The Relation of Stroke Admissions to Recent Weather, Airborne Allergens, Air Pollution, Seasons, Upper Respiratory Infections, and Asthma Incidence, September 11, 2001, and Day of the Week

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Background and Purpose—Some previous research links stroke incidence to weather, some links strokes to air pollution, and some report seasonal effects. Alveolar inflammation was proposed as the mechanistic link. We present a unified model of time, weather, pollution, and upper respiratory infection (URI) incidence.

Methods—We combined existing databases: US Environmental Protection Agency pollution levels, National Weather Service data, counts of airborne allergens, and New York City Health and Hospitals Corporation counts of stroke, asthma, and URI patients. We used autoregressive integrated moving average modeling (a statistical time series modeling technique) with stroke admissions as the response variable and day of week, holidays, September 11th, and other counts and levels as explanatory variables.

Results—Using a broad definition of stroke, there were 5.1 ± 2.3 stroke admissions per day: narrowly defined, 4.2 ± 2.1 strokes per day. There are relatively fewer strokes on Sundays (0.50 strokes; P < 0.0011), Saturdays (0.62; P < 0.0001), Fridays (0.38; P = 0.0009) and holidays (0.875; P = 0.0016). We found relatively small, independent exacerbating effects of higher air temperature (P = 0.0211), dry air (P = 0.0187), URIs, (P < 0.0001), grass pollen (P = 0.0341), sulfur dioxide (SO2; P = 0.0471), and suspended particles <10 μm in size (P = 0.0404). These effects are modest: ≤0.6, 0.6, 2.4, 1, 0.9, and 0.7 strokes per day, respectively. We did not find statistically significant exacerbating effects of other variables.

Conclusions—We found statistically significant, independent exacerbating effects of warmer, drier air, URIs, grass pollen, SO2, and particulate air pollution. The model supports the theory that links pulmonary inflammation to stroke. (Stroke. 2006;37:951-957.)

Key Words: air pollution ■ cerebrovascular accident ■ fungal spores ■ influenza, human ■ pollen ■ respiratory infections ■ weather

In 2003, 700 000 Americans suffered a new or recurrent stroke, and stroke prevalence was 5.5 million (2.6% of total population); 157 804 of them died.1 Understanding the epidemiology may help us understand the underlying pathophysiology and to develop treatment and prevention strategies. Existing literature suggests a link between ischemic stroke and season,2–7 day of the week,7,8 weather,3,9,10 air pollutants,11–13 and respiratory infections.14,15 These projects compared the number of new strokes, or stroke deaths, to the variable of interest for that article. None of them model all of these factors together. Time, seasons, weather, upper respiratory infections (URIs), and many air pollutants are interrelated. A unified model allows us to examine the relation of strokes to each of these factors while controlling for the others.

Seaton suggests that inflammation, especially pulmonary inflammation, is the mechanism connecting air pollution to stroke.16 Some epidemiologic research on myocardial infarction17,18 and overall mortality19 supports this theory. Researchers invoked this mechanism as the link between pollution and strokes.11,12 If inflammation links air pollution to stroke, we might see a statistical relationship between stroke and agents that exacerbate asthma. We explored these relationships with autoregressive integrated moving average (ARIMA) models (a statistical time series modeling technique).
Methods

Data Sources

Data were obtained from existing databases. Ongoing New York City Health and Hospitals Corporation (HHC), a quasi-independent city agency that operates 11 city hospital centers, continuous quality improvement, and billing databases supplied patient counts. Any visit to a clinic or emergency department (ED) with a primary or secondary diagnosis of URI (International Classification of Diseases, Ninth Revision [ICD-9] codes 460.0 to 465.9) counted as a URI visit. Any patient seen in an ED with a primary or secondary ICD-9 code between 493.0 and 493.9 was counted as an asthma visit. Admitted patients with a discharge diagnosis of ischemic stroke (ICD-9 codes 433.0 to 434.9) or stroke of undetermined origin (ICD-9 436) were counted as stroke patients (broad definition). We recounted the subset patients with ICD-9 3-digit code of 433 or 434 and fifth digit 1 (narrow definition). We then eliminated cases with ICD-9 433 as the only stroke diagnosis and recounted again. We eliminated cases admitted primarily for rehabilitation.

One author (L.B.) counted airborne allergens at a rooftop monitoring station in Newark, NJ, using the rotorod method. This is the closest American Academy of Allergy and Immunology–approved station to New York City. He counted allergens daily except during winter. Before 2003, he made winter measurements when convenient; since then, they have been made daily. On 773 of 781 (99%) winter days when pollen counts were made, the count was 0. On winter days without counts, we assumed a pollen count of 0 and interpolated fungal spore counts.

US Environmental Protection Agency provided air pollution data. Federal, city and state officials collaborate to operate the sites and record data. Ozone (O3), nitrogen dioxide (NO2), oxides of nitrogen, including NO2 (NOx), sulfur dioxide (SO2), and carbon monoxide (CO) were measured hourly at sites scattered geographically and in time throughout the city; we used daily averages. On rare days, a pollutant was not measured in New York City. After ensuring a high correlation, we used adjusted levels from nearby New Jersey stations on those days. PM10 (suspended airborne particles of ≤10 μm in their largest diameter) were measured at 14 sites, 3 of which were active during the entire study period. With some exceptions, PM10 measurements were made every 6 days, the same days for all stations. We used spline interpolation estimated levels for days between measurements.

The US National Weather Service provided hourly air temperature and humidity measurements from 3 sites in New York City. We used daily averages and maximum–minimum temperatures.

We examined some time dummy variables: seasons, days of the week (Monday . . .) major holidays (New Years, Martin Luther King Day, Easter, Memorial Day, July 4, Labor Day, Thanksgiving, and Christmas), major Jewish Holidays, and September 11, 2001. These values took a value of 1 on the specific day of the week, holiday, or September 11 and 0 on other days.

Statistical Analysis

We used SAS 9.1.3 (GPLOT, GCHART, EXPAND, UNIVARIATE, CORR, FREQ, REG, AUTOREG, NPAR1WAY, ARIMA, and POWER) for calculations and graphics. We modified Proc EXPAND spline interpolated output with maximum and minimum functions to keep values within probable values: counts ≥0 and ≤ever measured for that season. We used autoregression with a 365-day lag for bivariate comparisons between strokes counts and explanatory variables (see Table 3) or sine waves (Figure 1). We examined other time patterns of stroke with χ2 analysis of dummy variables and ARIMA modeling. We considered nonlinear functions; for allergens and pollutants, we only considered monotonic (constantly increasing) functions with effect delays of <14 days.

Preliminary analysis showed that ARIMA modeling was needed to avoid underestimating forecasted number of strokes. Criteria for inclusion are: (1) α<0.05, (2) positive coefficients (see Table 3) for factors known from literature to be exacerbating agents, and (3) Schwartz–Bayesian criterion statistic smaller with the term in the

Figure 1. Scatter plot of number of ischemic strokes per day for each day. The ARIMA 95% CIs are overlaid in yellow. Strokes per day for the 10-year study period, plotted with the 95% CIs of the broad definition ARIMA model. Scatter plot of number of ischemic strokes per day.
model than without it. The model was derived retrospectively on data from 1991 to 2003 and then tested prospectively in 2004 (Figure 1, dashed line). The response (dependent) variables were the daily count of strokes, broadly and narrowly defined, with and without ICD-9 433 as the only stroke diagnosis.

**Statistical Power Calculations**
Assuming no autocorrelation or cross-correlation, $r^2 = 0.1$ for a full model of 5 variables and a study of 3287 days. We had power $= 0.855$ to find a significant ($\alpha = 0.05$) effect of the fifth variable if that variable contributes $r^2 = 0.0025$. If that component $r^2 = 0.005$, then power $= 0.989$, and power $> 0.999$ when the $r^2 = 0.0075$.

**Results**
A total of 82% of the broad definition patients are narrow definition patients. ICD-9 433 as the only stroke diagnosis comprised 19% of broad definition and 9% of narrow definition patients. Unless otherwise noted, “stroke patients” are broadly defined and include ICD-9 433 (see Discussion).

**Univariate Analysis**
During the retrospective (January 1, 1995, to December 31, 2003; 3287 days) period, HHC admitted 16,906 ischemic

<table>
<thead>
<tr>
<th>Variable</th>
<th>Max</th>
<th>q75</th>
<th>Median</th>
<th>q25</th>
<th>Min</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>URI, count</td>
<td>3006</td>
<td>1134</td>
<td>866.3</td>
<td>580</td>
<td>87</td>
<td>875.9</td>
<td>390.9</td>
</tr>
<tr>
<td>Air temperature, °C</td>
<td>33.47</td>
<td>21.24</td>
<td>12.79</td>
<td>5.42</td>
<td>15.6</td>
<td>12.80</td>
<td>9.299</td>
</tr>
<tr>
<td>Relative humidity, %</td>
<td>100</td>
<td>76.5</td>
<td>64.75</td>
<td>54.75</td>
<td>22.88</td>
<td>65.70</td>
<td>14.86</td>
</tr>
<tr>
<td>Grass pollen, count</td>
<td>324</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>5.6</td>
<td>12.86</td>
</tr>
<tr>
<td>SO$_2$, ppm</td>
<td>0.096</td>
<td>0.014</td>
<td>0.009</td>
<td>0.005</td>
<td>0</td>
<td>0.0108</td>
<td>0.009124</td>
</tr>
<tr>
<td>PM $&lt;10\mu$m, mg/m$^3$</td>
<td>89.53</td>
<td>30.5</td>
<td>22.74</td>
<td>16.09</td>
<td>0</td>
<td>23.56</td>
<td>12.52</td>
</tr>
<tr>
<td>NO$_2$, ppm</td>
<td>0.073</td>
<td>0.027</td>
<td>0.019</td>
<td>0.014</td>
<td>0</td>
<td>0.02087</td>
<td>0.009961</td>
</tr>
<tr>
<td>NO$_x$, ppm</td>
<td>0.433</td>
<td>0.083</td>
<td>0.057</td>
<td>0.038</td>
<td>0</td>
<td>0.06596</td>
<td>0.03927</td>
</tr>
<tr>
<td>O$_3$, ppm</td>
<td>0.074</td>
<td>0.008</td>
<td>0.003</td>
<td>0.001</td>
<td>0</td>
<td>0.005843</td>
<td>0.007006</td>
</tr>
<tr>
<td>CO, ppm</td>
<td>5.124</td>
<td>1.624</td>
<td>0.888</td>
<td>0.595</td>
<td>0</td>
<td>1.149</td>
<td>0.7155</td>
</tr>
<tr>
<td>Total pollen, count</td>
<td>9301</td>
<td>112</td>
<td>24</td>
<td>2</td>
<td>0</td>
<td>351.1</td>
<td>1355</td>
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<tr>
<td>Strokes (narrow), count</td>
<td>14</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>4.219</td>
<td>2.152</td>
</tr>
<tr>
<td>Strokes (broad), count</td>
<td>15</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>5.144</td>
<td>2.390</td>
</tr>
</tbody>
</table>
stroke patients (broad definition), a mean of 5.1±2.4 per day; narrow definition statistics are 13,906 and 4.2±2.1. During the 366-day prospective period, statistics are 1885 patients (broad definition), 5.1±2.5 per day, and narrow definition 1506 admissions, 4.1±2.1 admissions per day. Distribution statistics are in Table 1.

### TABLE 3. ARIMA Models

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Coefficient</th>
<th>SE</th>
<th>( P )</th>
<th>Shift</th>
<th>Lag</th>
<th>Maximum Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Broad</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>4.621</td>
<td>0.307</td>
<td>&lt;0.0001</td>
<td>0</td>
<td>0</td>
<td>4.621</td>
</tr>
<tr>
<td>MA 14</td>
<td>0.039</td>
<td>0.018</td>
<td>0.027</td>
<td>0</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Sunday</td>
<td>-0.5</td>
<td>0.155</td>
<td>0.0011</td>
<td>0</td>
<td>0</td>
<td>-0.5</td>
</tr>
<tr>
<td>Saturday</td>
<td>-0.63</td>
<td>0.152</td>
<td>&lt;0.0001</td>
<td>0</td>
<td>0</td>
<td>-0.63</td>
</tr>
<tr>
<td>Friday</td>
<td>-0.39</td>
<td>0.116</td>
<td>0.0009</td>
<td>0</td>
<td>0</td>
<td>-0.39</td>
</tr>
<tr>
<td>Holiday</td>
<td>-0.76</td>
<td>0.24</td>
<td>0.0016</td>
<td>0</td>
<td>0</td>
<td>-0.76</td>
</tr>
<tr>
<td>URI</td>
<td>83E-5</td>
<td>18E-5</td>
<td>&lt;0.0001</td>
<td>0</td>
<td>0</td>
<td>2.496</td>
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<tr>
<td>Air temperature</td>
<td>0.103</td>
<td>0.006</td>
<td>0.0211</td>
<td>0</td>
<td>0</td>
<td>0.44</td>
</tr>
<tr>
<td>Relative humidity</td>
<td>-0.01</td>
<td>0.003</td>
<td>0.0187</td>
<td>12</td>
<td>0</td>
<td>-0.63</td>
</tr>
<tr>
<td>Grass pollen</td>
<td>0.011</td>
<td>0.003</td>
<td>0.0341</td>
<td>5</td>
<td>0</td>
<td>3.619</td>
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<tr>
<td>SO2</td>
<td>8.878</td>
<td>4.471</td>
<td>0.0471</td>
<td>0</td>
<td>0</td>
<td>0.857</td>
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<tr>
<td>PM10</td>
<td>0.008</td>
<td>0.004</td>
<td>0.0404</td>
<td>8</td>
<td>0</td>
<td>0.677</td>
</tr>
<tr>
<td><strong>Narrow</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>4.082</td>
<td>0.268</td>
<td>&lt;0.0001</td>
<td>0</td>
<td>0</td>
<td>4.082</td>
</tr>
<tr>
<td>MA 14</td>
<td>0.035</td>
<td>0.018</td>
<td>0.0453</td>
<td>0</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Sunday</td>
<td>-0.32</td>
<td>0.141</td>
<td>0.0251</td>
<td>0</td>
<td>0</td>
<td>-0.32</td>
</tr>
<tr>
<td>Saturday</td>
<td>-0.28</td>
<td>0.139</td>
<td>0.0444</td>
<td>0</td>
<td>0</td>
<td>-0.28</td>
</tr>
<tr>
<td>Friday</td>
<td>-0.24</td>
<td>0.107</td>
<td>0.0237</td>
<td>0</td>
<td>0</td>
<td>-0.24</td>
</tr>
<tr>
<td>Holiday</td>
<td>-0.57</td>
<td>0.219</td>
<td>0.0087</td>
<td>0</td>
<td>0</td>
<td>-0.57</td>
</tr>
<tr>
<td>URI</td>
<td>63E-5</td>
<td>16E-5</td>
<td>0.0001</td>
<td>0</td>
<td>0</td>
<td>1.888</td>
</tr>
<tr>
<td>Air temperature</td>
<td>0.011</td>
<td>0.005</td>
<td>0.0251</td>
<td>0</td>
<td>0</td>
<td>0.378</td>
</tr>
<tr>
<td>Relative humidity</td>
<td>-0.01</td>
<td>0.002</td>
<td>0.0095</td>
<td>12</td>
<td>0</td>
<td>-0.64</td>
</tr>
<tr>
<td>Grass pollen</td>
<td>0.009</td>
<td>0.003</td>
<td>0.0370</td>
<td>5</td>
<td>0</td>
<td>3.034</td>
</tr>
</tbody>
</table>

For strokes, bivariate comparisons with \( P<0.05 \) are shown with *; \( P<0.01 \) with **. The top half of the table models the broad definition of stroke; the bottom half models the narrow definition. Columns show the estimated equation coefficient, the SE of that estimate, the \( P \) value, the delay (shift or lag) of the effects, the maximum possible effect a variable in the ARIMA model could have on the No. of strokes. \( *MA 14* \) is the 14-day moving average term.
Bivariate Analysis

Broadly and narrowly defined strokes are highly correlated: \( r = 0.9216, r^2 = 0.8494; P < 0.0001 \). Workdays (not Sunday, Saturday, or holidays) form 69% of days sampled; 73% of strokes present on workdays \((P < 0.0001)\), as did 83% of URIs \((P < 0.0001)\). NO\(_2\) is a major component of NO\(_x\); \( r = 0.599 \).

Other variables show smaller correlations with each other and with strokes (Table 2).

The scatter plot of stroke admissions per day versus time (Figure 1) shows little seasonal variation; harmonic curve fit shows a slight peak in early September, and in early July, a trough that is 0.6 visits per day lower (Figure 1, green dashed line; \( P = 0.0415 \)). Other tests for yearly variation showed no statistically significant effect. On Sundays, 2359 (12.55%) stroke patients presented; 2802 (14.91%) on Monday; 2964 (15.77%) on Tuesday; 2879 (15.32%) on Wednesday; 2812 (14.96%) on Thursday; 2661 (14.16%) on Friday; and 2314 (12.31%) on Saturday \((P < 0.0001)\). Table 2 (and Figures 2 and 3, as well as supplemental Figures I and II, available online at http://stroke.ahajournals.org) shows bivariate relationships between strokes and other explanatory variables.

Multivariate Analysis

Table 3 shows our ARIMA models. Adjusted for the other factors, there are 0.5 fewer broadly defined strokes on Sundays \((P = 0.0011)\). Each 1 mg/m\(^3\) increase in PM10 should produce an additional 0.008 visits \((P = 0.0404)\); at the highest concentration of PM10 (89.53 mg/m\(^3\)), we would predict an additional 0.677 strokes. Other variables in the table are similarly interpreted. All ARIMA models fit well for both time periods; 95% of observed points fell within the 95% CIs. Figure 1 plots these (broad definition). We did not find independent statistically significant effects of September 11th, ED asthma visits, daily temperature change, or other pollutants. Eliminating the ICD-9 433 charts produced little change in either model except that for SO\(_2\); \( P = 0.0539 \).

Discussion

Compared with many other pollution studies,\(^{12,20,21}\) our study covers a small geographic area, with 1 set of pollutant definitions and regulatory standards. The study is large and long lasting. Patients come from 1 health care system. These reduce variability.

The counts of narrow definition strokes and broad definition strokes were highly correlated \((r = 0.9216)\), as was suggested previously by previous research.\(^{22}\) Broad and narrow definition models are similar (Tables 2 and 3). Eliminating ICD-9 433 charts and our narrow definition exclude poorly defined conditions that may not be strokes. Those restrictions also exclude strokes that, for various reasons, could not be fully worked up or narrowly defined. Most epidemiologic studies like ours used definitions that were as broad, or broader, than our “broad definition.”\(^{6,8,10–13,20}\) Piriyawat\(^{23}\) and Broderick\(^{24}\) verified the validity of these definitions by chart review. Where space limitations preclude thorough discussion of all models, we used the broad definition, including ICD-9 433 patients.

There are more URI visits on workdays, when clinics are open. The increase in stroke counts on workdays is relatively smaller. This may cause us to underestimate the effect of URIs on stroke (bivariate plot in Figure 2). If we include a URI workday interactive effect in the model, the URI effect...
increases. The interactive effect did not meet model entry criteria.

Seasons, allergens, pollutants, temperature, and URI incidence are inter-related. By potentially including all of these variables, we reduced the possibility of incorrectly modeling a variable that is temporally related but less causally connected (ie, an epiphénoménal). Our statistical power analysis suggests that we could find weak effects, and we found some. Unlike some previous studies, we report both probability values and effect magnitude. Our models show modest relationships (Table 3). Assuming causality, modest mitigation of adverse environmental effects might reduce some morbidity and mortality. This could be as beneficial to the overall group of stroke patients as intravenous thrombolysis has been.

Time and Weather
We noted fewer strokes on weekends, as did Oberg and Jakovljević. We found little evidence of seasonality in bivariate analysis and no significant effect after URI, grass pollen, and weather have been adjusted for. Other investigators, using different time series methods with fewer covariables, report time effects. Oberg found a complex yearly pattern. Kelly-Hayes reported a complex yearly pattern and Monday peaks. Shinkawa reported seasonal variation, a positive relationship to daily temperature change and a negative relationship to average daily temperature. The World Health Organization collaborative study involved data from many different cities and complex modeling. Unlike us, they found more strokes with lower temperature. Colder temperature exacerbates asthma; temperature may have both proinflammatory and countervailing effects on patients at risk for stroke. Rothwell did not find seasonal variation in stroke admissions in Edinburgh, UK. They speculate that seasonal variations in stroke death rates might be attributable to comorbid conditions including respiratory infection. Field did not find a seasonal pattern of hospitalizations in Canada. Wang reported a winter peak in Australia.

Although total pollen count would fit our ARIMA model, the subset grass pollen count fits better. This is consistent with the inflammatory theory; grass pollen is especially allergenic.

Pollution
Bivariate analysis (Table 2) shows statistically significant effects of PM10 (Figure 3), NO2, NOx, and CO. When atmospheric variables are cross-correlated with each other, one could be a marker for another. Our ARIMA models allow us to examine one atmospheric effect while controlling for the others and for the moving average effect. The broad definition model shows significant immediate PM10 and delayed SO2 effects. These trends were present but not statistically significant in the narrow definition model. Hong found small immediate PM10 and SO2 and delayed NOx, CO, and O2 effects. Maheswaran found that Englishmen and Welshmen who lived close to a major road (a PM10 source) had a relatively high incidence of stroke death. Complex, multinational APHEA (Air Pollution and Health: a European Approach) studies show some relationship between air pollution and cardiac disease but not to stroke. Tsai studied 12,748 stroke admissions with before and after case crossover designs. They found some effect for all pollutants except SO2.

Neither Hong nor Tsai describe controlling experiment-wise type I errors.

Seaton suggests that pulmonary inflammation links air pollution to stroke. Cold air, dry air, air pollutants, and URIs are known causes of pulmonary and sometimes systemic inflammation. Previous research links strokes to infections and positis inflammation as the mechanistic link.

Limitations
Counts of HHC URI patients is an approximate measure of the URI exposure for HHC patients at risk for stroke. Contact between these patients is variable. Some URI patients saw non-HHC physicians or no physician. PM10 is composed of particles of many sizes and chemical reactivity. Smaller and more chemically reactive particles may promote relatively more inflammation and strokes. Most PM10 measurements are interpolated. Some allergen measurements are interpolated. Some diagnoses of URI or stroke may be inaccurate, leading to inaccurate counts. Unbiased but inaccurate measurements generally cause us to underestimate the extent of statistical relationships.

Conclusions
With a fairly large study modeling weather, time factors, and pollutants, we found modest, independent exacerbating effects of low humidity, high temperature, dry air, grass pollen, URIs, SO2, and PM10 on stroke incidence. We did not find a September 11th effect. Stroke admissions were lower on weekends and holidays.

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