Showdown Over Clean Air Science

Industry and environmental researchers are squaring off over studies linking air pollution and illness in what some are calling the biggest environmental fight of the decade

Nine years ago, epidemiologist Joel Schwartz stumbled across a disturbing pattern of death. Schwartz, then at the Environmental Protection Agency (EPA), noted that when soot levels in the air of Steubenville, Ohio, rose on any given day in the 1970s and 1980s, the number of fatalities among residents would jump the next day—even when air pollution levels were supposedly safe. Schwartz went on to document the same chilling pattern in four more cities that track soot: Philadelphia; Detroit; St. Louis; and Kingston, Tennessee. Projecting these findings to the entire U.S. population, Schwartz estimated that 60,000 people could be dying each year—more than the annual number of car crash victims—from heart and lung diseases aggravated by tiny airborne particles. At scientific meetings in 1991 and 1992, recalls Schwartz, now at Harvard, the studies got "a tremendous amount of attention."

Today, the analysis is provoking a furor. Schwartz's findings and similar studies by other researchers lit the fuse of a political powder keg: a debate over whether industry should take costly steps to reduce the amount of soot and other pollutants released into the atmosphere. Heeding the results from Schwartz and others, on 16 July the EPA unveiled final rules designed to tighten ozone standards and clamp down on particles. The cost of implementing the rules—which EPA estimates at $9.7 billion per year for measures such as installing new equipment on power plants and diesel trucks—has sparked a fierce protest on Capitol Hill from industry groups and many state and local officials. So far, EPA has stood its ground. The agency has refused to scale back the standards, first proposed in November, and President Clinton has said he supports them. But now the bell has sounded for round two of what is shaping up to be the biggest environmental fight of the decade: Congress is about to consider legislation that would quash the standards.

Opponents argue that the science fails to support the new regulations, which would lower maximum ozone levels by a third and, for the first time, set acceptable airborne levels of fine particles less than 2.5 micrometers in diameter, called $PM_{2.5}$, which are generated mainly by burning fossil fuels. Although industry groups have sharply criticized the new ozone standards, arguing that the health benefits would be marginal compared to the costs, most of the scientific debate has centered on the limits on particulate matter.

Critics charge that Schwartz's population studies and others like it do not link individual pollutants to human health effects; instead, they argue, different factors—such as other pollutants and lifestyle factors—may be responsible for the increased death rate. Moreover, scientists have yet to propose a plausible explanation for how fine particles might harm the body (see sidebar on p. 469). Because of such shortcomings, the Air Quality Standards Coalition, representing 500 petroleum, automotive, and other industry and business groups, derides the science as "totally inadequate." Adds epidemiologist Suresh Moolgavkar of the Fred Hutchinson Cancer Research Center in Seattle, "EPA is espousing a certainty in its language that is simply not justified by the data."

But EPA Administrator Carol Browner contends that there are plenty of data to support the rule, even the particularly contentious $PM_{2.5}$ standard. The evidence comes from more than 60 published health studies that show a link between soot and adverse health effects in scores of cities, says John Bachmann, associate director for science policy in EPA's Office of Air Quality Planning and Standards. EPA acknowledges, however, that many questions remain about how fine particles cause harm. "All of us agree we need way more science," says Bachmann. However, he says, "We're not supposed to wait until people are dead in the streets." But many scientists say the problem is not the standard itself, but the levels EPA has chosen. "These studies can't readily lead to a specific number," says Johns Hopkins University epidemiologist Jonathan Samet. "It all makes sense to regulate $PM_{2.5}$. The question is, do we have the quantitative information to do it? That's where the debate begins."

SELECTED PARTICLE-POLLUTION STUDIES

Study	Design	Key Findings
Utah Valley (Pope *et al.*, 1989)	Hospital admissions & PM_{10} levels across period encompassing 13-month shutdown of steel mill	Admissions for respiratory disease higher when mill operating
Philadelphia (Schwartz & Dockery, 1992)	Daily mortality and total PM levels	Significant association, with greater risks for elderly and for death from chronic obstructive pulmonary disease
Six Cities (Dockery *et al.*, 1993)	Interviewed 8111 people for lifestyle factors and tracked deaths over 14 to 16 yrs.; used several PM measures	26% higher death rate in most polluted vs. least polluted city
American Cancer Society 151 cities (Pope *et al.*, 1995)	Used health information from 552,138 ACS volunteers, $PM_{2.5}$ for 50 cities	17% higher death rate in most polluted vs. least polluted city

Fine particle distinctions

Researchers have been well aware of the dangers of particles ever since several disastrous air pollution episodes in Europe and the United States in the middle of this century, such as a deadly week in London in 1952 when choking soot and sulfur dioxide—at least 10 times today's average levels—killed thousands, mostly children and elderly people with heart or lung ailments. Such incidents spurred controls on pollutants. Since 1971, EPA has ordered limits on levels of particles, which are composed of dust from soils, bits of carbon spewed by diesel vehicles and power plants, sulfates, and gases such as nitrogen oxides and volatile organics that condense onto seed particles. Initially, these rules covered particles up to 50 micrometers in diameter. But after studies showed that coarse particles tend to be safely expelled from the body's upper airways, the agency in 1987 restricted only finer particles, less than 10 micrometers in diameter (PM_{10}).

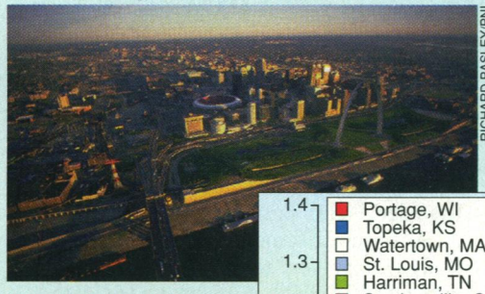
By the early 1990s, however, Schwartz's study and dozens like it had convinced many experts that the PM_{10} standard might not be protective enough, especially for the elderly, children, people with frail immune systems, and other vulnerable groups. In cities in the United States and other countries, death rates and hospital admissions for people suffering from cardiac problems and respiratory

Researchers and Lawmakers Clash Over Access to Data

In one corner of the battleground over new clean air standards (see main text), scientists and policy-makers are skirmishing over an issue close to their hearts and pocketbooks: who "owns" raw data. Industry groups have charged that the authors of a key study on the health effects of airborne particles have resisted sharing data collected with taxpayer money—a reanalysis of which, they argue, might weaken the scientific basis of the standards. The researchers, meanwhile, are reluctant to make the data widely available because it contains confidential information on their subjects.

The fight could have repercussions that reach far beyond this year's pollution debate: A House committee earlier this month directed the Environmental Protection Agency (EPA) to publicly release raw data from air pollution research it funds. Not everyone is sure that's a good idea. "The implications of this language could be quite significant in terms of setting precedents," says Anne Sassaman, extramural grants director at the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health.

The data-sharing commotion was sparked by a paper from the so-called Six Cities study, in which a Harvard team led by epidemiologist Douglas Dockery followed the health of about 8000 people over 14 to 16 years and found a link between variations in particulate matter (PM) levels and death rates. Besides tapping public databases on weather and PM levels, the researchers interviewed subjects and obtained death records. The NIEHS funded the data collection, while EPA grants paid for the analyses.



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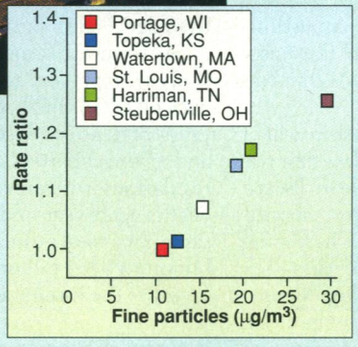

Data dust up. Congress wants raw data from the Six Cities study, which correlated relative death rates (Portage, Wisconsin, being 1) with particulate levels *(right)*. St Louis *(above)* came out in the middle.

Last January, however, EPA Assistant Administrator for Air and Radiation Mary Nichols urged the Harvard group to share its data. Congress, state governors, and others had requested the raw data, the letter said, and "given the strong interest," the data "should be made available ... as rapidly as possible." Industry groups appealed to Representative Tom Bliley (R–VA), chair of the House Commerce Committee, who asked EPA and NIEHS to obtain raw data from the Six Cities study and a related Harvard study and hand it over to the committee. Given the importance and cost of the proposed rules, Bliley wrote, "it is important that the public and affected parties have the ability to review all of the underlying data ... so they can be confident that EPA is basing its decisions on sound science."

The agencies said they did not have the data, and Harvard refused to turn them over to EPA. Dockery says that subjects' medical histories and lifestyle habits, as well as death records from state and local agencies, were obtained on condition that the information would be kept confidential. Even if a subject's name were deleted from a file, Dockery says, simply knowing the date of death could be a big enough clue to identify that person, as three of the six cities in the study have populations under 50,000. The Harvard group has, however, allowed at least 18 scientists over the past 15 years to review its data collection at Harvard.

Last April, Harvard's dean for academic affairs, James H. Ware, offered a second alternative: to share the data with the Health Effects Institute, a research center in Cambridge, Massachusetts, funded by industry and the EPA, which could convene a panel of scientists not affiliated with industry or environmental groups to oversee a reanalysis. EPA agreed, and a nine-scientist panel chaired by Arthur Upton of the Robert Wood Johnson Medical School in Piscataway, New Jersey, is expected to finish its work by June 1999.

This arrangement hasn't satisfied the industry critics, however. For example, American Petroleum Institute (API) President Charles DiBona told Ware in a 1 May letter that while "we commend" Harvard for "taking this step ... we do not believe it goes far enough" and that the data should be available "for review by any professionally qualified investigators who have a legitimate scientific interest," including API. Bliley lambasted EPA again last week, saying the agency "has so far withheld the facts."

Other lawmakers are also not appeased. A report accompanying the House version of the 1998 EPA appropriations bill earmarks $35 million for particle studies that EPA would fund at NIEHS and the Department of Energy, and requires that all the data from these studies "will become available to the public, with proper safeguards" covering such issues as confidentiality, first publication rights, and scientific fraud. The Senate funding bill does not contain such a directive; thus, it may not survive a House-Senate conference later this summer to settle differences in the bills.

If a data-release requirement were limited to just these studies, and if grantees were to know "up front" about the ground rules, it would not be onerous, says Sheila Newton, director of policy, planning, and evaluation for NIEHS. Some industry groups, such as the 40,000-member Small Business Survival Committee, however, are now lobbying Congress to require that data from all federally funded research be made public. That prospect concerns many researchers, who worry that wholesale release of raw data could lead to "data dredging," in which hired hands working for industry, environmental groups, or other advocacy groups might analyze it with sub-par methods to get answers favorable to their position. "There's no question that if you put in enough variables in a post hoc analysis, you can make these data or any data say whatever you want," says Dockery. "I would have deep concerns about giving up some of my data if I knew a priori someone wasn't going to do an honest job of analyzing it, if they had a political agenda," says one state scientist who asked not to be identified.

The furor has made EPA realize it needs to clarify its policy on data ownership, says Joe Alexander, acting chief of EPA's Office of Research and Development. Like most other agencies, EPA encourages extramural researchers to share data. But EPA told Bliley's committee that it almost never asks for raw data, except when investigating allegations of scientific fraud, or when data are prepared for approval of products. Alexander says one possibility under consideration is to set up a system like that at NASA, which requires agency-funded scientists to submit all their raw data. That, says Carl Mazza, science adviser in EPA's Air and Radiation Office, "would create a major issue for the way in which the scientific community operates." **–J.K.**

problems such as asthma seemed to rise and fall with daily particle levels. For example, a study led by biostatistician Richard Burnett of Health Canada found that in Ontario in the mid-1980s, for every 13 micrograms/meter^3 rise in daily levels of sulfates—a surrogate for overall $PM_{2.5}$—hospital admissions for respiratory and cardiac events shot up 3.7% and 2.8%, respectively.

Researchers also began to recognize that they needed to focus on finer particles—$PM_{2.5}$ or smaller—because animal studies using radioactively tagged particles and lung casts made from human cadavers had shown that such tiny particles are most likely to lodge deep in lungs. "The finer particles represent a completely different class of materials than the coarser PM_{10}, and it is logical that they probably have different activities and types of toxicity," says toxicologist Joseph Mauderly of the Lovelace Respiratory Research Institute in Albuquerque, New Mexico. The PM_{10} is mostly inert crustal dust, while the combustion-generated fine particles contain the nasty stuff—corrosive acids and metals—that can damage tissues.

Many experts, however, were skeptical of these red flags. Their main beef was that the daily mortality studies were unable to discern whether air pollution levels were significantly shortening lives or perhaps hastening by hours or days the deaths of very sick people already on the verge of dying. "People believed the studies were picking up a real phenomenon, but the interpretation was unclear," says Columbia University epidemiologist Patrick Kinney.

A more convincing set of findings came along in 1993, however, when a Harvard team headed by Douglas Dockery examined soot and other pollutant levels and 1429 deaths that occurred in 8111 adults the team followed for 14 to 16 years in six Eastern U.S. cities (known as the Six Cities study). The researchers interviewed subjects about weight, smoking, and other risk factors, correcting for these lifestyle differences, which had not been possible in earlier studies comparing city death rates. They found that the strongest association between any pollutant and death rates was with fine particles, and that the risk of death was 26% higher in the most polluted city—Steubenville—compared to the cleanest—Portage, Wisconsin. The results supported the findings of the daily studies and raised additional concerns by suggesting that the harmful effects of particles can build up over years.

A second long-term study 2 years later strengthened the case against airborne particles. Tapping an American Cancer Society (ACS) database of smoking, age, occupation, diet, and other data on over 550,000 volunteers in 151 cities, along with sulfate data and $PM_{2.5}$ readings for 50 cities, the Harvard group and environmental economist Arden Pope of Brigham Young University in Provo, Utah, found a 17% difference over 8 years in death rates between the cleanest and dirtiest cities. "We're not likely to see a study of this quality and magnitude [again] in our lifetimes," says Alan Krupnick, an economist with Resources for the Future, a Washington, D.C., think tank. "I think that pushed a lot of people over the edge," adds Kinney.

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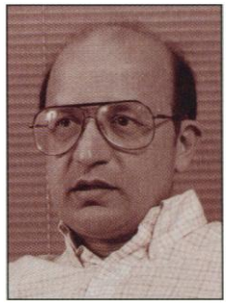
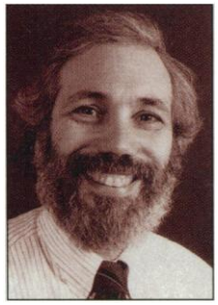


A Natural Resources Defense Council study extrapolated the results and came up with 64,000 annual deaths that were up to 2 years premature. Using this "body count" and its own analyses, EPA estimates that its regulations will prevent 15,000 premature deaths each year and 9000 hospital admissions, for a total estimated cost savings of $19 billion to $104 billion a year—about two to 12 times the estimated cost of compliance.

Industry chokes on rules

After a 1993 lawsuit brought by the American Lung Association forced EPA to stick to its mandated 5-year schedule for reviewing the latest evidence of particle health effects, critics of the science behind the new rules launched their assault. "We'd go to meetings and testify at hearings," says Dockery, "and they'd say, 'We get different results.' "



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—Joel Schwartz

Critics have saved most of their barrage for the mortality studies. Hutchinson's Moolgavkar, for instance, reanalyzed Schwartz's Philadelphia data on behalf of the American Iron and Steel Institute. When Moolgavkar took into account other air pollutants—ozone and nitrogen dioxide—and analyzed them all simultaneously, it was impossible to separate the health effects of particles from those of sulfur dioxide. "It is impossible to say one component is any more responsible than any other," says Moolgavkar.

Others point out that the long-term ACS and Six Cities studies captured only a fraction of the total pollution the subjects were exposed to over their lives. "How does that relate to what people are exposed to across their lifetimes? We really don't know," says Samet of Johns Hopkins, who nonetheless says he believes the link between daily mortality and particles is real. Biostatistician Fred Lipfert, a consultant who has worked for the Electric Power Research Institute in Palo Alto, California, also argues that the Harvard team "kind of just took a first cut at socioeconomic status," and that a more sedentary lifestyle in, say, Steubenville compared to Portage might account for the differences in mortality that the Six Cities study attributes to fine particles.

Other concerns center on how EPA estimated the potency of these tiny particles. Because only a few excess deaths and hospitalizations occur when the air contains low levels of particle pollution, the studies lack the statistical power to precisely estimate how dangerous particles are at these levels. So EPA assumed that the health threat increases in a linear fashion with dose, ignoring the possibility that the risk may taper off at lower levels. Adding to the uncertainty, few studies actually measured $PM_{2.5}$—most used PM_{10} or a surrogate such as sulfates. "There's very little information on the ratio" between PM_{10} and $PM_{2.5}$, says Yale epidemiologist Jan Stolwijk.

Moreover, without knowing what it is about particles that causes ill health effects, it's impossible to be sure that the regulations are targeting the right source, says toxicologist Roger McClellan, president of the Chemical Industry Institute of Technology in Research Triangle Park, North Carolina. For example, he says, a state might target diesel engines or clamp down on plow dust, when the problem is actually sulfates from power plants. Says McClellan: "We run a real hazard here of putting in place a new standard that we don't know how effective it will be."

A lot of hot air?

EPA scientists disagree, saying they are confident that the science supports their regulations. "We think we've done a totally legitimate, rational analysis of the studies we had," says the agency's Bachmann. He points to

Puzzling Over a Potential Killer's Modus Operandi

Experts may clash over the strength of the science behind the new clean air regulations (see main text), but they do agree on one thing: It's still a mystery how airborne particles could trigger a bout of asthma or cause someone to drop dead of a heart attack. A dozen labs are now racing to find a modus operandi.

This is not the first time that an unknown mechanism has bedeviled researchers trying to assess a potential environmental hazard. But unlike some other alleged risks—such as electromagnetic fields—it's apparent that the more particles one breathes, the greater the danger, says Keith Florig, a science policy expert at Carnegie Mellon University in Pittsburgh. "If you observe a strong enough dose response, that's pretty compelling," he says.

The best way to unravel a pollutant's mechanism is to study how it triggers health effects in animals. Until recently, however, researchers had drawn a blank. "I've done lots of studies" exposing healthy rats to diesel soot for nearly their entire lives at particle levels more than 10 times what people typically encounter, and "nothing happens," says toxicologist Joseph Mauderly of the Lovelace Respiratory Research Institute in Albuquerque, New Mexico.

But in a parallel to the epidemiological studies that first drew attention to the hazards of airborne particles, toxicologists in the last year or two have begun to find that sickly animals exposed to fine particles get sicker and sometimes die. For example, pulmonary biologist John Godleski of the Harvard School of Public Health in Boston found that rats with chronic bronchitis are especially vulnerable. When he exposed the animals to particles smaller than 2.5 micrometers ($PM_{2.5}$) strained from Boston air, at levels equivalent to about twice the current EPA daily limit for PM_{10} for 6 hours per day for three straight days, 37% of the bronchitic animals died; all the healthy rats survived.

Godleski has also tightened balloons around the coronary arteries of dogs to simulate angina, or cardiac chest pain, then exposed the dogs for 6 hours to $PM_{2.5}$. At particle concentrations of about 116 $\mu g/m^3$ and 175 $\mu g/m^3$, levels often reached in heavily polluted cities, the dogs' hearts developed arrhythmias that are commonly observed in people nearing a fatal heart attack. Godleski says these animal studies could help explain the observation that when particle pollution soars, "a lot of people are dying outside of the hospital. These could very well be sudden deaths" from heart attacks, he says.

Now that researchers have potential animal models for the health effects, they are trying to sort out whether a particle's chemical composition dictates how dangerous it is, and how it triggers health effects. "Nobody is sure what it is in, or on, or of the particles" that causes health effects, notes toxicologist Judith Zelikoff of New York University School of Medicine. Freshly created particles appear to be more toxic than aged particles, so the culprit may be some reactive chemical group—such as an acid, a metal, an organic compound, or a peroxide—attached to a particle's surface, says Morton Lippman, also at New York University School of Medicine. Others think that ultrafine particles, or those less than 0.1 micrometer in diameter, are the problem, because they are much more potent than larger particles at provoking immune responses in the lungs. "The problem is, none of these hypotheses really seems to be a solid explanation for all the effects," Mauderly says. "Probably they all contribute."

–J.K.

what he calls "overwhelming consistency"—more than 60 of 86 population studies linked health effects to fluctuations in particulate matter levels—and the coherence between deaths, hospitalization, and respiratory disease. Others point to a study published this month in *Environmental Health Perspectives* by EPA researcher Tracey Woodruff and colleagues at the Centers for Disease Control and Prevention in Atlanta. They found that infants in cities with high particle pollution levels are 25% more likely to die of sudden infant death syndrome than are those in cities with relatively clean air. "It certainly adds support," says California EPA epidemiologist Bart Ostro.

Schwartz also takes aim at the argument that pollutants other than particles may be blurring the picture. Cities with only one or two major airborne pollutants—such as Santa Clara, California, which has low air levels of sulfur dioxide and ozone in winter—still show a link between particle levels and health problems, he says. "This whole industry argument that it's all other pollutants is just not supported by the data," says Schwartz. New York University School of Medicine epidemiologist George Thurston says "it's a valid criticism" that some of the Harvard daily city studies underestimated the effects of other pollutants, but those contributions "just reduce" the estimated danger levels of particles. "It doesn't make [the effects] go away." Finally, Bachmann says, even if $PM_{2.5}$ itself is not the bad guy—if sulfates alone are the problem, for example—targeting it should also control whatever pollutant is taking lives.

Most experts contacted by *Science* agreed that EPA was justified in setting a standard for $PM_{2.5}$. "There's enough circumstantial evidence that it does make sense to begin to look at and regulate fine particles as a class," says Mauderly. At a minimum, Mauderly and others add, setting a standard will force the states to collect data that could help pin down $PM_{2.5}$ health effects. But they split on just how stringent that standard should be. "We have a tremendous amount of uncertainty as to what the dose-effect relationship is—how dangerous particles might be and under what circumstances," says Mauderly. "The scientific basis for [EPA's planned levels] is totally lacking," Stolwijk says. "You have to make several leaps of faith."

Yet while the studies "have their limitations," says environmental health scientist Arthur Upton of the Robert Wood Johnson Medical School in Piscataway, New Jersey, "I'm not aware that we can dismiss their findings as unimportant or irrelevant." Deciding whether to set a stringent standard, Upton says, "becomes a value judgment. It's not a scientific question. ... Do we dismiss the data? Or do we accept them as warning signs and act accordingly?"

EPA's judgment won't be the final word. The House Commerce Committee is considering a bill that would impose a 4-year moratorium on the standards while EPA does more monitoring and research. Congress may also try to kill the rules through a new law passed last year to shield small businesses from overly burdensome regulations. And the White House announced last month that EPA will conduct another scientific review, starting this year, before it implements the $PM_{2.5}$ standard. Congress is expected to set aside up to $35 million next year in EPA's budget for research on particles. And Upton is heading a reanalysis of the Six Cities and ACS studies by the Health Effects Institute, an industry- and EPA-funded research organization in Cambridge, Massachusetts. "It's a vexing question, and I wish I were Solomon and knew exactly what the right answer was," Upton says. "But we'll work on it."

–Jocelyn Kaiser