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Particulate Air Pollution and the Rate of Hospitalization for Congestive Heart Failure among Medicare Beneficiaries in Pittsburgh, Pennsylvania

Gregory A. Wellenius[1,2], Thomas F. Bateson[2,3], Murray A. Mittleman[1,3], and Joel Schwartz[2,3]

[1] Cardiovascular Epidemiology Research Unit, Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA.
[2] Department of Environmental Health, Harvard School of Public Health, Boston, MA.
[3] Department of Epidemiology, Harvard School of Public Health, Boston, MA.

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The authors used a case-crossover approach to evaluate the association between ambient air pollution and the rate of hospitalization for congestive heart failure among Medicare recipients (aged ≥65 years) residing in Allegheny County (Pittsburgh area), Pennsylvania, during 1987–1999. They also explored effect modification by age, gender, and specific secondary diagnoses. During follow-up, 55,019 patients were admitted with a primary diagnosis of congestive heart failure. In single-pollutant models, particulate matter with an aerodynamic diameter of <10 μm (PM_{10}), carbon monoxide, nitrogen dioxide, and sulfur dioxide—but not ozone—were positively and significantly associated with the rate of admission on the same day. The strongest associations were observed with carbon monoxide, nitrogen dioxide, and PM_{10}. The associations with carbon monoxide and nitrogen dioxide were the most robust in two-pollutant models, remaining statistically significant even after adjusting for other pollutants. Patients with a recent myocardial infarction were at greater risk of particulate-related admission; otherwise, there was no significant effect modification by age, gender, or other secondary diagnoses. These results suggest that short-term elevations in air pollution from traffic-related sources may trigger acute cardiac decompensation in heart failure patients and that those with certain comorbid conditions may be more susceptible to these effects.

aged; air pollution; cardiovascular diseases; disease susceptibility; heart failure, congestive; hospitalization; Medicare

Abbreviations: CHF, congestive heart failure; CI, confidence interval; ICD-9, *International Classification of Diseases*, Ninth Revision; PM_{10}, particulate matter with an aerodynamic diameter of <10 μm.

Congestive heart failure (CHF) affects approximately 5 million people in the United States (1). Age-adjusted incidence rates do not appear to be increasing (2, 3), but the prevalence is expected to increase as the population ages and heart failure mortality continues to decline (4). Hospital discharges for CHF have increased 164 percent over the past two decades from 377,000 in 1979 to 995,000 in 2001 (1). Thus, the identification of precipitating factors that lead to acute cardiac decompensation and subsequent hospitalization is of considerable public health interest.

Acute decompensation can be precipitated by pathologic, behavioral (5–9), and environmental factors such as extreme temperatures (5), smoking (10), and exposure to carbon monoxide and air particles with an aerodynamic diameter of less than 10 μm (PM_{10}) (11–14). Although a secondary diagnosis of CHF may affect pollution-related hospitalizations for ischemic heart disease (15, 16), subgroups of CHF patients more susceptible to environmental triggers have not been identified.

Accordingly, we evaluated the following specific hypotheses: 1) short-term elevations in PM_{10} are associated with an increased rate of cardiac decompensation and subsequent hospitalization for CHF, and 2) the increase in the rate is more pronounced for older persons and those with specific

Correspondence to Dr. Gregory A. Wellenius, Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Deaconess 306, Boston, MA 02215 (e-mail: gwelleni@bidmc.harvard.edu).

comorbid conditions. We evaluated these hypotheses by using the case-crossover study design (17), which is well suited to assessing the effects of transient exposures on the subsequent risk of acute events (18). Although our primary hypotheses relate to particulate matter, we also evaluated the association between ambient measures of other criteria pollutants and the rate of hospitalization for CHF.

MATERIALS AND METHODS

Study population

We obtained information on hospital admissions from the Centers for Medicare and Medicaid Services, which provides financial reimbursement of inpatient hospital admission costs for most US citizens aged 65 years or older. Cases were defined as persons admitted from the emergency room with a primary discharge diagnosis of CHF (*International Classification of Diseases*, Ninth Revision (ICD-9), codes 428.0 and 428.1) between January 1, 1987, and November 30, 1999, and residing in Allegheny County (Pittsburgh area), Pennsylvania, as noted in the Medicare claims record. For patients admitted multiple times, we considered only those admissions that occurred more than 14 days since the last included admission. Pittsburgh was chosen because it is one of the larger cities for which daily air quality data are available for many years. This study was granted an exemption from institutional review board review by the Harvard School of Public Health Human Subjects Committee.

Daily integrated (24-hour) measures of PM_{10} and hourly measures of ozone, carbon monoxide, sulfur dioxide, and nitrogen dioxide were obtained from the Aerometric Information Retrieval System of the US Environmental Protection Agency. The measurement methods used to determine ambient concentrations of each pollutant have been described elsewhere (19). Measures of PM_{10} were available from 17 monitoring sites, ozone from four sites, carbon monoxide from three sites, sulfur dioxide from 10 sites, and nitrogen dioxide from two sites. We computed local daily mean concentrations of each pollutant by using an algorithm that accounts for monitor-specific means and variances, as described previously (20). We excluded from analysis 2 days on which PM_{10} levels exceeded 150 $\mu g/m^3$, the current 24-hour Environmental Protection Agency standard.

We obtained National Weather Service data on daily mean ambient temperature, barometric pressure, and dew point from the EarthInfo CD-ROM entitled NCDC Surface Airways (EarthInfo, Inc., Boulder, Colorado) and calculated apparent temperature (an index of human discomfort) as described previously (21–23).

Study design and statistical analysis

We used the case-crossover study design to assess the effect of changes in daily mean concentrations of PM_{10}, sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone on the rate of hospitalization for acute decompensated CHF. Our primary exposure of interest was mean daily PM_{10} concentrations. Exposure during the case period was defined as mean PM_{10} concentration either on the day of admission (lag 0) or 1–3 days preceding admission (lags 1–3). Control periods were chosen by using the time-stratified approach (24, 25) such that exposures during the case period were compared with exposures occurring on all other days of the same month (before or after the event day) that fell on the same day of the week as the case period (26).

We performed conditional logistic regression, stratifying on each hospitalization, to obtain estimates of odds ratios and 95 percent confidence intervals associated with an interquartile-range increase in the mean daily level of each pollutant. In this paper, effect estimates are reported as percent change in rate of hospitalization. In all analyses, we modeled the mean apparent temperature at lag 0 as a quadratic function, and mean apparent temperature at lag 1 and mean barometric pressure at lag 0 as linear functions of continuous variables. We modeled PM_{10}, sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone as linear functions of continuous variables. We first evaluated the effect of PM_{10} separately at lags of 0–3 days in single-pollutant models. On the basis of the results of this analysis, we selected a single lag for all subsequent analyses. Pollutants were first considered separately by using single-pollutant models and then jointly by using two-pollutant models. We assessed the assumption of linearity by using standard methods, including examining the shape of the dose-effect curve fitted with fractional polynomials and linear splines, and found the assumption of linearity over the range of our data to be reasonable.

We examined effect modification by considering categories of age ($\geq$80 vs. 65–79 years as the referent), gender, and the presence of secondary diagnoses of atrial fibrillation (ICD-9 code 427.31), other cardiac arrhythmias (ICD-9 code 427, except 427.31), chronic obstructive pulmonary disease (ICD-9 codes 490–496), essential hypertension (ICD-9 code 401), type 2 diabetes (ICD-9 codes 250.x0 and 250.x2), acute myocardial infarction within the past 30 days (ICD-9 code 410), old myocardial infarction (ICD-9 code 412), angina pectoris (ICD-9 code 413), other forms of ischemic heart disease (ICD-9 codes 411 and 414), and acute respiratory infections (ICD-9 codes 460–466 and 480–487).

All reported p values are based on two-sided tests. A p value of <0.05 was considered statistically significant. All analyses were performed by using SAS statistical software, version 8 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

There were 55,019 admissions from the emergency room with a primary discharge diagnosis of CHF among Medicare beneficiaries residing in Allegheny County (Pittsburgh area), Pennsylvania, between January 1, 1987, and November 30, 1999. Of these cases, 37.4 percent were patients admitted only once for CHF during the observation period, and 86.8 percent were patients admitted five or fewer times. Among patients admitted more than once, the median time between admissions was 154 days. Age on the day of admission ranged from 65 to 108 years (mean, 78.9; standard deviation, 7.78). Other characteristics of the cases are summarized in table 1.

TABLE 1. Characteristics of congestive heart failure cases among Medicare beneficiaries in Allegheny County, Pennsylvania, 1987–1999

	No. of cases ($n = 55,019$)	%
Age ≥80 years	25,713	46.7
Male gender	22,333	40.6
White race	47,674	86.7
Primary diagnosis		
ICD-9* code 428.0†	54,346	98.8
ICD-9 code 428.1‡	673	1.2
Secondary diagnoses		
Ischemic heart disease	21,232	38.6
Atrial fibrillation	14,139	25.7
COPD*	12,579	22.9
Essential hypertension	9,182	16.7
Type 2 diabetes	7,670	13.9
Other arrhythmias	6,639	12.1
Acute respiratory infections	3,123	5.7
Old myocardial infarction	2,212	4.0
Recent myocardial infarction	2,024	3.7
Angina pectoris	1,968	3.6

* ICD-9, *International Classification of Diseases*, Ninth Revision; COPD, chronic obstructive pulmonary disease.
† Congestive heart failure, unspecified.
‡ Left heart failure.

The distribution of average daily concentrations of particulate and gaseous air pollutants is shown in table 2, and pairwise correlations between pollutants are shown in table 3.

PM_{10} and the rate of hospitalization for CHF

Initially, we estimated the effect of PM_{10} separately for lags of 0–3 days and found a 3.07 (95 percent confidence interval (CI): 1.59, 4.57; $p < 0.0001$) percent increase in the rate associated with an interquartile-range increase in PM_{10} on the day of admission (lag 0). When we controlled for the effect at lag 0, PM_{10} levels 1–3 days before the admission day were not associated with an altered rate of hospitalization. Additionally, the use of a 2-day moving average (average of lags 0 and 1) did not materially alter the results. Therefore, in subsequent analyses, we considered PM_{10} levels on the day of admission only. Controlling for ambient temperature and barometric pressure rather than apparent temperature also did not materially alter the results. Including only the first observed admission for each patient yielded a qualitatively similar, but less precise effect estimate.

Daily concentrations of other air pollutants were highly correlated with PM_{10} levels (table 3). We used two-pollutant models to evaluate potential confounding by simultaneous exposure to these co-pollutants (table 4). Controlling for either ozone or sulfur dioxide did not materially alter the estimated effect of PM_{10}. However, in two-pollutant models controlling for either carbon monoxide or nitrogen dioxide, the effect of PM_{10} was negligible.

Gaseous co-pollutants and the rate of hospitalization for CHF

In single-pollutant models, daily fluctuations in ambient levels of carbon monoxide, nitrogen dioxide, and sulfur dioxide—but not ozone—were positively and significantly associated with the rate of hospitalization for CHF on the same day (table 4). In two-pollutant models, the effects of both carbon monoxide and nitrogen dioxide were not materially changed by adjustment for most other measured pollutants, including PM_{10}. Ozone was not significantly associated with the rate of hospitalization for CHF in either single-pollutant or two-pollutant models.

Identification of susceptible subgroups

The effect of PM_{10} was more than threefold greater in patients with a secondary diagnosis indicating a myocardial

TABLE 2. Distribution of average daily concentrations of air pollutants in Allegheny County, Pennsylvania, 1987–1999

	% of days missing	Mean (SD*)	Percentile				
			5	25	50	75	95
PM_{10}* ($\mu g/m^3$)	0.78	31.06 (20.10)	8.89	16.31	25.69	40.39	70.49
Carbon monoxide (ppm)	0.23	1.03 (0.53)	0.42	0.68	0.91	1.23	2.04
Nitrogen dioxide (ppb)	0.93	26.48 (8.02)	15.10	20.61	25.70	31.30	41.02
Ozone (ppb)	2.90	24.30 (12.23)	7.01	14.60	23.15	31.96	46.37
Sulfur dioxide (ppb)	0.02	14.78 (9.88)	3.98	7.70	12.24	18.98	33.93
Temperature (°C)	0	11.09 (9.88)	−5.36	3.03	11.74	19.83	25.00
Apparent temperature† (°C)	0	10.32 (10.97)	−6.12	0.80	9.79	19.92	27.56

* SD, standard deviation; PM_{10}, particulate matter with an aerodynamic diameter of <10 μm.
† Defined as a person's perceived air temperature by using the formula $AT = -2.653 + (0.994 \times Ta) + (0.0153 \times Td^2)$, where AT is the apparent temperature, Ta is the air temperature in degrees Celsius, and Td is the dew-point temperature in degrees Celsius.

TABLE 3. Pearson's pairwise correlation coefficients among air pollutants in Allegheny County, Pennsylvania, 1987–1999

	Carbon monoxide	Nitrogen dioxide	Ozone	Sulfur dioxide
PM_{10}*	0.57	0.64	0.29	0.51
Carbon monoxide	1	0.70	−0.25	0.54
Nitrogen dioxide		1	−0.04	0.52
Ozone			1	−0.19
Sulfur dioxide				1

* PM_{10}, particulate matter with an aerodynamic diameter of <10 μm.

infarction within the past 30 days (rate ratio = 9.62, 95 percent CI: 3.14, 16.52 vs. rate ratio = 2.80, 95 percent CI: 1.29, 4.32; $p_{\text{homogeneity}} = 0.042$). Similarly, the effect of carbon monoxide was approximately twofold greater in patients with a recent myocardial infarction, but this difference in the rate ratios did not reach statistical significance (rate ratio = 8.99, 95 percent CI: 3.34, 14.95 vs. rate ratio = 4.36, 95 percent CI: 3.12, 5.62; $p_{\text{homogeneity}} = 0.12$). In contrast, the effect of neither PM_{10} nor carbon monoxide was significantly stronger for patients with a secondary diagnosis of an old myocardial infarction. The effect of either pollutant did not vary significantly by age, gender, or the presence of any other secondary diagnosis examined.

DISCUSSION

Heart failure patients may remain asymptomatic for extended periods if compensatory mechanisms and/or treatment is sufficient to balance the cardiac dysfunction. Factors that commonly disturb this balance include treatment noncompliance, uncontrolled hypertension, atrial fibrillation, acute respiratory infections, and myocardial ischemia or infarction (5–9). Although short-term increases in ambient particle levels have been associated with cardiovascular morbidity and mortality (27, 28), relatively few studies have examined their effect on CHF morbidity. We found that short-term increases in mean daily levels of ambient particles and/or other pollutants may also precipitate acute cardiac decompensation leading to hospitalization, most notably in patients with a recent myocardial infarction.

In single-pollutant models, PM_{10}, carbon monoxide, nitrogen dioxide, and sulfur dioxide (but not ozone) were significantly associated with CHF admissions—carbon monoxide, nitrogen dioxide, and PM_{10} most strongly. Previous studies found similar results for these three pollutants (13, 14, 29) or for only carbon monoxide and nitrogen dioxide, but not PM_{10} (30). In two-pollutant models, associations with carbon monoxide and nitrogen dioxide were the most robust, as noted before (12, 14, 29). However, given the high correlation among ambient measures of PM_{10}, carbon monoxide, and nitrogen dioxide, two-pollutant modeling is of limited value in disentangling their effects.

Generally, the effect estimates derived from single-pollutant models (table 5) in the current study are similar to those from previous reports. For example, previous estimates of the increase in CHF morbidity range from 2 percent to 7 percent (13, 14, 29, 30) for a 1-ppm increase in ambient carbon monoxide. Previous estimates of the effects of PM_{10} have also been similar (14, 30, 31) although not always statistically significant. For instance, Schwartz and Morris (12) found a 0.99 (95 percent CI: 0.37, 1.60) percent higher rate of admissions for CHF associated with a 10-$\mu g/m^3$ increase in 2-day mean PM_{10}. Hoek et al. (32) found that a 10-$\mu g/m^3$ increase in the 7-day mean concentration of PM_{10} was associated with a 0.44 (95 percent CI: −0.51, 1.40) percent increase in the risk of CHF mortality. Two other studies (33, 34) reported an association between ambient

TABLE 4. Percent increase (and 95% confidence interval) in the rate of hospital admission for congestive heart failure associated with an interquartile-range increase in pollutant levels in single-pollutant and two-pollutant models,* Allegheny County, Pennsylvania, 1987–1999

Pollutant (IQR†)	Single pollutant		Adjusted for PM_{10}†		Adjusted for carbon monoxide		Adjusted for nitrogen dioxide		Adjusted for ozone		Adjusted for sulfur dioxide	
	% increase	95% CI†	% increase	95% CI	% increase	95% CI	% increase	95% CI	% increase	95% CI	% increase	95% CI
PM_{10} (24 μg/m^3)	3.07	1.59, 4.57	NA†		−1.10	−3.02, 0.86	0.52	−1.46, 2.53	2.80	1.29, 4.33	2.18	0.37, 4.02
Carbon monoxide (0.55 ppm)	4.55	3.33, 5.79	5.18	3.49, 6.89	NA		4.84	3.06, 6.66	4.35	3.08, 5.64	4.51	3.15, 5.90
Nitrogen dioxide (11 ppb)	4.22	2.61, 5.85	4.05	1.83, 6.31	−0.37	−2.59, 1.89	NA		3.73	2.10, 5.39	3.79	1.93, 5.67
Ozone (17 ppb)	−1.60	−3.77, 0.61	−1.96	−4.14, 0.27	0.13	−2.12, 2.44	−1.19	−3.38, 1.06	NA		−1.41	−3.58, 0.81
Sulfur dioxide (11 ppb)	2.36	1.05, 3.69	1.35	−0.27, 2.99	0.10	−1.35, 1.57	0.68	−0.82, 2.21	2.02	0.68, 3.37	NA	

* In models controlling for barometric pressure and apparent temperature.
† IQR, interquartile range; PM_{10}, particulate matter with an aerodynamic diameter of <10 μm; CI, confidence interval; NA, not applicable.

TABLE 5. Summary of effect estimates from single-pollutant models expressed for standard increments in each air pollutant, Allegheny County, Pennsylvania, 1987–1999

Pollutant	Increment	Increase in rate (%)	95% CI*
PM_{10}*	10 μg/m^3	1.27	0.66, 1.88
Carbon monoxide	1 ppm	8.43	6.14, 10.77
Nitrogen dioxide	10 ppb	3.83	2.37, 5.30
Ozone	10 ppb	−0.95	−2.23, 0.36
Sulfur dioxide	10 ppb	2.14	0.95, 3.35

* CI, confidence interval; PM_{10}, particulate matter with an aerodynamic diameter of <10 μm.

particles and CHF mortality, but differences in exposure metrics for ambient particles prevent direct comparison to the current study.

Our effect estimate for PM_{10} from the current study is similar to that of the National Morbidity, Mortality, and Air Pollution Study (NMMAPS), a large multicity study. With a 10-μg/m^3 increase in same-day PM_{10}, we found a 1.27 (95 percent CI: 0.66, 1.88) percent increase in CHF hospitalizations, while the National Morbidity, Mortality, and Air Pollution Study found a 0.84 (95 percent CI: 0.51, 1.18) percent increase in total cardiovascular disease hospitalizations among Medicare beneficiaries aged 65 years or older in Pittsburgh and a 1.02 (95 percent CI: 0.76, 1.27) percent increase in 14 cities combined (26).

Agent(s) responsible for the observed associations

In studies carried out in single cities, it is not possible to clearly distinguish the effects of multiple pollutants that covary strongly over time. Therefore, the effect we are attributing to ambient particles may be mediated at least in part by gaseous co-pollutants.

Three pieces of evidence support ambient particles as the responsible agent. First, ambient measures of gaseous pollutants at a central site are poorly correlated with personal exposure to those pollutants. For example, one study (35) found this to be true of nitrogen dioxide. Instead, ambient measures of both nitrogen dioxide and carbon monoxide were strongly and significantly associated with personal measures of exposure to particulate matter with an aerodynamic diameter of less than 2.5 μm and even more so with personal exposure to elemental carbon, a surrogate for traffic-related particles. Second, several large multicity studies have concluded that gaseous co-pollutants do not confound the association between PM_{10} and daily deaths (28, 36, 37), and it may in fact be inappropriate to control for them. Third, biologic plausibility is evidenced by animal toxicologic and human panel studies, which suggest that particulate-related decompensation of heart failure patients may be mediated by relative increases in sympathetic nervous system activity (38, 39), inappropriate changes in vasomotor tone (40), or triggering or exacerbation of myocardial ischemia (41, 42). In contrast, carbon monoxide has been shown to have vasodilatory (43) and antiarrhythmic (44) properties in laboratory animals, both of which would be expected to reduce the risk of acute decompensation.

Most consistent with our data is the interpretation that elevations in a combination of ambient particles, carbon monoxide, and nitrogen dioxide are responsible for the association. In urban areas, the primary source of carbon monoxide is motor vehicle emissions, which also contribute significantly to ambient levels of nitrogen dioxide and PM_{10}. Thus, motor vehicle emissions may be the responsible exposure. This interpretation is supported by recent epidemiologic studies showing that living in proximity to major roadways is associated with increased rates of cerebrovascular (45), cardiopulmonary (46), and all-cause (47) mortality. Additionally, a study of 14 US cities (48) found that the magnitude of the association between PM_{10} and cardiovascular hospital admissions increased significantly as the proportion of particles from highway vehicles increased. As discussed above, toxicologic evidence points to particles as the most likely culprit. However, toxicologic studies that examine the cardiovascular effects of traffic-related pollutant mixtures are still needed.

If causal, the results of the current study are noteworthy. Among those aged 65 years or older, the rate of hospitalization with a primary diagnosis of CHF is estimated as 222 per 10,000 person-years (49). If we take this as the underlying rate of hospitalization in the target population at the median PM_{10} concentration and assume that PM_{10} is an adequate marker of the pollution episodes responsible for the observed associations, then the daily PM_{10} levels over the median value resulted in an approximately 1.5 percent excess rate of admission. Although this relative increase in rate is small, the absolute increase in hospital admissions may be quite high given that 995,000 hospitalizations for CHF took place in the United States in 2001 (1).

Identification of susceptible subgroups

Previous studies suggest that CHF patients are at greater risk of pollution-related hospitalization for ischemic heart disease (15) and acute myocardial infarction (16), as well as nonaccidental mortality (50, 51). However, to our knowledge, subgroups of CHF patients at increased risk of pollution-related acute decompensation have not been identified previously.

We did not confirm, for either PM_{10} or carbon monoxide, recent reports that patients with diabetes may be particularly susceptible to the effects of ambient particles (16, 52–54), presumably because of increased endothelial dysfunction.

The possibility that patients with a history of myocardial infarction may be at greater risk for pollution-related events was evaluated among Medicare beneficiaries in Cook County, Illinois (54). The association between PM_{10} and all-cause mortality was more than twice as large among patients with versus without a history of myocardial infarction. We found that the association between PM_{10} and the rate of admission for CHF was nearly threefold greater among patients with a recent myocardial infarction than those without. A smaller increase in the association, not statistically significant, was observed for carbon monoxide.

Enhanced susceptibility was much less pronounced among patients with an old infarct, suggesting that the remodeling myocardium may be more susceptible to pollution.

Limitations

First, particle concentrations were measured by using PM_{10}, whereas particulate matter with an aerodynamic diameter of less than 2.5 μm is the currently regulated measure based on studies suggesting their greater toxicity. Second, the use of ambient PM_{10} levels rather than personal exposure measures, while highly correlated with indoor and personal PM_{10} levels (55), will result in some nondifferential misclassification, tending to underestimate risk. Third, admission dates may have differed from the date of symptom onset, resulting in some exposure misclassification and underestimation of the true relative risk. Fourth, disease misclassification is also possible as a result of diagnostic or coding errors, although these errors are likely unrelated to pollution levels. While the direction of the resulting bias is expected to be toward the null, the magnitude is expected to be small.

A potential limitation inherent to research using administrative data sets is the lack of information on chronic risk factors for disease. However, a strength of the case-crossover design used in this study is that self-matching ensures that, within strata, there is no variability in—or confounding by—chronic risk factors, whether measured or unmeasured.

Summary and implications

Short-term increases in a combination of particulate air pollution, carbon monoxide, and nitrogen dioxide were associated with acute decompensation and subsequent hospitalization of heart failure patients, especially those with a recent myocardial infarction. This and other studies suggest that motor vehicle emissions are the responsible exposure. Because of the large number of hospitalizations for CHF, even a modest increase in rate can account for a large number of admissions, which may be preventable.

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