

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Ischemic Heart Disease Events Triggered by Short-Term Exposure to Fine Particulate Air Pollution

C. Arden Pope, III, Joseph B. Muhlestein, Heidi T. May, Dale G. Renlund, Jeffrey L. Anderson and Benjamin D. Horne

Circulation 2006;114:2443-2448; originally published online Nov 13, 2006;

DOI: 10.1161/CIRCULATIONAHA.106.636977

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

Copyright © 2006 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circ.ahajournals.org/cgi/content/full/114/23/2443>

Subscriptions: Information about subscribing to *Circulation* is online at
<http://circ.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21202-2436. Phone 410-5280-4050. Fax: 410-528-8550. Email:
journalpermissions@lww.com

Reprints: Information about reprints can be found online at
<http://www.lww.com/static/html/reprints.html>

Ischemic Heart Disease Events Triggered by Short-Term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD; Joseph B. Muhlestein, MD; Heidi T. May, MSPH; Dale G. Renlund, MD; Jeffrey L. Anderson, MD; Benjamin D. Horne, PhD, MPH

Background—Recent evidence suggests that long-term exposure to particulate air pollution contributes to pulmonary and systemic oxidative stress, inflammation, progression of atherosclerosis, and risk of ischemic heart disease and death. Short-term exposure may contribute to complications of atherosclerosis, such as plaque vulnerability, thrombosis, and acute ischemic events. These findings are inconclusive and controversial and require further study. This study evaluates the role of short-term particulate exposure in triggering acute ischemic heart disease events.

Methods and Results—A case-crossover study design was used to analyze ischemic events in 12 865 patients who lived on the Wasatch Front in Utah. Patients were drawn from the cardiac catheterization registry of the Intermountain Heart Collaborative Study, a large, ongoing registry of patients who underwent coronary arteriography and were followed up longitudinally. Ambient fine particulate pollution (particles with an aerodynamic diameter $\leq 2.5 \mu\text{m}$; $\text{PM}_{2.5}$) elevated by $10 \mu\text{g}/\text{m}^3$ was associated with increased risk of acute ischemic coronary events (unstable angina and myocardial infarction) equal to 4.5% (95% confidence interval, 1.1 to 8.0). Effects were larger for those with angiographically demonstrated coronary artery disease.

Conclusions—Short-term particulate exposures contributed to acute coronary events, especially among patients with underlying coronary artery disease. Individuals with stable presentation and those with angiographically demonstrated clean coronaries are not as susceptible to short-term particulate exposure. (*Circulation*. 2006;114:2443-2448.)

Key Words: air pollution ■ angina ■ coronary disease ■ ischemia ■ myocardial infarction

Exposure to elevated concentrations of ambient particulate matter (PM) air pollution has been implicated as a risk factor for cardiovascular disease and mortality.¹⁻⁵ Long-term repeated exposure to PM has been linked to ischemic heart disease. The empirical patterns of PM mortality associations are consistent with the hypothesis that PM exposure contributes to pulmonary and systemic oxidative stress, inflammation, atherosclerosis, and increased risk of ischemic heart disease and death.⁴ Long-term PM exposure has been associated with subclinical chronic inflammatory lung injury⁶ and subclinical atherosclerosis.⁷ In heritable hyperlipidemic rabbits, PM exposure accelerated progression of atherosclerotic plaques and increased vulnerability to plaque rupture.⁸ PM-potentiated vascular inflammation and atherosclerosis also were observed in a recent study of apolipoprotein E-deficient (hyperlipidemic) mice exposed to environmentally relevant concentrations of fine PM.⁹

complications of atherosclerosis by increasing the risk of atherosclerotic plaque rupture, thrombosis, and precipitation of acute ischemic events. Evidence that short-term exposure to PM air pollution can trigger myocardial infarction (MI) has been observed in several general population studies.¹⁰⁻¹⁵ Increased short-term PM exposure also has been associated with ischemic stroke,^{16,17} ECG ST-segment depression,^{18,19} increased plasma viscosity,²⁰ increased circulating markers of inflammation,²¹⁻²⁸ and changes in cardiac autonomic function as indicated by various measures of heart rate variability.^{27,29-33} Related evidence also shows that short-term PM exposure is associated with vasculature alterations. For example, PM- and ozone exposure-induced arterial vasoconstriction in healthy adults³⁴ was associated with impaired vascular reactivity and endothelial function in patients with diabetes,³⁵ and increased blood pressure in cardiac rehabilitation patients³⁶ and adults with lung disease.³⁷ Evidence of pathophysiological or mechanistic pathways that plausibly link PM exposure to cardiopulmonary disease and death is reviewed and discussed in more detail elsewhere.^{1,4,5}

The present study evaluates the role of environmentally relevant short-term increases in exposures in triggering acute ischemic heart disease events. This study takes advantage of

Editorial p 2430 Clinical Perspective p 2448

Short-term PM exposures also may play a role in triggering acute ischemic heart disease events. Short-term elevated PM exposures and related inflammation may contribute to acute

Received May 3, 2006; revision received September 11, 2006; accepted September 15, 2006.
From the Cardiovascular Department, LDS Hospital and Intermountain Medical Center (J.B.M., H.T.M., D.G.R., J.L.A., B.D.H.) and University of Utah (J.B.M., D.G.R., J.L.A.), Salt Lake City, and Brigham Young University (C.A.P.), Provo, Utah.
Correspondence to C. Arden Pope III, PhD, 142 FOB, Brigham Young University, Provo, UT 84602-2363. E-mail cap3@byu.edu
© 2006 American Heart Association, Inc.

a large, ongoing, and unique registry of well-characterized patients who underwent coronary arteriography and who have been followed up over time.³⁸ Research participants lived in a well-defined area with long-term daily monitoring of particulate air pollution and with substantial daily variability in PM concentrations resulting from densely populated mountain valley topography and frequent temperature inversions.³⁹ The specific objective of this study is to explore the potential role of short-term exposure to fine PM in triggering acute ischemic heart disease events in these well-characterized cardiac catheterization patients.

Methods

Study Area and Participants

Approximately 80% of the population of Utah resides on a relatively narrow strip of land that fronts the west side of the Wasatch mountain range. The Wasatch Front area is bordered on the east by the Wasatch Mountains and on the west largely by the Great Salt Lake, Utah Lake, and smaller mountain ranges. It is ≈ 10 to 15 miles wide from east to west and ≈ 80 miles long from north to south with 3 nearly contiguous metropolitan areas: the city of Ogden and surrounding communities to the north with a 2003 total population of 469 000, Salt Lake City and surrounding communities located in the center with a 2003 total population of 1 005 000, and Provo/Orem and surrounding communities to the south with a 2003 total population of 407 000.

Study participants included patients drawn from the cardiac catheterization registry of the Intermountain Heart Collaborative Study,³⁸ a population of patients undergoing coronary arteriography at the LDS Hospital (Salt Lake City, Utah). At the time of index hospitalization, these patients presented with 1 of 3 general clinical conditions that indicated coronary angiography: acute MI, an unstable pattern of chest pain suggesting unstable angina (such as progressive symptoms or symptoms at rest), or a stable pattern of chest pain suggesting stable angina (exertional symptoms only, including a positive stress test result) or stable noncoronary syndromes necessitating angiography. Male and female patients of unrestricted age were included in the registry. The study was approved by the institutional review board of the hospital.

A total of 26 643 participants were enrolled between 1994 and 2004, including mostly patients from throughout Utah and from neighboring western states. The present analysis includes the 12 865 study participants who lived in the Wasatch Front study area and who had their event on a date when air pollution and weather data were available. This analysis also included identifiable subsequent MI events. Participants were followed up until death or December 31, 2004. Deaths were determined from electronic hospital records, State of Utah Health Department death certificates, and national Social Security Administration death records. MI events subsequent to the index hospitalization were identified by searching the Intermountain Healthcare electronic medical records database.

Baseline Participant Variables

Baseline participant variables, including various individual risk factors, were determined or derived from physician-provided information on the standard angiographic report form used at the LDS Hospital. These included age, gender, smoking, body mass index (BMI), congestive heart failure (CHF), hypertension, hyperlipidemia, diabetes, family history of early coronary artery disease (CAD), and number of severely diseased coronary vessels. Smoking included active or previous (>10 pack-years) tobacco use. BMI was calculated from height and weight. CHF was physician reported based on clinical symptoms. Hypertension was physician reported for systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or use of antihypertensive agents. Hyperlipidemia was physician reported for total cholesterol ≥ 200 mg/dL, low-density lipoprotein level ≥ 130 mg/dL, or use of cholesterol-lowering med-

ication. Diabetes was determined based on physician-reported fasting blood sugar level ≥ 126 mg/dL or use of an antidiabetic medication. Family history was based on self-reported information that a first-order relative had suffered cardiovascular death, MI, or coronary revascularization at <65 years of age. The number of severely diseased coronary vessels was defined as 0, 1, 2, or 3 coronary arteries with $\geq 70\%$ maximal stenosis as determined at angiography.

Weather and Pollution Data

Wasatch Front communities share common weather patterns. During low-level temperature inversion episodes, PM concentrations become elevated because local emissions become trapped in a stagnant air mass near the valley floor. Daily weather data from January 1, 1993 through December 31, 2004, including temperature, dewpoint temperature, and the clearing index, were collected from the National Weather Service (Salt Lake City International Airport station). The clearing index ranges from 0 to 1050. Low index values reflect stagnant air conditions; high values reflect greater diffusion pollution potential.

Particulate air pollution data for PM₁₀ (particles with an aerodynamic diameter $\leq 10\text{-}\mu\text{m}$ cut point) and PM_{2.5} (particles with an aerodynamic diameter $\leq 2.5\text{-}\mu\text{m}$ cut point) were obtained from the Utah Department of Environmental Quality, Division of Air Quality (Salt Lake City, Utah). Monitoring was conducted in accordance with the US Environmental Protection Agency federal reference method.⁴⁰ Data from monitoring sites along the Wasatch Front from January 1, 1993 to December 31, 2004 were collected (Table 1). Three observations of extremely high PM₁₀ concentrations caused by extreme windstorms were deleted. In Ogden and Provo/Orem, PM₁₀ monitoring was conducted at a single community-based site with monitoring completeness of 82% and 93%, respectively. In Salt Lake City, the centrally located, community-based air monitoring center (SLC AMC) was replaced by monitoring at another site (SLC Hawthorne) with concurrent overlapping monitoring for >1 year. Daily PM₁₀ data were available from 1 or both of these sites for 95% of the days. In addition, PM₁₀ data were collected from another Salt Lake City monitoring site (SLC North). Daily PM₁₀ concentrations between all of the Wasatch Front sites were highly correlated ($r=0.72$ to 0.85). PM₁₀ concentration ratios between monitors were calculated using no-intercept regression models, and missing values were estimated from this ratio and monitored PM₁₀ data at the nearest monitoring site with nonmissing data.

For PM_{2.5}, daily monitoring at the SLC Hawthorn and Lindon sites and every third day monitoring at the Ogden site began in January 1998. Missing PM_{2.5} concentrations were estimated from season- and clearing index-specific ratios of PM_{2.5} to PM₁₀. When the clearing index is low, indicating stagnant air conditions, there is little windblown dust but a buildup of primary and secondary PM from vehicles, industry, wood burning, and other local sources, resulting in a relatively high PM_{2.5}/PM₁₀ ratio. High clearing index values reflect more wind movement, which clears local combustion-source pollutants but results in more localized windblown dust. Under such conditions, lower PM_{2.5}/PM₁₀ ratios prevail. Furthermore, the PM_{2.5}/PM₁₀ ratio tends to be higher during winter months (December through February) for various reasons, such as more frequent and severe temperature inversions; more space heating, including wood burning; and the ground surface being more likely to be frozen or snow covered. For each of the 3 Wasatch Front metropolitan areas, the PM_{2.5}/PM₁₀ ratios were estimated for 10 different air stagnation levels (clearing index ≤ 100 , 101 to 200, 201 to 500, 501 to 999, and 1000 to 1050) and 2 seasonal periods (winter months, December through February, versus nonwinter months) using regression models and available daily PM_{2.5} and PM₁₀ data. The resulting estimated regression coefficients produce direct estimates of the clearing index season-specific correlations between PM_{2.5} and PM₁₀ that also are estimates of the clearing index season-specific PM_{2.5}/PM₁₀ ratios. In all 3 areas and for all 10 clearing index- and season-specific conditions, regression coefficients were highly statistically significant ($P<0.0001$), indicating strong correlations between PM_{2.5} and PM₁₀. Missing PM_{2.5} data were estimated by applying these PM_{2.5}/PM₁₀ ratios (Table 1). Such imputation of missing data can result in

TABLE 1. Summary of Available Particulate Air Pollution Data (1993–2004)

Monitoring Sites		n	Mean	SD	Maximum
Ogden	PM ₁₀ monitored	3589	28.5	16.5	163
Ogden	PM ₁₀ monitored+estimated	4381	28.5	16.5	163
Ogden	PM _{2.5} monitored	773	10.8	10.6	108
Ogden	PM _{2.5} monitored+estimated	4381	10.9	9.7	108
SLC Hawthorne	PM ₁₀ monitored	2634	27.7	17.4	162
SLC Hawthorne	PM ₁₀ monitored+estimated	4381	27.2	16.8	162
SLC Hawthorne	PM _{2.5} monitored	2309	11.3	11.9	94
SLC Hawthorne	PM _{2.5} monitored+estimated	4382	10.6	10.8	94
Provo/Orem, Lindon	PM ₁₀ monitored	4057	32.7	21.1	240
Provo/Orem, Lindon	PM ₁₀ monitored+estimated	4381	32.5	20.8	240
Provo/Orem, Lindon	PM _{2.5} monitored	2332	10.1	9.8	82
Provo/Orem, Lindon	PM _{2.5} monitored+estimated	4383	10.6	11.1	144
SLC AMC	PM ₁₀ monitored	2260	35.9	20.4	161
SLC North	PM ₁₀ monitored	4032	45.1	25.1	199

less variability in estimated exposures. As reported in Table 1, the means and the standard deviations for the monitored plus estimated data were similar to the monitored data.

Statistical Analysis

In this analysis, the primary exposure variable was PM_{2.5}, but PM₁₀ was also considered. Concentrations on the concurrent day and previous 1 to 3 days and 2- to 4-day lagged moving average concentrations were evaluated. The primary outcome variables were presentation with MI or unstable angina at the time of index hospitalization and subsequent incident MI during follow-up (after the index hospitalization), analyzed separately and in pooled analysis. Elevated concentrations of PM air pollution were hypothesized to increase the risk of these acute coronary events. Stable presentation at the index hospitalization also was analyzed as an outcome variable. However, because treatment for stable presentation is more likely to be elective with regard to its timing, it was hypothesized that this presentation is less associated with particulate air pollution.

This analysis uses the case-crossover design,^{41,42} which is an adaptation of the retrospective case-control design. This approach matches exposures at the time of or shortly before the event of interest with ≥1 periods when the event did not occur (control or referent periods) and evaluates potential excess risk using conditional logistic regression. Details of the use of conditional logistic regression in case-crossover studies with application to air pollution exposure are given elsewhere.^{43,44} Because individuals who experience an acute event serve as their own controls, there is perfect matching on all participant-specific characteristics that do not vary over time; thus, this approach controls for participant-specific risk factors by design. Furthermore, by choosing matching referent periods close in time (before and after the event) and on the same day of the week, this approach structures the analysis so that various time-dependent risk factors such as day of the week, seasonality, long-term time trends, and long-term changes in individual characteristics between multiple events for the same patient also are controlled for by design. In this analysis, referent or control period exposures were matched on day of the week in the same month and year as the ischemic event, resulting in up to 4 control periods per event. The details of this specific time-stratified referent selection approach and a statistical exposition on why it allows unbiased conditional logistic regression estimates and avoids bias that can occur as a result of time trends in air pollution exposure are presented elsewhere.^{43,44} Temperature and dewpoint temperature were included as linear and quadratic terms in the conditional logistic regression model. Additionally, analyses stratified by various baseline participant variables, risk factors, and number of severely diseased coronary vessels were conducted.

The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

Results

Baseline participant characteristics are summarized in Table 2. Of those presenting with MI or unstable angina, only 21% had a history of smoking; however, most were hypertensive or hyperlipidemic,

TABLE 2. Baseline Participant Characteristics

Characteristic	MI+Unstable Angina (n=4818)	Stable Presentation (n=8047)	Subsequent MI (n=1173)
Age, y	63±13	60±16	65±13
Male gender, %	69	55	68
Smoking, %	21	11	20
BMI, kg/m ²	29±6	28±6	30±14
MI, %	41	0	100
CHF, %	12	15	21
Hypertension, %	60	39	58
Hyperlipidemia, %	60	31	50
Diabetes, %	22	14	24
Family history, %	45	21	35
Risk factors, %*			
0	12	42	16
1	22	21	26
2	19	19	25
3	26	13	21
4+	11	5	11
Diseased vessels, %			
0	19	68	19
1	35	13	31
2	22	8	22
3	24	11	28

Proportions are given in percent; averages, in mean±SD.

*Risk factors include CHF, hypertension, hyperlipidemia, diabetes, and family history of early CAD.

TABLE 3. Number of Ischemic Events and Percent Increase in Risk (and 95% CIs) Associated With a 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$

Event	Events, n	Increase, %	95% CI
Index MI and unstable angina	4818	4.81	0.98–8.79
Subsequent MI	1173	3.23	–3.87–10.85
All acute coronary events	5991	4.46	1.07–7.97
All acute coronary events excluding observations using imputed $\text{PM}_{2.5}$ data	3940	4.24	0.33–8.31
Stable presentation	8047	–2.57	–5.39–0.34

and many also had CHF, diabetes, or a family history of early CAD. When CHF, hypertension, hyperlipidemia, diabetes, and family history of early CAD were treated as underlying individual “risk factors,” the majority of the MI and unstable angina participants had multiple risk factors. In comparison, those with stable presentation were relatively less likely to smoke and had less underlying chronic cardiovascular disease.

Table 3 presents estimated increased risk (and 95% confidence intervals [CIs]) for acute coronary events associated with a 10- $\mu\text{g}/\text{m}^3$ increase in concurrent-day $\text{PM}_{2.5}$. Index MI/unstable angina and subsequent MI were not significantly different in terms of their associations with $\text{PM}_{2.5}$. On the basis of estimates from pooled analysis, a 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ was associated with a 4.5% (95% CI, 1.1 to 8.0) increase in risk of presenting with an acute coronary event. The effect estimate was nearly the same when observations using imputed PM data were excluded. The association between $\text{PM}_{2.5}$ and stable presentation was negative and not statistically significant.

Figure 1 presents risk estimates for different lag structures. Increased risk was more strongly associated with $\text{PM}_{2.5}$ than with PM_{10} . Although there is autocorrelation in daily PM exposures, the strongest associations were with concurrent-day or the 2-day-lagged moving average (mean of the concurrent and previous day), indicating the relative importance of more recent exposure. The distributed lag structure also partially reflects the

fact that clinical presentation and subsequent angiography follow onset of symptoms.

Figure 2 presents $\text{PM}_{2.5}$ risk estimates for all acute coronary events after stratification by event type and individual characteristics. The $\text{PM}_{2.5}$ effect estimates were nearly the same for unstable angina, index MI, and subsequent MI, indicating that pooling these events was appropriate. Observed differences in $\text{PM}_{2.5}$ effect estimates for age, gender, smoking, BMI, underlying disease, and risk factor strata were not statistically significant ($P>0.05$). However, significantly larger $\text{PM}_{2.5}$ effect estimates were observed for individuals who had at least 1 severely diseased coronary vessel compared with those who did not (interaction $P=0.01$). Excluding participants who, on the basis of coronary arteriography, were found not to have seriously diseased coronary arteries clearly resulted in stronger $\text{PM}_{2.5}$ associations.

Discussion

The results of this analysis indicate that short-term ambient $\text{PM}_{2.5}$ exposure is associated with acute ischemic heart disease events. Similar results have been observed in a study of MI events in Boston,¹⁰ a study of first MI hospitalization in Rome,¹¹ a study of emergency hospitalizations for MI in 21 US cities,¹² and a study of hospital readmissions for MI, angina, dysrhythmia, or heart failure of MI survivors in 5 European cities.¹³ The present study is unique with regard to its use of a large registry of well-characterized patients who underwent coronary arteriography and lived in a well-defined geographic area with adequate long-term daily pollution monitoring. No other study has been able to explore differential effects for patients with differing levels of angiographically demonstrated CAD. Although the effect estimates of a 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ are relatively small (during winter temperature inversions, 24-hour $\text{PM}_{2.5}$ concentrations can exceed 100 $\mu\text{g}/\text{m}^3$), these effects may be of significant public health importance because such exposure to fine PM is relatively ubiquitous in urban environments and essentially involuntary.

A primary strength of the case-crossover study design used in this analysis is that the effect estimates are probably not due to

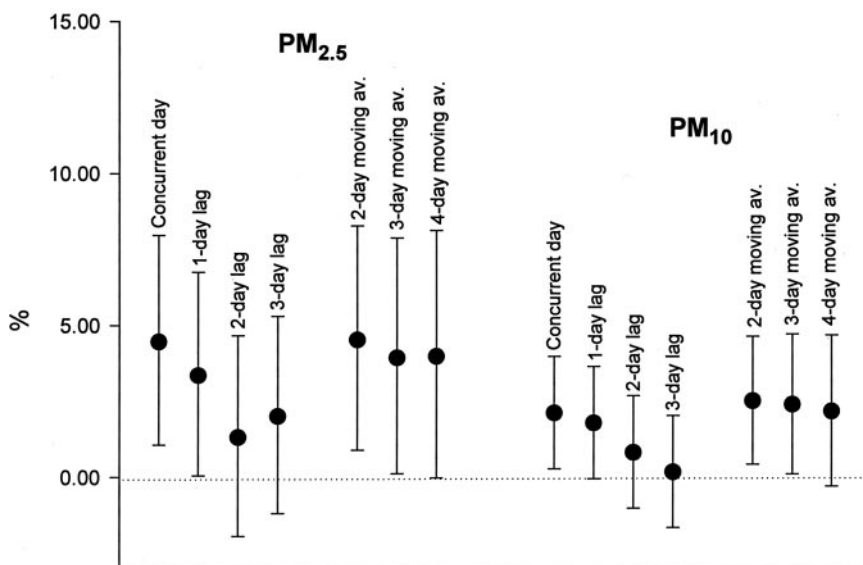


Figure 1. Percent increase in risk (and 95% CI) of acute coronary events associated with 10 $\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$ or PM_{10} for different lag structures. av. Indicates average.

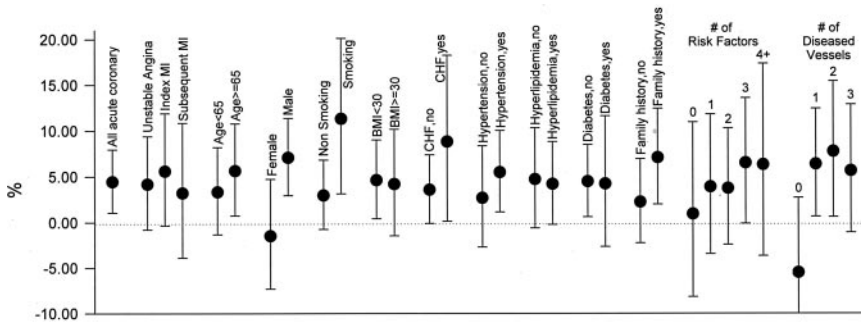


Figure 2. Percent increase in risk (and 95% CI) of acute coronary events associated with 10 µg/m³ of PM_{2.5} stratified by various characteristics.

confounding by age, gender, smoking, underlying chronic disease, or other individual-level characteristics. In this case-crossover study design, individuals serve as their own controls, and individual-level characteristics are controlled for by design. Similarly, long-term time trends, seasonality, day of the week, and long-term changes in individual characteristics between multiple events for the same patient are controlled for by matching. Furthermore, it has been demonstrated that the time-stratified referent selection strategy used in this analysis allows unbiased conditional logistic regression estimates and avoids the bias that can occur as a result of time trends in air pollution exposure.^{43,44}

Although this study includes well-defined and characterized subjects, the design allows only the evaluation of pollution-related risk for those who had an event, required index catheterization, and were available for study entry. It is unclear how these limitations affect the generalizability of the results, but they place the emphasis of analysis on events that are less likely to have been fatal. In this study, only ≈5% of index MI events were fatal, defined as death within 30 days of the event. Although a quantitative review of the literature suggests that there may be differential effects of PM pollution on fatal versus nonfatal events, the use of different study designs and PM measures requires some caution when comparing effect estimates.⁵ Furthermore, clinical presentation and subsequent angiography follow onset of symptoms and in some cases may be on a different calendar date, resulting in some exposure misclassification and affecting the estimated distributed lag structure.

The results of this study provide some information regarding the related issue of plausibility. Is it plausible that clinically relevant ischemic cardiovascular events could be triggered by environmentally relevant exposures of only a day or 2? It seems implausible that short-term PM exposure could trigger a clinically relevant ischemic cardiac event in someone without pre-existing CAD. In fact, PM_{2.5} associations with acute ischemic heart disease events were observed only for individuals who had at least 1 severely diseased coronary vessel (with ≥70% stenosis as determined at angiography). These findings are consistent with the suggestion that short-term elevated PM exposure and related inflammation contribute to acute complications of atherosclerosis, including plaque vulnerability, thrombosis, and acute ischemic events, but only in persons with existing disease.

A primary limitation of the design used in this study is that it allowed analysis of only very short-term acute exposure and its potential to trigger ischemic heart disease events. As discussed elsewhere, long-term repeated exposure to elevated concentrations of PM may contribute to oxidative stress, low-

moderate-grade inflammation, and the initiation and progression of atherosclerosis and related cardiovascular disease.^{1,4,5,7} Further study is required to evaluate long-term risk. However, this study does provide evidence that short-term exposure to elevated concentrations of fine particulate air pollution contributes to the triggering of acute ischemic heart disease events. Individuals with stable presentation and without seriously diseased coronary vessels are not as susceptible to risk from short-term exposure to fine particulate pollution.

Sources of Funding

This study was supported by Deseret Foundation, Salt Lake City, Utah, and funds from the Mary Lou Fulton Professorship, Brigham Young University, Provo, Utah.

Disclosures

None.

References

1. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, Luepker R, Mittleman M, Samet J, Smith SC Jr, Tager I. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation*. 2004;109:2655–2671.
2. Pope CA III, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA*. 2002;287:1132–1141.
3. Dockery DW, Pope CA, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG, Speizer FE. An association between air pollution and mortality in six US cities. *N Engl J Med*. 1993;329:1753–1759.
4. Pope CA III, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krewski D, Godleski JJ. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. *Circulation*. 2004;109:71–77.
5. Pope CA III, Dockery DW. Health effects of fine particulate air pollution: lines that connect. *J Air Waste Manage Assoc*. 2006;56:709–742.
6. Souza MB, Saldiva PHN, Pope CA III, Capelozzi VL. Respiratory changes due to long-term exposure to urban levels of air pollution: a histopathologic study in humans. *Chest*. 1998;113:1312–1318.
7. Künzli N, Jerrett M, Mack WJ, Beckerman B, LaBree L, Gilliland F, Thomas D, Peters J, Hodis HN. Ambient air pollution and atherosclerosis in Los Angeles. *Environ Health Perspect*. 2005;113:201–206.
8. Suwa T, Hogg JC, Quinlan KB, Ohgami A, Vincent R, van Eeden SF. Particulate air pollution induces progression of atherosclerosis. *J Am Coll Cardiol*. 2002;39:935–942.
9. Sun Q, Wang A, Jin X, Natanzon A, Duquaine D, Brook RD, Aguinaldo JGS, Fayad ZA, Fuster V, Lippmann M, Chen LC, Rajagopalan S. Long-term air pollution exposure and acceleration of atherosclerosis and vascular inflammation in an animal model. *JAMA*. 2005;294:3003–3010.
10. Peters A, Dockery DW, Muller JE, Mittleman MA. Increased particulate air pollution and the triggering of myocardial infarction. *Circulation*. 2001;103:2810–2815.
11. D'Ippoliti D, Forastiere F, Ancona C, Agabiti N, Fusco D, Michelozzi P, Perucci CA. Air pollution and myocardial infarction in Rome: a case-crossover analysis. *Epidemiology*. 2003;14:528–535.

12. Zanobetti A, Schwartz J. The effect of particulate air pollution on emergency admissions for myocardial infarction: a multicity case-crossover analysis. *Environ Health Perspect*. 2005;113:978–982.
13. von Klot S, Peters A, Aalto P, Bellander T, Berglind N, D'Ippoliti D, Elosua R, Hörmann A, Kulmala M, Lanki T, Löwel H, Pekkanen J, Picciotto S, Sunyer J, Forastiere F. Ambient air pollution is associated with increased risk of hospital cardiac readmissions of myocardial infarction survivors in five European cities. *Circulation*. 2005;112:3073–3079.
14. Peters A, von Klot S, Heier M, Trentinaglia I, Hörmann A, Wichmann HE, Löwel H. Exposure to traffic and the onset of myocardial infarction. *N Engl J Med*. 2004;351:1721–1730.
15. Sullivan J, Sheppard L, Schreuder A, Ishikawa N, Siscovick D, Kaufman J. Relation between short-term fine-particulate matter exposure and onset of myocardial infarction. *Epidemiology*. 2005;16:41–48.
16. Hong Y-C, Lee J-T, Kim H, Kwon H-J. Air pollution: a new risk factor in ischemic stroke mortality. *Stroke*. 2002;33:2165–2169.
17. Wellenius GA, Schwartz J, Mittleman MA. Air pollution and hospital admissions for ischemic and hemorrhagic stroke among Medicare beneficiaries. *Stroke*. 2005;36:2549–2553.
18. Pekkanen J, Peters A, Hoek G, Tiittanen P, Brunekreef B, de Hartog J, Heinrich J, Ibaldo-Mulli A, Kreyling WG, Lanki T, Timonen KL, Vanninen E. Particulate air pollution and risk of ST-segment depression during repeated submaximal exercise tests among subjects with coronary heart disease. *Circulation*. 2002;106:933–938.
19. Gold DR, Litonjua AA, Zanobetti A, Coull BA, Schwartz J, MacCallum G, Verrier RL, Nearing BD, Canner MJ, Suh H, Stone PH. Air pollution and ST-segment depression in elderly subjects. *Environ Health Perspect*. 2005;113:883–887.
20. Peters A, Doring A, Wichmann H-E, Koenig W. Increased plasma viscosity during an air pollution episode: a link to mortality? *Lancet*. 1997;349:1582–1587.
21. Peters A, Fröhlich M, Döring A, Immervoll T, Wichmann H-E, Hutchinson WL, Pepys MB, Koenig W. Particulate air pollution is associated with an acute phase response in men: results from the MONICA-Augsberg study. *Eur Heart J*. 2001;22:1198–1204.
22. Tan WC, Qiu D, Liam BL, Ng TP, Lee SH, van Eeden SF, D'Yachkova Y, Hogg JC. The human bone marrow response to acute air pollution caused by forest fires. *Am J Respir Crit Care Med*. 2000;161:1213–1217.
23. Salvi S, Blomberg A, Rudell B, Kelly F, Sandstrom T, Holgate ST, Frew A. Acute inflammatory responses in the airways and peripheral blood after short-term exposure to diesel exhaust in healthy human volunteers. *Am J Respir Crit Care Med*. 1999;159:702–709.
24. Salvi SS, Nordenhall C, Blomberg A, Rudell B, Pourazar J, Kelly FJ, Wilson S, Sandstrom T, Holgate ST, Frew AJ. Acute exposure to diesel exhaust increases IL-8 and GRO- α production in healthy human airways. *Am J Respir Crit Care Med*. 2000;161:550–557.
25. Ghio AJ, Kim C, Devlin RB. Concentrated ambient air particles induce mild pulmonary inflammation in healthy human volunteers. *Am J Respir Crit Care Med*. 2000;162:981–988.
26. Ghio AJ, Huang YT. Exposure to concentrated ambient particles (CAPs): a review. *Inhal Toxicol*. 2004;16:53–59.
27. Pope CA III, Hansen ML, Long RW, Nielsen KR, Eatough NL, Wilson WE, Eatough DJ. Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects. *Environ Health Perspect*. 2004;112:339–345.
28. Rückerl R, Ibaldo-Mulli A, Koenig W, Schneider A, Woelke G, Cyrus J, Heinrich J, Marder V, Frampton M, Wichmann HE, Peters A. Air pollution and markers of inflammation and coagulation in patients with coronary heart disease. *Am J Respir Crit Care Med*. 2006;173:432–441.
29. Pope CA III, Verrier RL, Lovett EG, Larson AC, Raizenne ME, Kanner RE, Schwartz J, Villegas GM, Gold DR, Dockery DW. Heart rate variability associated with particulate air pollution. *Am Heart J*. 1999;138:890–899.
30. Gold DR, Litonjua A, Schwartz J, Lovett E, Larson A, Nearing B, Allen G, Verrier M, Cherry R, Verrier R. Ambient pollution and heart rate variability. *Circulation*. 2000;101:1267–1273.
31. Liao D, Duan Y, Whitsel EA, Zheng Z, Heiss G, Chinchilli VM, Lin H-M. Association of higher levels of ambient criteria pollutants with impaired cardiac autonomic control: a population-based study. *Am J Epidemiol*. 2004;159:768–777.
32. Park SK, O'Neill MS, Vokonas PS, Sparrow D, Schwartz J. Effects of air pollution on heart rate variability: the VA Normative Aging Study. *Environ Health Perspect*. 2005;113:304–309.
33. Schwartz J, Park SK, O'Neill MS, Vokonas PS, Sparrow D, Weiss ST, Kelsey K. Glutathione-S-transferase M1, obesity, statins, and autonomic effects of particles. *Am J Respir Crit Care Med*. 2005;172:1529–1533.
34. Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F. Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adults. *Circulation*. 2002;105:1534–1536.
35. O'Neill MS, Veves A, Zanobetti A, Samat JA, Gold DR, Economides PA, Horton ES, Schwartz J. Diabetes enhances vulnerability to particulate air pollution-associated impairment in vascular reactivity and endothelial function. *Circulation*. 2005;111:2913–2920.
36. Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, Eagan-Bengston E, Gates KA, Hartley H, Suh H, Gold DR. Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation*. 2004;110:2184–2189.
37. Linn WS, Gong H Jr. Air pollution, weather stress, and blood pressure. *Am J Public Health*. 2001;91:1345–1346.
38. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, Renlund DG, Muhlestein J. Which white blood cell subtypes predict increased cardiovascular risk? *J Am Coll Cardiol*. 2005;45:1638–1643.
39. Pope CA III, Hill RW, Villegas GM. Particulate air pollution and daily mortality on Utah's Wasatch Front. *Environ Health Perspect*. 1999;107:567–573.
40. US Environmental Protection Agency. Revised requirements for the designation of reference and equivalent methods for PM_{2.5} and ambient air quality surveillance for particulate matter; final rule. *Fed Reg*. 1997;62:5725–5726.
41. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol*. 1991;133:144–153.
42. Maclure M, Mittleman MA. Should we use a case-crossover design? *Annu Rev Public Health*. 2000;21:193–221.
43. Janes H, Sheppard L, Lumley T. Overlap bias in the case-crossover design, with application to air pollution exposures. *Stat Med*. 2005;24:285–300.
44. Janes H, Sheppard L, Lumley T. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. *Epidemiology*. 2005;16:717–726.

CLINICAL PERSPECTIVE

It has previously been demonstrated that long-term exposure to particulate air pollution contributes to cardiovascular disease, including the progression of atherosclerosis and risk of ischemic heart disease and death. This study extends that risk to include short-term exposures of ≤ 24 hours of ambient fine particulate air pollution. By analyzing 12 865 patients who lived on the Wasatch Front in Utah, we determined that short-term particulate exposures are associated with a significantly increased risk of acute ischemic coronary events, especially for those with established coronary artery disease. This information emphasizes that even short-term pollution episodes of only 1 or a few days may put patients at risk. Although any single high-air-pollution day results in only a modest increase in the risk of an acute ischemic event, the additive risk over time may result in substantial adverse clinical impact. The present study suggests that future research should investigate effective interventions to reduce the cardiovascular risks associated with high-air-pollution days. On the basis of these results, patients with established heart disease might do well to move to areas with a lower burden of fine particulate air pollution levels. If moving is not possible, patients may at least be wise to stay indoors during the more polluted days and to ensure adequate filtering of their indoor air. Given the ubiquitous and involuntary nature of the exposure, this study provides support for the need for increased public efforts to improve overall air quality.