicted PM10 values (i.e., from the trace element estimated PM2.5 and CP) were highly correlated with the measured PM10 ($r = 0.98$). Daily maximum temperature records were also obtained for nearby Toronto Pearson International Airport from Environment Canada. The overall means/maxima of pollution (as measured at Breadalbane Street) and temperature (two sites) are presented in Table 1. The most notable contrasts among the three summers are the relatively high pollution concentrations and warm temperatures recorded during 1988.

STATISTICAL METHODS

Data Detrending and Prefiltering

Kinney and Ozkaynak (1991), in their study on the relationship between mortality and pollution/weather, point out that, because O_3 and mortality have sinusoidal seasonal cycles that are opposite in sign, the overall apparent correlation of the two series is negative, when in fact their correlation is positive once such seasonal cycles are removed. Also, Thurston *et al.* (1992a), in their study of respiratory admissions and pollution in several New York State metropolitan areas, reported that during the summer months of June, July, and August the seasonal (low-frequency) components of environmental and admissions data can exhibit an apparent negative correlation, whereas the higher frequency components in the same period are positively correlated. Thus, in order to properly examine "short-term" (i.e., day-to-day) associations between the environmental variables and hospital admissions, the influence of potentially confounding seasonal cycles must first be addressed. Because of the relatively small sample size (about 6 weeks for each summer), the use of high-pass filtering, which cuts off both ends of the series (e.g., ± 7 days for 15-day moving average filters), was not practical. Therefore, elimination of the seasonal component (and a reduction in data autocorrelation) was accomplished by regressing each data series on sine and cosine curves of annual cycles and utilizing the residuals of this model in subsequent analyses. This is the same statistical approach previously employed in the above-mentioned analysis of New York State pollution/admissions data (Thurston *et al.*, 1992a), in which this data prefiltering was shown to successfully eliminate negative long-wave associations, thereby clarifying the short-wave pollutant–morbidity correlations.

Daily hospital admission counts are expected to also be influenced by a day-of-week pattern. If left unaddressed, such patterns may bias associations between pollution and health effects, and they were therefore eliminated in this work by regressing each variable on day-of-week dummy indicator variables. This is functionally equivalent to taking deviations from the mean of each day of the week, as was done by Bates and Sizto (1983, 1986, 1987).

Data Analysis

After detrending and removing the day-of-week effects from both the environmental and admission data, correlations with lags (i.e., cross-correlation functions, CCFs) were calculated between the hospital admissions and the various pollution/temperature series. Bates and Sizto's past papers (1983, 1986, 1987, 1989) reported significant associations between hospital admissions and pollution/temperature variables lagged up to 2 days prior to hospital admissions. Burnett *et al.* (1994) reported significant associations between hospital admissions and pollution lagged up to 3 days. While these lagged pollution/temperature associations with health effects are suggestive of a causal association, these time series variables are not purely random, and interpretation of such results should be made with caution. For example, if the same extent of correlation was also found on the

other side of cross-correlation (i.e., the association of hospital admissions with "future" pollution), then the interpretation of a causal association could not be rationalized. Thus, observation of both sides of the cross-correlation function provides useful guidance in interpreting the results. For this reason, cross-correlations for up to both plus and minus 3 days were considered for both the raw and prefiltered data.

Another important factor in interpreting cross-correlation results is the autocorrelation function (ACF), the correlation of a variable with itself over time, for each of the variables in question. When both of the variables to be correlated are themselves not autocorrelated, interpretation of CCFs are unambiguous. However, if one or both of the variables are autocorrelated, then CCFs tend to have smooth peaks or waves around otherwise sharp peaks, making interpretation of temporal sequence in the association ambiguous. In order to circumvent this problem, Haugh and Box (1977) suggested addressing the autocorrelation in each variable prior to CCF. In the present analysis, the initial detrending (by sine and cosine functions) should remove most or all long-wave positive autocorrelation present.

Changing filters twice a day (9 AM and 5 PM) made it possible to examine the pollution concentration averaged over different time periods. Daytime aerosol acidity levels appeared to be slightly higher than the nighttime levels, on average, but preliminary cross-correlation analyses between H^+ pollution and hospital admissions showed no notable difference in results among the 9 AM–9AM, 5 PM–5 PM, 5 PM–9 AM, and 9 AM–5 PM periods. Therefore, the 9 AM–5 PM values were selected in order to make the interpretation of cross-correlation days unambiguous, and also to match the exposure time window of these pollutants to the time when outdoor air pollution exposures were most likely (i.e., daytime).

Since sulfates and acid aerosols were measured only at the Breadalbane Street station during the summer of 1988, data analyses of the combined 3 years were conducted using only this downtown site. As shown by Thurston *et al.* (1994), while the extent of H^+ neutralization varies somewhat throughout the metropolitan area, the H^+ measurements among the three sites were highly correlated ($r \sim 0.90$) during 1986 and 1987, indicating that the use of a single central site for H^+ is adequate for these analyses. However, because spatial variability and representativeness of central site pollutant measurements may still have influenced any reported associations between pollution and hospital admissions, both the average of three sites and the downtown data were also examined during 1986 and 1987 for their association with hospital admissions. Similarly, associations for the average of the two MOEE sites (vs the downtown site alone) were also analyzed for O_3, NO_2, and SO_2, even though these pollutants were also highly correlated across monitoring sites in Toronto.

Guided by the CCF analyses, regressions of the hospital admission series were performed on same-day and lagged pollution and temperature variables. Considering all of the possible lag combinations of temperature and pollution variables results in an unwieldy array of regression runs. Therefore, a directed and relatively "conservative" approach was taken: the temperature lag having the highest association with a hospital admissions series was first chosen, and all possibly

significant pollution lags (based on the CCF analyses) were also entered, one at a time, into regressions on the respective hospital admissions' categories in order to identify the strongest pollution lag, after incorporation of temperature influences.

The distributional properties of each variable and of the residuals of each hospital admissions' regression were also determined. Normality was tested using the Shapiro–Wilk statistic provided by the Statistical Analysis System (SAS) package (SAS Institute, 1988). The occurrence of extreme pollution levels is not an everyday event, even in summer, and it is possible that the small numbers of very high pollution days may overly influence the association with hospital admissions. This suggests that a logarithm or square-root transformation of these series may be appropriate. However, such an operation may also have the undesirable effect of reducing the measurement signal-to-noise ratio of the pollutant data. Therefore, to allow comparisons among these possibilities, cross-correlation and regression analyses were calculated using both transformed and untransformed dependent variables.

RESULTS

Exploratory Analyses

The distributional and autocorrelation characteristics of each variable were evaluated both before and after the detrending and day-of-week control steps. All the environmental variables, except temperature, NO_2, and O_3 series, were significantly different from the normal distribution. However, all the hospital admission series distributions were found to be not different from normal for each year, indicating that, for example, a Poisson regression was not required, and that ordinary least-squares regressions was appropriate. Among the raw hospital admission series, the control series showed strong autocorrelation ($r = 0.59$ with lag 1 day), while the total respiratory and total asthma series did not show significant autocorrelation ($r = 0.02$ and 0.03, respectively). All the raw pollution/temperature variables showed modest significant 1-day-lag autocorrelations, ranging from $r = 0.27$ for sulfur dioxide to $r = 0.46$ for temperature. Autocorrelations of all the pollution/temperature variables were lowered by the prefiltering steps, with the maximum filtered 1-day autocorrelation being that for temperature ($r = 0.34$). Moreover, after the detrending and day-of-week control, none of the hospital admission series were significantly autocorrelated ($-0.14 < r < 0.08$), indicating that an autoregressive term would not be required in the subsequent regression modeling.

Cross-correlations among the environmental variables were also examined to assess the extent and temporal structures of pollution/weather associations. The results of cross-correlation with log- and square-root-transformed variables were found to be essentially the same as for the untransformed data, and therefore only the results from untransformed data are analyzed here. The highest correlation between temperature and a pollution variable was with ozone ($r = 0.60$ at lag 0 day). The highest correlations among the pollution variables, and between the pollution and temperature, almost always occurred with zero lag. The same-day bivariate correlations among the variables are therefore shown in Table 2, ranging

TABLE 2

SAME-DAY BIVARIATE INTERCORRELATION OF ENVIRONMENTAL VARIABLES, 1986, 1987, AND 1988 SUMMERS COMBINED (n = 121), AFTER THE DETRENDING AND DAY-OF-WEEK CONTROL

	H^+	$SO_4^=$	O_3	FP	CP	PM10	TSP	SO_2	NO_2	T_{max}
H^+	1.00									
$SO_4^=$	0.82	1.00								
O_3	0.51	0.71	1.00							
FP	0.61	0.84	0.72	1.00						
CP	0.45	0.56	0.65	0.72	1.00					
PM10	0.60	0.80	0.75	0.97	0.86	1.00				
TSP	0.49	0.65	0.64	0.70	0.69	0.75	1.00			
SO_2	0.17	0.36	0.41	0.41	0.46	0.45	0.32	1.00		
NO_2	0.24	0.45	0.62	0.56	0.63	0.62	0.56	0.38	1.00	
T_{max}	0.39	0.58	0.68	0.39	0.56	0.68	0.61	0.38	0.56	1.00

from r = 0.17 (between acid aerosol and sulfur dioxide) to r = 0.97 (between PM10 and FP mass).

After detrending and day-of-week control, the three summer data series were pooled, and cross-correlation between hospital admissions and the environmental variables were computed. Again, the results of cross-correlation with log and square-root transformation were essentially the same as with the untransformed data, and therefore only the results from untransformed data are presented here. Figure 1 shows admissions' cross-correlations with the gaseous pollutants and with temperature for the pooled three-summer dataset. The stronger correlations

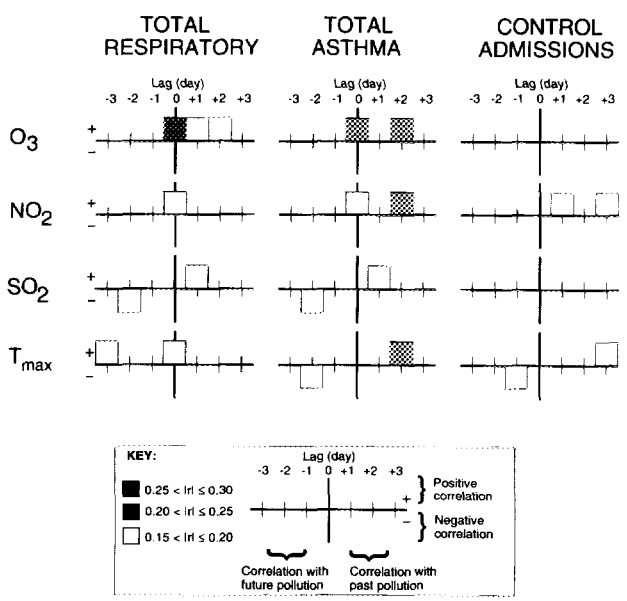

FIG. 1. Cross-correlations between daily hospital admissions and gaseous pollutants and temperature in Toronto, Ontario: 1986, 1987, and 1988 summers combined (after detrending and day-of-week control).

on the right side of the centerline indicate that pollution or temperature precedes the hospital admissions. The highest association was $r = 0.28$ between total respiratory admissions and maximum ozone without a lag. Temperature, NO_2, and SO_2 associations with respiratory/asthma admissions were weaker and less definitive. The figure shows that weaker correlations (e.g., white boxes) can occur on either side of the centerline, but stronger associations (e.g., gray or black boxes) tend to appear on the right side, or at the centerline, which is consistent with a causal relationship between pollution exposure and subsequent admissions. Figure 2 shows analogous cross-correlation results for the various particle pollution metrics. The strongest and most consistent correlations are with H^+, although FP, PM10, and TSP also show significant correlations with same-day total respiratory admissions. Most notable is that the coarse thoracic particles (CP) and the nonthoracic particles (TSP-PM10) are not significantly correlated with the total respiratory admissions, as would be expected on biological plausibility grounds, and that none of the various air pollution metrics are correlated with the control admissions.

In order to obtain a preliminary picture of the environmental–hospital admissions' relationships, the mean number of daily hospital admissions were calculated for each quartile of each environmental variable under study. For example, Fig. 3 displays these quartile means for total respiratory admissions as a function of H^+, O_3, and temperature for both the raw (Figs. 3a–3c) and filtered (Figs. 3d–3f) data. In both cases, the upper quartiles of the environmental variables

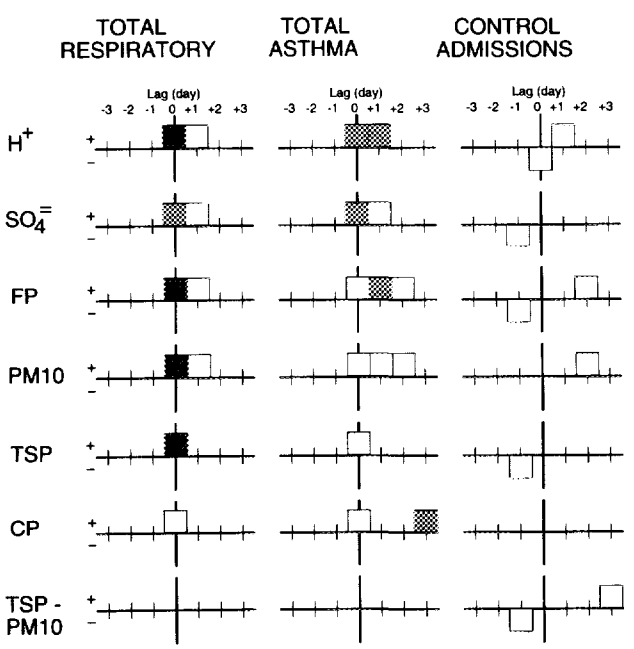

FIG. 2. Cross-correlations between daily hospital admissions and various metrics of particulate pollution in Toronto, Ontario: 1986, 1987, and 1988 summers combined (after detrending and day-of-week control).

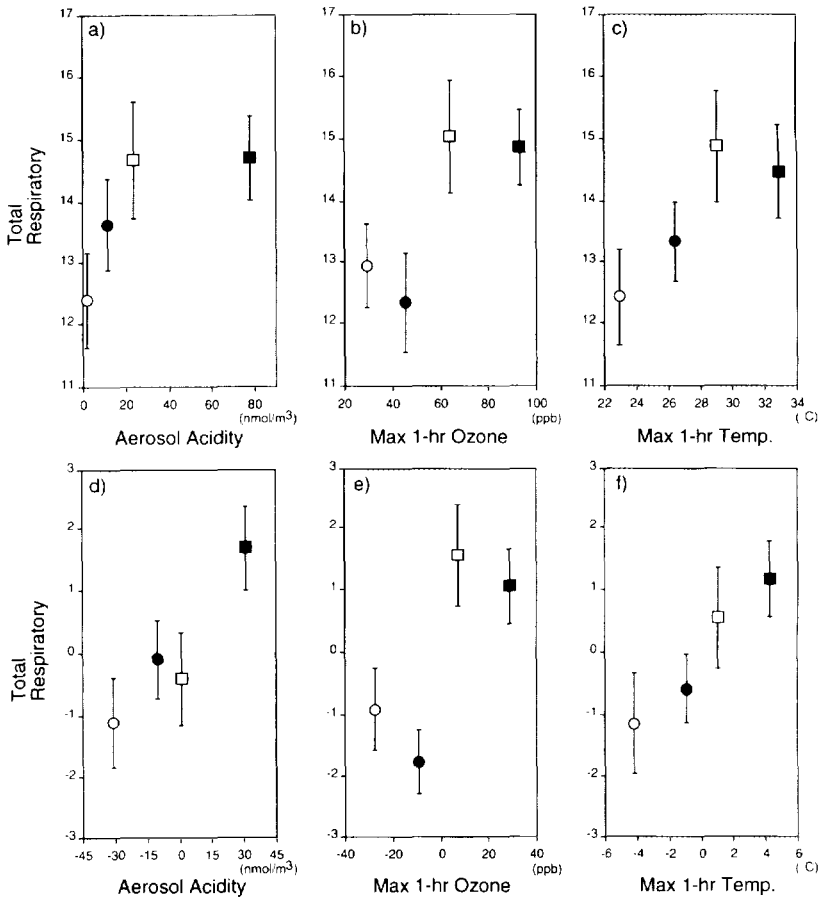

FIG. 3. Mean of total respiratory admissions for each pollution/temperature quartile for both the raw (a–c) and filtered (d–f) 1986–1988 data series (Q1, ○; Q2, ●; Q3, □; Q4, ■).

(designated by squares in Fig. 3) generally exhibit higher average daily admissions rates than the lower quartiles. The increase with increasing pollutant concentration and temperature is especially evident for the filtered data (Figs. 3d–3f), after the potentially confounding effects of long-wave and day-of-week trends have been removed. The pollutant plots suggest that increases in admissions with concentration do not occur until the upper quartiles, especially for H^+. In contrast, the temperature–admissions relationship appears throughout the temperature range, even in the lowest two quartiles (≤27°C, or ≤80°F), which may be biologically implausible. In any event, there is an apparent temperature–admissions relationship which cannot be compensated for in the simple bivariate pollutant–admissions plots shown here, indicating a need for regression analyses to simultaneously account for the temperature association when assessing the various pollutant–admissions relationships suggested by these quartile plots.

Regression of Hospital Admission on Pollutants and Temperature

Tables 3 and 4 show the hospital admissions–environmental metric regression results for the pooled three-summer data set for total respiratory and for asthma admissions, respectively. The CCF results often indicated a distributed lag model (regression model with multiple lags of the same "independent" variable), but since both the pollution and temperature variables were often still moderately autocorrelated in the short wave (e.g., one day to the next), only one lag of a pollution variable was entered in the regression at a time. Initial regression results presented are for temperature and only one pollutant at a time. Regressions for SO_2 and NO_2 consistently yielded nonsignificant pollution coefficients and are not shown. As expected from the relatively unautocorrelated filtered admissions series, Durbin–Watson statistics indicated no significant autocorrelation in any of the regression residuals. For both total respiratory admissions and asthma admissions, the 0-day-lagged O_3 coefficient consistently had the highest degree of statistical significance.

In order to investigate the extent to which the regression coefficients of the various particulate pollution metrics are independent of the very strong O_3 associations noted in the single pollutant regressions, a limited number of simulta-

TABLE 3
SIMULTANEOUS REGRESSIONS OF 1986–1988 TORONTO DAILY SUMMERTIME TOTAL RESPIRATORY ADMISSIONS ON TEMPERATURE AND VARIOUS POLLUTION METRICS

Temp, pollutant model specification	Pollutant regr coefficients (adm/poll unit[a])	*P* value (one-way)
	Single pollutant models	
T(LG0), O_3 (LG0)	0.0528 ± 0.0197	0.004
T(LG0), H^+(LG0)	0.0227 ± 0.0096	0.010
T(LG0), $SO_4^=$(LG0)	0.0106 ± 0.0054	0.028
T(LG0), FP(LG0)	0.0828 ± 0.0367	0.013
T(LG0), CP(LG0)	0.1228 ± 0.0895	0.086
T(LG0), PM10(LG0)	0.0642 ± 0.0290	0.015
T(LG0), TSP(LG0)	0.0242 ± 0.0160	0.066
T(LG0), TSP-PM10(LG0)	0.0180 ± 0.0196	0.180
	Two pollutant models	
T(LG0), O_3(LG0)	0.0503 ± 0.0205	0.008
H^+(LG1)	0.0153 ± 0.0089	0.044
T(LG0), O_3(LG0)	0.0508 ± 0.0207	0.008
$SO_4^=$(LG1)	0.0062 ± 0.0046	0.089
T(LG0), O_3(LG0)	0.0404 ± 0.0233	0.043
FP(LG0)	0.0434 ± 0.0429	0.157
T(LG0), O_3(LG0)	0.0388 ± 0.0241	0.055
PM10(LG0)	0.0339 ± 0.0344	0.164
T(LG0), O_3(LG0)	0.0360 ± 0.0228	0.059
TSP(LG0)	0.0127 ± 0.0175	0.235

[a] Pollution units are nmole/m^3 for H^+ and $SO_4^=$, ppb for O_3, and μg/m^3 for FP, CP, PM10, TSP, and TSP-PM10.

TABLE 4
SIMULTANEOUS REGRESSIONS OF 1986–1988 TORONTO DAILY SUMMERTIME TOTAL ASTHMA ADMISSIONS ON TEMPERATURE AND VARIOUS POLLUTION METRICS

Temp, pollutant model specification	Pollutant regr coefficients (adm/poll unit[a])	*P* value (one-way)
	Single pollutant models	
T(LG2), O_3(LG0)	0.0346 ± 0.0124	0.003
T(LG2), H^+ (LG0)	0.0185 ± 0.0072	0.010
T(LG2), $SO_4^=$(LG0)	0.0065 ± 0.0037	0.042
T(LG2), FP(LG0)	0.0334 ± 0.0241	0.084
T(LG2), CP(LG0)	0.0670 ± 0.0571	0.122
T(LG2), PM10(LG0)	0.0248 ± 0.0180	0.087
T(LG2), TSP(LG0)	0.0193 ± 0.0105	0.035
T(LG2), TSP-PM10(LG0)	0.0237 ± 0.0155	0.065
	Two pollutant models	
T(LG2), O_3(LG0)	0.0276 ± 0.0132	0.019
H^+(LG1)	0.0105 ± 0.0075	0.081
T(LG2), O_3(LG0)	0.0289 ± 0.0135	0.017
$SO_4^=$(LG1)	0.0026 ± 0.0040	0.261
T(LG2), O_3(LG0)	0.0265 ± 0.0142	0.033
FP(LG1)	0.0132 ± 0.0273	0.315
T(LG2), O_3(LG0)	0.0290 ± 0.0146	0.025
PM10(LG1)	0.0039 ± 0.0208	0.425
T(LG2), O_3(LG0)	0.0252 ± 0.0174	0.076
TSP(LG0)	0.0071 ± 0.0134	0.298

[a] Pollution units are nmole/m^3 for H^+ and $SO_4^=$, ppb for O_3, and μg/m^3 for FP, CP, PM10, TSP, and TSP-PM10.

neous pollutant regressions were also conducted, as presented in Tables 3 and 4. In each case, the model contained both T and O_3 as dependent variables, and the strongest lag of the various particulate pollution metrics were then individually added to that "base" model. For both total respiratory and asthma admissions, H^+ was the only particulate pollution metric which remained significant in the model with T and O_3. The O_3 and H^+ coefficients in this model were not significantly correlated with each other ($r = -0.11$) and were very similar in magnitude to those from their single pollutant regressions, indicating that their coefficients are statistically independent of one another. In contrast, the various particulate mass, and to a lesser extent $SO_4^=$, coefficients were significantly correlated with the O_3 coefficient in the simultaneous regressions (e.g., $r = 0.63$ for TSP). Thus, although the particulate matter mass measures initially appeared to be significantly correlated with hospital admissions, and some remained significant even after the consideration of temperature effects via regression, it seems clear that these apparent associations were merely a statistical by-product of interpollutant confounding resulting from the shared day-to-day variations in dispersion conditions. This points out the importance of considering as many pollutants as possible in such analyses, in order to diminish the chances of being misled as to which of the many ambient air pollutants is actually culpable for any noted air pollution–health effects associations.

In order to aid in the interpretation of the regression results in Tables 3 and 4, it is useful to estimate the implied pollutant mean effect and relative risk (RR) for H^+ and O_3. Each represents an effect metric which standardizes the regression coefficients, taking into account the scale and concentration range differences among the pollutants. Mean effect is calculated here as the product of the mean pollution level and its corresponding regression coefficient divided by the mean hospital admission levels, times 100. RR is calculated as the maximum pollution level deviation from the mean, multiplied by its corresponding regression coefficient, divided by the mean hospital admission, plus one. For the T, O_3, and H^+ simultaneous models shown in Tables 3 and 4, the resulting mean effect estimate of summertime acid haze pollution was 24% of total respiratory admissions (21 ± 9% for O_3, 3 ± 2% for H^+) and 21% of asthma admissions (18 ± 8% for O_3, 3 ± 2% for H^+). In contrast, the estimated relative risk of admission for the highest H^+ concentration (RR = 1.41 ± 0.30 for asthma, and RR = 1.40 ± 0.23 for total admissions) was higher than that for the highest O_3 concentration (RR = 1.31 ± 0.15 for asthma, and RR = 1.37 ± 0.15 for total admissions). Thus, while O_3 clearly dominates the summertime air pollution association with admissions, on average, a substantial increase in respiratory admissions (by as much as 40% above the average) is apparently also associated with peak acid aerosol episodes, which typically occur several times each summer in Toronto.

Table 5 shows a comparison of analogous admissions–environmental factor regressions for both Toronto, Ontario and Buffalo, New York (Thurston *et al.*, 1992a) during the summer of 1988. This is the only period when acid aerosol data were simultaneously collected by the NYUMC in both of these neighboring cities (approximately 60 miles apart and separated by Lake Ontario). It should be noted that the Toronto 1988 dataset has a smaller sample size (n = 42, July 10 through August 17) than Buffalo data (n = 92, June 1 through August 31), and the Buffalo H^+ samples were 24-hr averages. Also, the fact that different health care systems

TABLE 5
COMPARISON OF REGRESSIONS OF DAILY SUMMERTIME RESPIRATORY ADMISSIONS ON POLLUTION AND TEMPERATURE IN TORONTO, ONTARIO AND BUFFALO, NEW YORK 1988 SUMMER

City and year	Respiratory admissions category	Temp, pollutant model specification	Pollutant regr coeff (adm/μg/m^3/10^6, persons ± SE)	Pollutant mean effect (% ± SE)	Max/mean pollutant rel risk (±SE)
Toronto, 1988 summer	Total respiratory (mean = 14.1/day)	T(LG2), $SO_4^=$(LG1)	0.07 ± 0.03**	13.3 ± 5.3	1.41 ± 0.16
		T(LG2), H^+(LG1)	0.18 ± 0.09*	7.7 ± 3.9	1.50 ± 0.25
		T(LG2), O_3(LG1)	0.011 ± 0.005*	26.4 ± 11.8	1.34 ± 0.15
Toronto, 1988 summer	Total asthma (mean = 9.5/day)	T(LG2), $SO_4^=$(LG1)	0.04 ± 0.02*	13.0 ± 6.8	1.40 ± 0.21
		T(LG2), H^+(LG0)	0.13 ± 0.07*	8.1 ± 4.5	1.53 ± 0.29
		T(LG2), O_3(LG1)	0.007 ± 0.004*	25.3 ± 14.9	1.32 ± 0.19
Buffalo, 1988 summer	Total respiratory (mean = 25.0/day)	T(LG2), $SO_4^=$(LG0)	0.11 ± 0.04**	8.0 ± 2.7	1.22 ± 0.12
		T(LG2), H^+(LG0)	0.35 ± 0.12**	6.4 ± 2.2	1.47 ± 0.16
		T(LG2), O_3(LG2)	0.015 ± 0.008*	18.4 ± 9.9	1.25 ± 0.09
Buffalo, 1988 summer	Total asthma (mean = 7.1/day)	T(LG2), $SO_4^=$(LG1)	0.03 ± 0.02*	7.0 ± 3.9	1.29 ± 0.12
		T(LG2), H^+(LG1)	0.09 ± 0.05*	5.6 ± 3.3	1.43 ± 0.26
		T(LG2), O_3OLG3)	0.006 ± 0.002**	23.9 ± 10.1	1.25 ± 0.14

* $P < 0.05$ (one-way test).
** $P < 0.01$ (one-way test).

are employed in the United States and Canada may have influenced the rate of emergency hospital admissions to some extent. However, the two cities experience similar summer haze pollutant exposures (Thurston *et al.*, 1994). In all cases, the distribution of the model residuals were not statistically significantly different from normal, confirming the appropriateness of the ordinary least-squares regression model employed. All the corresponding regression mean effects and relative risks at the two locations agree within one standard error, although the "optimal" model lag specification of the pollutants varies in some cases. In the case of H^+, the relative risk estimated from the highest H^+ day (August 4, 1988 in both cities) was 1.50 ± 0.25 in Toronto and 1.47 ± 0.16 in Buffalo. Overall, these two independent analyses confirm each other remarkably well.

Hospital admissions regressions were also conducted for subsets of the 3-year database in order to determine the sensitivity of the O_3 and H^+ individual pollutant model results to extreme values. As shown in Table 6, elimination of the 2 ozone days having daily maximum concentrations greater than the U.S. National Ambient Air Quality Standard (NAAQS) of 120 ppb had little effect on the results, indicating that the ozone association exists even for concentrations below that standard. For concentrations below 80 ppb, however, the O_3 slope declined appreciably, and the O_3 slope for asthma even becomes nonsignificant. The increase in the size and significance of the ozone coefficients with the inclusion of higher O_3 concentration days is consistent with biological expectations. Also interesting is that the elimination of the highest H^+ days during the 3-year period lowered the O_3 slopes and significances more than eliminating the days with $O_3 > 120$ ppb. Overall, these sensitivity analyses indicate that ozone's association with respiratory and asthma hospital admissions exists at levels below 120 ppb and suggests that high H^+ concentrations (e.g., $H^+ > 100$ nmole/m^3) may potentiate the O_3 association with hospital admissions.

DISCUSSION AND CONCLUSIONS

These analyses of Toronto, Ontario pollution and hospital admissions' data indicate that exacerbations of preexisting respiratory disease, including asthma, are associated with community exposures to elevated levels of summertime haze O_3 and H^+. However, before such correlative or "ecological" associations can be judged as implying a cause-and-effect relationship, they should first be tested for their internal and external consistency with causality.

TABLE 6
SENSITIVITY ANALYSES OF 1986–1988 SUMMERTIME O_3 AND H^+ COEFFICIENTS

		Total respiratory coefficients		Total asthma coefficients	
Model	*n*	O_3 (adm/day/ppb)	H^+ (adm/day/nmole/m^3)	O_3 (adm/day/ppb)	H^+ (adm/day/nmole/m^3)
All days	120	0.053 (0.004)*	0.023 (0.010)	0.035 (0.003)	0.018 (0.006)
O_3 <120 ppb	118	0.052 (0.006)	0.022 (0.013)	0.029 (0.012)	0.017 (0.010)
O_3 <80 ppb	97	0.044 (0.057)	0.035 (0.087)	0.018 (0.166)	0.023 (0.110)
H^+ <100 nmole/m^3	114	0.045 (0.015)	0.035 (0.045)	0.028 (0.017)	0.022 (0.070)

* One-way *P* values.

Sir A. Bradford Hill has carefully enunciated a list of widely accepted criteria helpful in evaluating whether causality exists between environment and disease (Hill, 1965). Hill's first criterion is the *strength of association,* which is indicated in this analysis by the consistent statistical significance of acid aerosols and ozone in regressions, even after incorporating the effects of temperature, and by the sizable relative risks estimated in this research for these pollutants' maximum concentrations. The second criterion is the *consistency of the observed association* with work in other places and by different persons, which is satisfied by the previously cited past hospital visits/admissions studies conducted by the same and other authors for Ontario and New York State. The third criterion is the *specificity of the association* to particular types of persons and disease, which is shown here by the finding of air pollutant associations with respiratory disease categories, but not with "control" diseases. The fourth criterion is the *temporality of association,* which in this case is strongly evident by the lagged associations of health effects following (but not preceding) air pollution exposures. The fifth criterion is the presence of a *biological gradient,* which is indicated here by the positive pollutant regression slopes. The sixth criterion is *biological plausibility,* which is supported by past pollution episode effects (e.g., the London fog of 1952) and by a considerable and growing body of animal toxicity and controlled human exposure studies indicating measurable respiratory effects by both O_3 and acid aerosols at high concentration (e.g., see U.S. EPA, 1986, 1989; Lippmann, 1993). The seventh criterion is *coherence* with other available information regarding the disease and its manifestation. As discussed in detail by Bates (1992), the association between hospital admissions and air pollution found here is in concordance with a body of published results considering air pollution and other health indices such as mortality, emergency room visits, ambulance use, lung function, and symptoms. The eighth criterion is *experimental confirmation* by intervention, which has not yet been undertaken, but would only be possible in this case if dramatic remedial action were to be taken to abate these pollutants in the atmosphere. Hill's final criterion is to *judge by analogy* to other environmental agents which have been shown in the past to have a causal relationship. In this case, the best analogy possible is not to another ambient agent, but to these same agents (acid aerosols and ozone) at a much higher concentration. Both of these pollutants have been shown to be acutely lethal to animals when breathed in high concentration (e.g., see Doull *et al.,* 1980), suggesting that the hospitalization of humans at lower levels is plausible. Overall, while not all criteria have been fully and strongly satisfied, collective consideration of these criteria supports the conclusion that a causal relationship exists between ambient summer haze air pollution exposure and the acute exacerbation of preexisting respiratory disease (e.g., asthma), leading to increased incidence of respiratory hospital admissions.

The H^+ association found with total respiratory and asthma admissions in this work is supportive of Bates and Sizto's earlier speculation that $SO_4^=$ and O_3 could be acting as surrogates for the overall effects of "acid summer haze" air pollution, including acid aerosols. The various simultaneous regressions, sensitivity analyses, mean effects, and relative risk calculations conducted for this work indicate that the effects are predominantly associated with O_3 and H^+. Indeed, the mean

effects analyses indicated that these two pollutants were associated with 24% of all respiratory hospital admissions during the study periods (21% with O_3, 3% with H^+). Also, certain analyses, as well as recent independent laboratory human studies of normal and asthmatic subjects, suggest a possible potentiation of the effects of one acidic haze component on the other. For example, Linn *et al.* (1992) reported that the exposure of exercising human subjects to acidic aerosols, in addition to O_3, can result in larger reductions in lung function than the exposure to O_3 alone. Animal studies by Schlesinger *et al.* (1992) have also indicated that there can be interactions of effects, both antagonistic and synergistic, between ozone and strong acid aerosols. Similarly, Last (1991) found synergistic effects of acute O_3 exposures as low as 120 ppb and sulfuric acid as low as 5 to 20 $\mu g/m^3$ (100 to 400 nmole/m^3 H^+) in laboratory rats (as indicated by biochemical analyses of lung tissue and lavage fluids). Also, Thurston *et al.* (1992b), in their pilot study of asthmatic children at a camp exposed to acid summer haze, found that the number of asthma exacerbations was most heightened on a day when both O_3 and H^+ were elevated. Thus, there appears to be a consistency among this work and preliminary studies of various human and animal health outcomes that suggests that these two pollutants are of key importance in the summertime mix of air pollutants, and that there may also be a potentiation of these pollutants' adverse respiratory effects by the coexposure of both H^+ and O_3 in the ambient environment.

This research also provides relevant insights into the modeling and interpretation of particulate matter health effects. These analyses considered 10 different pollution variables, of which 7 were various particulate matter metrics. In the initial analysis, virtually every pollutant measure was significantly correlated with respiratory hospital admissions. Even nonthoracic particle mass (TSP-PM10) approached statistical significance, which is biologically implausible. This association is likely due to the moderate to high correlation among the various pollutants, which results from the general influences of atmospheric dispersion conditions on all of them. Only by directly intercomparing the relative strengths of associations displayed by the various gaseous pollutants and metrics of particle mass and composition was it possible to begin to sort out their relative importances. Overall, it was found here that, in Toronto during the summertime, particulate matter effects were secondary to the effects of O_3 for the health outcomes considered, and that, after controlling for these O_3 associations, the relative particle metric strengths of association with health effects were generally $H^+ > SO_4^= > FP > PM10 > TSP$. This result is similar to that found by past cross-sectional epidemiological analyses of various particulate matter metrics' associations with mortality (Ozkaynak and Thurston, 1987) and with morbidity (Ostro, 1990). These results are biologically plausible in that the largest (i.e., nonthoracic) particles are least associated with admissions, while the smallest and most irritant particles (i.e., submicrometer acid aerosols) are indicated to be most strongly associated with adverse health effects. Thus, these results suggest that what a particle is made of is more important to human health than the particle's mass, per se. Moreover, it is important to note that these results also clearly indicate that any statistical analysis of PM10 which fails to consider all the other major copollutants

(e.g., O_3), and/or the compositional variations (e.g., in the H^+/PM10 ratio) of PM10 that occur both spatially and over time, may well yield confounded and misleading results.

The above conclusions regarding particulate matter associations may appear to be in conflict with a number of recent publications indicating significant associations by PM10 with increased hospital admissions (e.g., Pope, 1989, 1991; Sunyer *et al.*, 1991, 1993; Tseng *et al.*, 1992; Schwartz *et al.*, 1993), but this is not necessarily the case. Actually, there are many important differences between the various data and analytical methods employed in these other studies versus those employed here. First and foremost of these differences is that the composition of the PM10 measured in each of these other locales is not the same as that of the PM10 measured in Toronto, Ontario. For example, the aerosol analyzed by Pope (1989, 1991) in Utah Valley was dominated by emissions from a local steel mill, while the Seattle aerosol analyzed by Schwartz *et al.* (1993) was dominated by wood smoke. In short, the aerosol mass collected by a PM10 sampler can vary dramatically in composition between locales, as well as between seasons at a single locale. Thus, it is not surprising that results can vary among PM10 mass studies, given that particles with differing compositions and irritancies are likely to have differing health implications. As previously noted by Thurston (1983), the grouping of all particles into one total mass measurement may be as misleading as would the grouping together of all gases as "total gases" without consideration as to whether a gas is, for example, oxygen or ozone. In the research reported here, the acidity of an aerosol has been confirmed to be one important particulate matter attribute to be considered, but more needs to be known about the nature of ambient PM10 particles, so that more appropriate epidemiology and control strategies can be applied to this problem. A major step toward this goal would be the immediate implementation of aerosol composition analyses (e.g., ionic and elemental analyses) of the PM10 samples presently being widely collected in Canada, the United States, and elsewhere. The key research and regulatory question, then, is not at what mass concentration level PM10 may cause health effects, but what kind or characteristics of particles cause the health effects noted to date?

Although the sample size of this study (three summer periods of about 6 weeks each) is smaller than that of Bates and Sizto's study (nine summers, 8 weeks each), or that of the Lipfert and Hammerstrom (1992) study (six summers, 8 weeks each), our results for comparable pollutants showed considerable consistency with those from these past southern Ontario studies: significant associations were found for both O_3 and $SO_4^=$ with total respiratory and asthma admissions to acute care hospitals in Toronto, Ontario. Furthermore, independent regression results from the 1988 Toronto and Buffalo data were consistent. However, unlike past southern Ontario studies, SO_2 was not shown to be significantly associated with respiratory admissions, which may be due to the fact that, unlike other pollutants, the mean summertime SO_2 levels in Toronto have fallen considerably over the intervening years (e.g., see Bates and Sizto, 1987). Most pertinent to this study, an association between directly measured H^+ and hospital admissions has now been demonstrated for the first time in the Toronto region, indicating that H^+ can have a large effect on respiratory admissions on the most polluted days (RR

= 1.5 at H^+ = 391 nmole/m^3). Moreover, consideration of Hill's criteria for inferring causality was found to support the conclusion of a causal relationship between human exposure to the levels of summertime haze air pollution experienced in Toronto, Ontario and acute exacerbations of preexisting respiratory disease, as manifested by increased hospital admissions for respiratory causes, including asthma.

Finally, the results reported in this paper must also be viewed in light of the conclusions of its companion paper (Thurston *et al.*, 1994). Together, these two investigations suggest that, not only are acidic summertime haze air pollutants being advected to Toronto, Ontario from upwind regions of the United States, but also that this transported pollution has measurable adverse health consequences in that city. Thus, to ameliorate this environmental health problem in Toronto and its vicinity, cooperation between the United States and Canada will clearly be required.

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