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EDITORIAL

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Cardiovascular Risks from Fine Particulate Air Pollution

Douglas W. Dockery, Sc.D., and Peter H. Stone, M.D.

More than a decade ago, prospective epidemiologic studies showed that mortality was increased among people living in communities with elevated concentrations of fine particulate air pollution.[1,2] Subsequent research has shown that particulate air pollution is statistically and mechanistically linked to increased cardiovascular disease.[3] New data are beginning to shed light on which persons are at heightened risk.

In this issue of the *Journal,* Miller et al.[4] report on data from the Women's Health Initiative (WHI) observational study, which greatly expands our understanding of how fine particulate pollution affects health. Earlier long-term prospective cohort studies showed an association between levels of air pollution consisting of particulate matter of less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) and an elevated risk of death from all causes and from cardiovascular disease.[1,2,5] The WHI study broadens the scope by finding that nonfatal cardiovascular events are also strongly associated with fine particulate concentrations in the community. Earlier work relied solely on death certificates to define the rate of death from cardiovascular disease. In the WHI study, cardiovascular events and mortality were defined by objective review of medical records. The earlier studies were designed to identify risk factors for respiratory disease[1] and cancer[2] and therefore had limited ability to adjust for cardiovascular risk factors. The WHI observational study was designed to assess the risk of cardiovascular events and therefore could exclude cardiovascular risk factors as explanations for the observed associations with air pollution.

Earlier studies did not include data on the full range of regulated community air pollutants — that is, $PM_{2.5}$ (and the larger particle fraction, PM_{10}), sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone. The WHI study considered all of these community air pollutants and found cardiovascular risk associated only with $PM_{2.5}$ concentrations. Whereas earlier work compared levels of air pollution and rates of death between various cities, the WHI investigators were also able to compare areas within individual cities. Their analysis demonstrated a relationship between increased levels of fine particul pollution and higher rates of death and complications from cardiovascular and cerebrovascular disease, depending not only on which city a person lived in but also on where in that city she lived.

Perhaps most important, the WHI study established a stronger statistical association between fine particulate air pollution a

death from coronary heart disease than that found in earlier studies. In the WHI study, Miller et al. found an increased relative risk of 1.76 for death from cardiovascular disease for every increase of 10 μg per cubic meter in the mean concentration of $PM_{2.5}$.[4] By comparison, a study by the American Cancer Society showed that each increase of 10 μg per cubic meter in the mean $PM_{2.5}$ concentration was associated with an increased relative risk of 1.12 for death from cardiovascular disease, 1.18 for death from ischemic heart disease (the largest proportion of deaths), and 1.13 for death fror arrhythmia, heart failure, or cardiac arrest.[5]

Samples in previous studies consisted of subjects from the entire population of the cities being investigated. The WHI analysis was restricted to postmenopausal women with no history of cardiovascular health problems. A 22-year follow-up c a cohort of nonsmoking white adults in California showed an increased risk of death from coronary heart disease with risin levels of fine particulate air pollution in women but not in men.[6] Does this suggest that the WHI population, or women in general, are more sensitive to the cardiovascular effects of particulate air pollution?

Women have a distinctly different profile of coronary disease. In the Women's Ischemia Syndrome Evaluation study, the cluster of conditions that increase the risk of vascular disease (e.g., hypertension, diabetes, obesity, and inactivity) was seen more frequently in postmenopausal women than in men.[7] Women's coronary arteries are smaller in size and tend to harbor more diffuse atherosclerosis than do men's arteries, and women's microvessels appear to be more frequently dysfunctional than those of men.[7] Indeed, in the Euro Heart Survey, although women were less likely than men to have fixed atherosclerotic obstructive disease, among patients undergoing elective diagnostic angiography for angina, women with confirmed coronary disease had twice the risk of death or myocardial infarction as that of men.[8] These findings suggest tha sex may not define susceptibility to air pollution but, rather, may be an indicator of an underlying cardiac substrate that put women at increased risk.

Characteristics that define increased cardiovascular susceptibility to particulate air pollution have also been identified in m Stronger associations between fine particulate concentrations and abnormal variability in heart rate were reported in asymptomatic men with higher Framingham cardiovascular risk scores.[9] $PM_{2.5}$ was more strongly associated with impaire autonomic cardiovascular function in men with genotypic and phenotypic indicators of increased systemic inflammation an oxidative stress than in those without these markers.[10] However, the increased susceptibility was not found among men taking statins, which both improve lipid profiles and reduce systemic inflammation.

The mechanisms by which fine particulate air pollution influence the risk of cardiovascular disease are still under investigation. There is evidence that inhalation of particulate air pollution creates and exacerbates both pulmonary and systemic inflammation and oxidative stress, leading to direct vascular injury, atherosclerosis, and autonomic dysfunction.[3] Buildup of atherosclerotic plaque, measured by the carotid intima–media thickness, is higher in communities with higher mean $PM_{2.5}$ concentrations.[11] Particulate air pollution has been found to lead to rapid and significant increases in fibrinoge plasma viscosity, platelet activation, and release of endothelins, a family of potent vasoconstrictor molecules.[3]

Taken together, these studies suggest that the status of cardiovascular risk factors has a substantial effect on susceptibility t the adverse effects of particulate air pollution. A particularly appealing aspect of the design of the WHI study is the range c data collected on all subjects, including demographic and lifestyle characteristics, cardiovascular risk factors, medical history, diet, and medications. With this wealth of data, the next generation of analyses should be able to focus risk stratification even further to identify the characteristics of persons who are most susceptible to the adverse effects of air pollution.

A multifaceted approach that encompasses both public health and medical interventions is needed to reduce the burden of cardiovascular disease attributable to air pollution. Comprehensive management of the harmful effects of fine particles mu

start with intensive efforts to reduce this destructive form of air pollution. Fine particulate air pollution results not only from the combustion of carbonaceous fuels in our vehicles, power plants, and factories but also from secondary particles produced by oxidation of gaseous pollutants emitted by these same sources. The evidence that has accumulated thus far regarding the health threat from $PM_{2.5}$ pollution is convincing enough to have prompted the Environmental Protection Agency (EPA) to lower the short-term (24-hour) standard for fine particulate concentration that communities must achieve. Unfortunately for public health, the EPA failed to follow the recommendation of its science advisers and reduce the long-term standard for fir particles.[12] The findings of the WHI study strongly support the recommendation for tighter standards for long-term fine particulate air pollution.

Even with tighter standards, people will continue to be exposed to fine particulate air pollution. Although the public health burden of cardiovascular disease attributable to air pollution is large, the evidence suggests that individual risks are modest. If the WHI and other studies can identify intrinsic and acquired individual factors that lead to increased adverse cardiovascular responses to air pollution, then it should be possible to offer focused interventions to persons who are at greatest risk and thereby ameliorate at least some of the patient-specific damages of air pollution.

Dr. Dockery reports receiving a stipend from Industrial Economics for participation in an expert-opinion study. No other potential conflict of interes relevant to this article was reported.

Source Information

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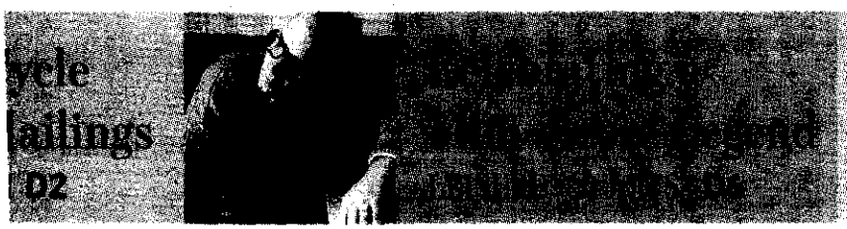

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Teri Agins helps track down a hard-to-find classic scent — ASK TERI D7

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tcoustic sales have increased 50% a year in .S. for the past four years and are poised to ate more than $3 million in revenue in says **StJohn Group** Inc., the Bellingham, ., company that sells the line domestically. typical customer for this has probably even ventured into a hi-fi store," says John ell, StJohn's co-founder.

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Increased Heart Risk Linked to Air Pollution

Study of 58,600 Older Women Finds Danger Grows in Cities With Higher Soot Levels From Autos and Power Plants

By KEITH J. WINSTEIN

BREATHING common urban air pollution is much more deadly than previously thought, according to a major study published in today's New England Journal of Medicine.

Today's study, which followed 58,600 postmenopausal women for seven years, found the added risk of cardiovascular death from living in the most-polluted areas including Cincinnati and Riverside, Calif. was roughly 150%. Breathing air heavily polluted by soot from automobiles and power plants may raise the risk of death for older women at nearly the same rate as smoking cigarettes. The study focused on the most deadly kind of soot, known as fine particulate matter, which comes from burning fossil fuels like gasoline, diesel fuel and coal.

Previous studies had concluded the risk was much lower. That research found that soot was responsible for increasing deaths from heart disease and stroke in the most polluted cities by about 40% over the least polluted, such as Santa Fe and Honolulu. That impact is comparable to the relatively consistent inhalation of second-hand smoke that comes from living with a smoker.

Dirty Air Risk

A new study shows that breathing polluted air sharply raises the risk of dying from cardiovascular disease. A few highlights:

- Older women living in the most polluted cities had about a **150% increased risk** of death from heart attack and stroke.
- The danger arose from a type of soot that is generated by **burning fossil fuels.**
- **Pittsburgh and Riverside, Calif.,** are among the cities with the highest soot levels.

In the new study, the approximate 150% increased risk is close to the impact of being an active smoker, said C. Arden Pope, a professor at Brigham Young University who played a big role in the two previous major U.S. soot studies but was not involved in the study published today. "It's stunning," Mr. Pope said.

Each increase of fine soot levels by 10 micrograms a cubic meter is associated with an increased risk of cardiovascular death of about 76%. For example, on average, women in Nashville, Tenn., where the 2005 level was 15 micrograms, would have an approximately 76% greater chance of dying from cardiovascular causes than women in Honolulu, Hawaii, where the 2005 level was five micrograms.

Today's findings may lend more ammunition to those who want the Environmental Protection Agency to lower the legal limit for fine particles in the air, said Rogene F. Henderson, a pollution expert who heads the agency's outside panel of scientists. The current limit was set in 1997 at an annual average of 15 micrograms a cubic meter.

Last year, Ms. Henderson's panel voted 20-2 to recommend lowering the limit to 13 to 14 micro-

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The Shape of Clothes to Come

o Silhouettes, Deep Hues

to wear, emerged in fashion in the 1910s in may be harder for

Increased Heart Risk Is Linked to Air Pollution

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grams a cubic meter. Nevertheless, the agency's administrator, Stephen L. Johnson, announced in October that he wouldn't follow the scientists' recommendation to change the standard.

Mr. Johnson argued at the time that the science wasn't definitive enough to justify a limit below 15 micrograms a cubic meter. Today's study could shift that balance, Ms. Henderson said, but it isn't clear when the EPA will next revisit the matter. The Clean Air Act requires the agency to review and reissue its air-quality regulations every five years. Historically, the EPA has done so every 10 years.

An EPA spokesman said "it's too soon to say" how much weight the agency will give the new findings in reviewing pollution standards, but that the study "will be considered as part" of the process. The spokesman also noted that the agency did tighten standards for soot levels in a 24-hour period. An editorial accompanying the study's publication said that the findings "strongly support" recommendations by Ms. Henderson and other scientists for tightening EPA standards.

The new, higher risk estimate may be more accurate than previous studies, said Mr. Pope, the Brigham Young professor, since researchers now have access to better air-quality measurements thanks to stepped-up monitoring by states and the EPA. Or it may indicate that soot harms women more than men. The findings only included women because the study was part of the $725 million Women's Health Initiative that Congress launched in 1991. Only postmenopausal women who didn't already have heart disease were included in the study.

Nobody knows exactly why soot leads to heart disease. One possibility is that the tiny particles inflame the lungs, which release chemicals into the bloodstream that harm the heart, said Douglas W. Dockery, a Harvard expert who wrote an accompanying editorial.

The researchers declined to release some additional statistics that weren't included in today's New England Journal, including the actual cardiovascular death risks measured in various cities or at various levels of exposure. All of that information eventually will be released, said Joel D. Kaufman, the University of Washington doctor who led the study.

Overall, the country's air has been getting cleaner— the total levels of fine particles decreased 10% from 1999 to 2003, according to the EPA. Roughly 30% of the population still lives in areas above the EPA's legal limit for the annual average.

And while soot levels in some historically polluted areas—such as Southern California and the Southeast—improved markedly in the past few years, other places, such as the Northeast, aren't improving, the EPA says. Several Northeastern states have sued the EPA to try to force more-stringent regulations, saying power plants in the Midwest are responsible for their higher levels.

The EPA also regulates several other air pollutants, including ozone, lead and carbon monoxide. But soot—and, particularly, the tiniest particles in soot—is "considered to be the worst," said Deborah Shprentz, a consultant who works for the American Lung Association. The World Health Organization recommends that governments adopt a long-term level of 10 micrograms a cubic meter, but few if any countries have adopted the WHO's recommendation, says Dan Greenbaum, an expert at the Health Effects Institute in Cambridge, Mass. Most countries don't even regulate fine particulate matter, according to Mr. Greenbaum and others.

What's In Your Air?

Average annual levels of outdoor fine particulate matter in selected cities in 2005

Metropolitan area	Level*	Metropolitan area	Level*	Metropolitan area	Level*	Metropolitan area	Level*	Metropolitan area	Level*
Pittsburgh, PA	21.4	Little Rock-North Little Rock, AR	16.1	Bridgeport, CT	14.4	Trenton, NJ	13.0	Rochester, MN	11.4
Riverside-San Bernardino, CA	21.0	Hickory-Morganton-Lenoir, NC	16.0	Champaign-Urbana, IL	14.4	Columbia, MO	12.9	Des Moines, IA	11.3
Cincinnati, OH-KY-IN	20.0	Roanoke, VA	16.0	Erie, PA	14.4	Flint, MI	12.9	Jacksonville, NC	11.3
Bakersfield, CA	19.8	Rockford, IL	16.0	Huntsville, AL	14.4	Fort Worth-Arlington, TX	12.9	Seattle-Bellevue-Everett, WA	11.3
Birmingham, AL	19.6	Houston, TX	15.9	Wilmington-Newark, DE-MD	14.4	Phoenix-Mesa, AZ	12.9	Topeka, KS	11.3
Cleveland-Lorain-Elyria, OH	19.4	Kokomo, IN	15.9	Montgomery, AL	14.3	Tallahassee, FL	12.9	Wichita, KS	11.3
Visalia-Tulare-Porterville, CA	18.8	Charlotte-Gastonia-Rock Hill, NC-SC	15.8	Fort Smith, AR-OK	14.1	Eugene-Springfield, OR	12.8	McAllen-Edinburg-Mission, TX	11.2
Canton-Massillon, OH	18.6	Gary, IN	15.8	Kansas City, MO-KS	14.1	Mobile, AL	12.8	Ventura, CA	11.2
Detroit, MI	18.6	Grnsboro-Winston-Salem-H. Point, NC	15.8	Merced, CA MSA	14.1	Myrtle Beach, SC	12.8	Jamestown, NY	11.1
Louisville, KY-IN	18.5	Greenville-Spartanburg-Anderson, SC	15.8	Salt Lake City-Ogden, UT	14.1	Madison, WI	12.7	Missoula, MT	11.1
Lancaster, PA	18.2	Toledo, OH	15.8	Sharon, PA	14.1	Rocky Mount, NC	12.7	Tampa-St. Petersburg-Clearwater, FL	11.1
St. Louis, MO-IL	18.2	Columbus, GA-AL	15.7	Fayetteville, NC	14.0	Springfield, MA	12.7	Corpus Christi, TX	11.0
Huntington, Ashland, WV, KY, OH	18.1	Fort Wayne, IN	15.7	Grand Rapids-Muskegon-Holland, MI	14.0	Dallas, TX	12.5	Oklahoma City, OK	10.8
Steubenville-Weirton, OH-WV	18.1	Lafayette, IN	15.7	Richmond-Petersburg, VA	14.0	Kenosha, WI	12.5	Spokane, WA	10.8
York, PA	18.1	Ann Arbor, MI	15.6	Waterbury, CT	14.0	Omaha, NE-IA	12.5	Jacksonville, FL	10.7
Hamilton-Middletown, OH	17.9	Athens, GA	15.5	Modesto, CA	13.9	Stockton-Lodi, CA	12.5	Providence-Fall River-Warwick, RI-MA	10.7
Indianapolis, IN	17.9	Harrisburg-Lebanon-Carlisle, PA	15.5	New Haven-Meriden, CT	13.9	Albany-Schenectady-Troy, NY	12.4	Sioux Falls, SD	10.7
Los Angeles-Long Beach, CA	17.8	Gadsden, AL	15.4	Tuscaloosa, AL	13.9	Nassau-Suffolk, NY	12.4	Sioux City, IA-NE	10.6
Charleston, WV	17.6	Terre Haute, IN	15.4	Kalamazoo-Battle Creek, MI	13.8	Saginaw-Bay City-Midland, MI	12.4	Brockton, MA	10.5
Chicago, IL	17.5	Newark, NJ	15.3	Boston, MA-NH	13.7	Charleston-North Charleston, SC	12.3	Manchester, NH	10.5
Dayton-Springfield, OH	17.4	Davenport-Moline-Rock Island, IA-IL	15.2	Jackson, MS	13.7	Chico-Paradise, CA	12.3	Nashua, NH	10.5
Baltimore, MD	17.2	Jersey City, NJ	15.2	Decatur, AL	13.6	Tulsa, OK	12.3	Ocala, FL	10.5
Atlanta, GA	17.0	Clarksville-Hopkinsville, TN-KY	15.1	Iowa City, IA	13.6	Minneapolis-St. Paul, MN-WI	12.2	Wilmington, NC	10.3
New York, NY	17.0	Columbia, SC	15.1	Raleigh-Durham-Chapel Hill, NC	13.6	Waterloo-Cedar Falls, IA	12.2	Lewiston-Auburn, ME	10.2
Washington, DC-MD-VA-WV	17.0	Owensboro, KY	15.1	Goldsboro, NC	13.5	Worcester, MA-CT	12.2	Denver, CO	10.1
Fresno, CA	16.9	Springfield, IL	15.1	Green Bay, WI	13.5	Newburgh, NY-PA	12.1	Medford-Ashland, OR	10.1
Youngstown-Warren, OH	16.9	Johnson City-Kingsport-Bristol, TN-VA	15.0	Lansing-East Lansing, MI	13.5	Pensacola, FL	12.0	Provo-Orem, UT	10.0
Johnstown, PA	16.8	Nashville, TN	15.0	Norfolk-V. Beach-Nwprt News, VA-NC	13.5	Portland, ME	11.9	Burlington, VT	9.9
Reading, PA	16.8	Hagerstown, MD	14.9	Bloomington-Normal, IL	13.4	Cedar Rapids, IA	11.8	Lawrence, MA--NH	9.9
Evansville-Henderson, IN-KY	16.7	Memphis, TN-AR-MS	14.9	Danbury, CT	13.4	Monmouth-Ocean, NJ	11.8	Lincoln, NE	9.9
Macon, GA	16.7	Milwaukee-Waukesha, WI	14.9	Lynchburg, VA	13.4	Pittsfield, MA	11.8	Orlando, FL	9.9
Chattanooga, TN-GA	16.6	Savannah, GA	14.9	Middlesex-Somerset-Hunterdon, NJ	13.4	San Diego, CA	11.8	Miami, FL	9.6
Columbus, OH	16.5	South Bend, IN	14.8	State College, PA	13.4	San Jose, CA	11.8	San Francisco, CA	9.5
Philadelphia, PA-NJ	16.5	Buffalo-Niagara Falls, NY	14.7	Dothan, AL	13.2	Greenville, NC	11.7	Las Vegas, NV-AZ	9.4
Akron, OH	16.4	Orange County, CA	14.7	Florence, AL	13.2	New London-Norwich, CT-RI	11.7	Portland-Vancouver, OR-WA	9.2
Muncie, IN	16.4	Albany, GA	14.6	Stamford-Norwalk, CT	13.2	Syracuse, NY	11.6	Oakland, CA	9.1
Parkersburg-Marietta, WV-OH	16.4	Allentown-Bethlehem-Easton, PA	14.5	Asheville, NC	13.1	Appleton-Oshkosh-Neenah, WI	11.5	Reno, NV	9.0
Knoxville, TN	16.3	Bergen-Passaic, NJ	14.5	Benton Harbor, MI	13.1	Hartford, CT	11.5	Albuquerque, NM	8.1
Wheeling, WV-OH	16.2	Decatur, IL	14.5	Texarkana, TX-Texarkana, AR	13.1	Sacramento, CA	11.5	Honolulu, HI	5.0
Augusta-Aiken, GA-SC	16.1	Peoria-Pekin, IL	14.5	Scranton-Wilkes-Barre-Hazleton, PA	13.0	Tacoma, WA	11.5		
Lexington, KY	16.1	St. Joseph, MO	14.5	Springfield, MO	13.0	Panama City, FL	11.4		

*In micrograms per cubic meter of air

Source: U.S. Environmental Protection Agency