SELECTED KEY STUDIES ON
PARTICULATE MATTER AND HEALTH: 1997 - 2001

NEW STUDIES CONFIRM THAT CURRENT LEVELS OF
PARTICULATE AIR POLLUTION ARE HARMFUL TO HUMAN
HEALTH

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More than 800 new scientific studies related to the effect of airborne particulates on human health have been published since 1996, when EPA last reviewed the standards for particulate matter. The new studies validate the earlier research and address the most important arguments raised by industry critics. Taken together, the studies confirm the relationship between particulate air pollution, illness, hospitalization, and premature death. The major themes of the new research are that the:

- Major long-term studies have been fully validated.
- New short-term studies from across the U.S. and around the world confirm the mortality effects.
- New analyses show that lives may be shortened by months or years, rather than days.
- Recent studies of laboratory animals and humans have identified cardiac responses to particles, thus elucidating possible biologic mechanisms for mortality.
- New studies demonstrate that infants and children, particularly asthmatic children, are especially sensitive to the effects of fine particle pollution.

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As part of this effort, the Health Effects Institute, jointly sponsored by industry and EPA, has committed substantial resources to research on PM.

As a result of this infusion of research funds, hundreds of scientific papers and research reports have been published since EPA last issued its “Air Quality Criteria for Particulate Matter” in 1996.

This annotated bibliography presents the findings of some of the most significant new research studies that advance our understanding of the harmful health effects of particulate air pollution. The peer-reviewed papers cited here represent a small sample of the scientific articles on the health effects of particulate air pollution published since 1996. This bibliography does not attempt to be comprehensive: exclusion does not imply that a study is unimportant; inclusion does not imply endorsement.

LONG-TERM STUDIES OF MORTALITY

Prospective Cohort Epidemiological Studies Are Validated in Independent Reanalysis

Two landmark prospective cohort studies reported that chronic exposure to particulate pollution increases the risk of premature mortality. In the 1993 Six Cities Study, Harvard University researchers followed the health of more than 8,000 people in six small cities that fell along a gradient of air pollution concentrations for a period of 14 to 16 years. As particle concentrations increased, there was an almost directly proportional increase in the death rate in the residents studied. Residents of the most polluted city in the study, Steubenville, Ohio, had a 26 percent increased risk of premature mortality, compared to the residents of the cleanest city studied, Portage, Wisconsin. The increased risks were associated with a difference in ambient fine particle concentrations of 18.6 micrograms per cubic meter.

The 1995 American Cancer Society study reported an association between fine particle air pollution and premature death by cardio-pulmonary and other causes in a study group of over half a million people in 151 U.S. cities. All cause mortality increased by 17 percent with a 24.5 microgram per cubic meter difference in fine particle pollution between the cleanest and dirtiest city studied.

These original studies used statistical techniques to adjust for age, and to control for the effects of smoking, diet, and occupational exposure.

Health Effects Institute funded researchers, led by Dr. Dan Krewski of the University of Ottawa, undertook a reanalysis of the original studies and a quality audit of the underlying data. Researchers performed an extensive sensitivity analysis using alternative statistical methods, and considering the role of 20 potential confounders such as other pollutants, climate, and socio-economic factors on study results. The sensitivity analysis largely confirmed the original results of the Harvard Six Cities Study and the American Cancer
Society Study. In addition, the sensitivity analysis identified higher educational status as a factor associated with reduced risk to air pollution exposure, and reported an association between sulfur dioxide pollution and mortality.


**Chronic Exposure to Particulate Pollution Shortens Lives by One to Three Years**

There have been two recent attempts to quantify the extent of life shortening predicted by the long-term epidemiological studies. Dutch scientist Dr. Burt Brunekreef made such an estimate in a paper prepared for the World Health Organization’s consideration of revisions to the Air Quality Guidelines for Europe. Using risk ratios reported in the Harvard Six Cities Study and the Study of the American Cancer Society cohort, Brunekreef conducted a life table analysis to estimate the effect of particulate air pollution on the survival rate of 25 year-old Dutch men. An extrapolation based on U.S. life tables yields an estimated diminished life expectancy of 1.31 years due to ambient pollution.

Dr. C. Arden Pope III, of Brigham Young University, analyzed reductions in life expectancy in the U.S. population due to chronic exposure to particulate matter. He applied relative risks for premature death derived from the prospective cohort studies, and estimated loss of life expectancy ranging from one to three years, depending upon assumptions about the age at which susceptibility to the effects of air pollution begins.


**DAILY MORTALITY STUDIES**

90-City National Morbidity, Mortality and Air Pollution Study (NMMAPS) Shows that Contemporary Levels of Air Pollution are Killing People

The Health Effects Institute, which is jointly funded by EPA and industry, commissioned an original nationwide study of the short-term effects of air pollution on human health, known as the National Morbidity, Mortality and Air Pollution Study, or NMMAPS. A
team of investigators led by Dr. Jonathan Samet of the Johns Hopkins University School of Public Health developed and applied a standardized methodology for examining pollution effects across many cities. Investigators from Johns Hopkins University and Harvard University developed and applied state-of-the-art statistical techniques to examine the effects of multiple pollutants, the extent of life-shortening, and the degree of "exposure measurement error" due to reliance on centrally located air quality monitors.

In its study of the 90 largest U.S. cities, NMMAPS found strong evidence linking daily increases in particulate pollution to increases in death. On average, overall mortality increased by 0.5 percent for every 10 microgram per cubic meter increase in \( \text{PM}_{10} \) measured the day before death. The effect was slightly greater for deaths due to heart and lung disease than for total deaths. This risk ratio is somewhat lower than reported by earlier meta-analyses, perhaps due to certain methodological assumptions such as a one-day lag.

Samet et al. report that the relative increases in daily mortality partly reflect life shortening on the order of months. The association between particulate matter and mortality persists even when other pollutants are included in the statistical model. Their analyses also provide evidence against arguments that exposure measurement error could explain the associations between particulate matter and adverse health effects.

In addition, in a study of 14 U.S. cities, NMMAPS found strong and consistent associations between particulate air pollution and hospital admissions among the elderly. Hospital admissions data was obtained from the Medicare program. The cities were selected for study because they had daily \( \text{PM}_{10} \) measurements.

For each 10 microgram per cubic meter increase in \( \text{PM}_{10} \), there was approximately a 1 percent increase in hospital admissions for cardiovascular disease, and about a 2 percent increase in admissions for pneumonia and chronic obstructive pulmonary disease. Cities studied were Birmingham, AL, Boulder, CO, Canton, OH, Chicago, IL, Colorado Springs, CO, Detroit, MI, Minneapolis/St. Paul, MN, Nashville, TN, New Haven, CT, Pittsburgh, PA, Provo/Orem, UT, Seattle, WA, Spokane, WA, and Youngstown, OH.

Investigators concluded that the complementary analyses of mortality and morbidity provide "new and strong evidence" linking particulate air pollution at current levels to adverse health effects.

Some of the results from the NMMAPS study were published in an article in the New England Journal of Medicine. Samet, et al. examined the effect of five of the most widespread outdoor air pollutants – particulate matter, ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide in 20 of the largest cities in the United States. The study was specifically designed to address many of the criticisms of earlier single-city studies. The study found consistent evidence that relatively small daily increases in particulate pollution were followed by daily increases in death rates, particularly from heart- and lung-related causes. Study authors noted that other analyses have demonstrated that the
amount of life lost due to particulate pollution goes beyond just a few days. The study
investigators also reported an association between summertime ozone levels and
mortality.

The New England Journal of Medicine article concludes, "there is consistent evidence
that the levels of fine particulate matter in the air are associated with the risk of death
from all causes and from cardiovascular and respiratory illness. These findings
strengthen the rationale for controlling the levels of respirable particles in outdoor air."

2000.

Samet, J.M., Zeger, S.L., Dominici, F., Curriero, F., Coursac, I., Dockery, D.W., Schwartz, J., and Zanobetti, A. The
National Morbidity, Mortality, and Air Pollution Study. Part II: Morbidity, Mortality and Air Pollution in the United

Samet, J.M., Dominici, F., Curriero, F.C., Coursac, I., and Zeger, S.L. Fine Particulate Air Pollution and

Air Pollution Effects Persist for Several Days, Increasing the Overall Risk of
Exposure

Epidemiological studies have used different assumptions about the number of days
following exposure to air pollution that effects will occur. Some studies have assumed
that effects occur the day after exposures. However, toxicological evidence suggests that
effects of exposure may be observed over several subsequent days. In an analysis using
data from New Haven, Birmingham, Pittsburgh, Canton, Detroit, Chicago,
Minneapolis, Colorado Springs, Spokane, and Seattle, Dr. Joel Schwartz, of the
Harvard School of Public Health, has shown that statistical models that assume a one day
lag, such as NMMAPS, grossly underestimate the effect of PM$_{10}$ on mortality. Assuming
that effects continue over several days, as demonstrated by this analysis, roughly doubles
the relative risk of premature mortality.


PM$_{2.5}$ from Motor Vehicles and Coal Combustion is Linked to Increased Mortality

Investigators from Harvard Medical School used data on the elemental composition of
size-fractionated particles to identify the sources of fine particles in six eastern U.S. cities
that have been the subject of a long-term air pollution study: Watertown, MA,
Kingston-Harriman, TN, St. Louis, MO, Steubenville, OH, Portage, WI, and
Topeka, KS. For example, lead was used as a tracer for motor vehicle exhaust, selenium
for coal combustion, and silicon for soil and crustal matter. Each of these fractions was
examined in association with daily mortality rates in each city. The study reported that a
10 μg/m³ increase in PM$_{2.5}$ from mobile sources accounted for a 3.4% increase in daily mortality, while the equivalent increase in fine particles from coal combustion sources accounted for a 1.1% increase. Fine particles from crustal sources were not associated with mortality. The study concludes that "the results indicate that combustion particles in the fine fraction from mobile and coal combustion sources, but not fine crustal particles, are associated with increased mortality."


**Daily Mortality Studies Pour In From Cities Around the World**

Studies in new locations and by additional investigators with consistent results help strengthen the case for a causal relationship.

EPA's 1996 review of the PM standards cited over two dozen short-term epidemiological studies. Since then, time series studies reporting an association between short-term exposure to particulate matter and early mortality have been published for these U.S. cities: Philadelphia; Ogden, Salt Lake City, and Provo/Orem, Utah; Seattle; Santa Clara County, California; and Buffalo. Additional studies have been published for these major cities all over the world: Toronto; Mexico City; London; Edinburgh; Birmingham, UK; Rotterdam; Helsinki; Madrid; Rome; Milan; Brisbane; Sydney; Delhi; Bangkok; and Seoul and Ulsan, Korea. Many of the new studies have evaluated the sensitivity of the estimated PM effects to the inclusion of other pollutants in the statistical model. Overall, the associations of PM with adverse effects continue to be consistently observed, and sometimes, effects of other air pollutants such as ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide are also reported.

A multi-city study of the short-term health effects of air pollution on mortality and hospital emergency admissions was initiated by the European Union Environment Programme. The study, known as Air Pollution and Health: A European Approach or APHEA, investigated the effects of several pollutants on mortality in 12 European cities. The study reported positive associations with sulfur dioxide and PM$_{10}$, and daily increases in mortality, with stronger and more consistent associations observed in western European cities.

A quantitative meta-analysis by Jonathan Levy et al. of the Harvard School of Public Health set out to compare mortality estimates from over twenty daily time series studies. Their analysis estimated that mortality rates increased by approximately 0.7 percent per 10 microgram per cubic meter increase in PM$_{10}$ concentrations. Investigators reported "our model finds compelling evidence that the PM$_{10}$-mortality relationship is stronger in locations with higher PM$_{2.5}$/PM$_{10}$ ratios, supporting the hypothesized role of fine particles."

001492
"HARVESTING" THEORY DISPROVEN

Mortality Reported in Short Term Community Health Studies is Not Due to "Harvesting"

Numerous short-term epidemiological studies have reported that short-term increases in air pollution are followed by an increased number of deaths. Some have argued that the associations between day to day variations in mortality and air pollution represent a "harvesting" effect, that is, the advancement of death by a few days in people already about to die from other causes. If air pollution advances death of the very frail by only a few days (the "harvesting" hypothesis), then you would expect that an increase in daily deaths would be followed by a decrease in deaths within a few days.

Professors Scott Zeger and Francesca Dominici of the Johns Hopkins School of Public Health developed a statistical technique to examine harvesting using data on total suspended particulate matter (TSP) and total mortality in Philadelphia. They found that removing the shortest term fluctuations from their time series increased rather than decreased the estimates of pollution effects. This is the opposite of what would be expected if "harvesting" accounted for all the deaths.

As part of the NMMAPS study, Dr. Joel Schwartz of the Harvard School of Public Health studied this issue using data from Boston. He reported that for chronic obstructive pulmonary disease and ischemic heart disease, most of the deaths seem to be advanced by a few months on average. The statistical approach did not allow estimates of life shortening beyond two months. In contrast, for pneumonia, the analysis showed that some deaths are brought forward by a few days, consistent with the harvesting hypothesis. Effect estimates increased when examining longer time periods, suggesting that cumulative exposures are more harmful than daily exposures. Overall, these results suggest that the short-term epidemiological studies underestimate the number of early deaths.


Most Air Pollution Related Deaths Are Being Advanced By Months to Years

While the association between particulate air pollution and mortality is generally acknowledged to be causal, critics have claimed that the public health impact is minor, because people are dying just a few days early. This theory is sometimes called "harvesting." This study is based on an examination of daily deaths and hospital admissions in Chicago for the years 1988-1993. If people are dying a few days early, then the death rate should drop a few days after the air pollution event. The analysis shows that this is not the case. The results confirm findings previously reported for Boston and Philadelphia, using a different methodology. The author concludes that the results indicate that air pollution may be increasing the overall number of people at risk of death, and that most of the deaths are being advanced by months to years.


PM-Mortality Relationship Is Linear, With No Thresholds

No Threshold is Evident for the Effect of PM$_{10}$ on Daily Deaths

In the Schwartz and Zanobetti study, Harvard University researchers applied a statistical method to examine the shape of the dose-response relationship between air pollution and daily deaths in ten U.S. cities. The cities studied were New Haven, Birmingham, AL, Pittsburgh, Detroit, Canton, OH, Chicago, Minneapolis-St. Paul, Colorado Springs, Spokane, and Seattle. Simulation studies demonstrated that the method used can detect threshold and other nonlinear relationships in epidemiologic studies. But when used to analyze the association between PM$_{10}$ and mortality, no evidence of a threshold was found, and the associations appeared to be linear down to the lowest levels studied. This is consistent with earlier results.

An analysis of data for the 20 largest U.S. cities from 1987-1994 from the NMMAPS study also reported that a linear model, without a threshold, was most appropriate for assessing the effects of particulate air pollution on daily mortality for total mortality and for mortality from cardiovascular and respiratory causes, but not for other causes of mortality. Daniels et al conclude: "...the continued demonstration of adverse effects of air pollution over recent decades, even as concentrations of pollutants have declined, suggests that exposures have not yet gone below no-effects thresholds, if such exist."


EXPOSURE MEASUREMENT ERROR CRITICISM REFUTED

Air Quality Monitors Can Be Used to Track Exposure to Fine Particles

Epidemiological studies generally rely on centrally located air quality monitors to assess exposure to ambient air pollutants. Some have argued that these monitors do not represent actual exposures, because people spend a large portion of their day indoors.

A study by Dutch scientist Nicole Janssen et al., of 10 – 12 year old school children in Wageningen, The Netherlands compared personal exposure to fine particles with classroom concentrations, and with ambient measurements at an outdoor location. Researchers found that personal fine particle concentrations were highly correlated with ambient concentrations. This finding supports the use of ambient monitoring measurements as an indicator of exposure to fine particles in epidemiological time series studies.

Dr. David Mage, of U.S. EPA’s Office of Research and Development, and colleagues, demonstrated that human exposure to fine particles of ambient origin is highly correlated in time to ambient PM concentrations measured at monitoring stations within the communities being studied.

The NMMAPS study discussed above also addressed the issue of measurement error, through the development of a model to systematically test what effect the relationship between personal exposure and ambient exposure might have on the observed increase in mortality associated with PM. While data to test the model is limited, “theoretical and actual analyses generated appear to refute the criticisms that exposure measurement error could explain the associations between PM and adverse health effects.”


Criteria for Asserting Causality Have Been Met

In responding to an article by Dr. John Gamble, Epidemiologist for Exxon Biomedical Sciences, Dr. David Bates, Professor Emeritus of Medicine at University of British Columbia, has re-evaluated the recent evidence health evidence regarding particulate matter and mortality. Determination of causality does not rest on any one study. Instead,
a weight of evidence approach is used to evaluate the scientific literature across a series of criteria such as coherence, consistency, strength of association, temporality, analogy, and biologic plausibility. Dr. Bates asserts that all of these criteria have been met by an avalanche of new data that strengthen the case for a causal relationship.


Kunzli, N. and Tager, I.B. Comments on “PM$_{2.5}$ and Mortality in Long-term Prospective Cohort Studies: Cause-Effect or Statistical Associations?” and Gamble, John. Reply to Kunzli and Tager Regarding Causality in PM$_{2.5}$ Cohort Studies. Environ Health Perspect 107-5, 1999; Correspondence.

People With Pre-Existing Cardiac or Respiratory Conditions Have Higher Than Average Risk of Death from Exposure to Particles

Canada’s national health insurance system enables access to detailed health records of patients. This permitted Dr. Mark Goldberg and colleagues at McGill University to conduct a detailed analysis of particle pollution and mortality in Montreal. Investigators were able to link individual deaths in Montreal to medical information up to five years before death. These data were used in conjunction with clinical expertise to define susceptible subgroups at risk of premature death from several different measures of particulate pollution. Subjects with acute lower respiratory disease, congestive heart failure, and a combination of cardiovascular diseases died at higher rates for increases in each of the three particulate matter measures. Associations with coefficient of haze and predicted PM$_{2.5}$ were reported for subjects with cancer, chronic coronary artery disease, and coronary artery disease, while effects of sulfate were associated with acute and chronic upper respiratory disease.


“Coarse” Particles are Also Linked with Disease and Death

This study by Dr. Morton Lippmann and colleagues from the New York University School of Medicine attempted to identify components of particulate matter and other air pollution mixtures that were associated with excess daily deaths and hospital admissions of the elderly in the Detroit metropolitan area. Investigators reported that deaths from respiratory diseases were associated with PM$_{10}$ and total suspended particulates. Unexpectedly, they found that relative risks for PM$_{10,2.5}$, the coarse particle fraction, were similar to those for PM$_{2.5}$, and even higher in the case of ischemic heart disease and stroke. The authors conclude that “the finding of elevated and significant effects for
PM\textsubscript{10,2.5} suggests that there may still be a rationale to consider the health effects of the coarse fraction as well as the fine fraction of PM."


BIOLOGIC MECHANISMS AND CARDIAC EFFECTS

Air Pollution Tied to Low Heart Rate Variability, a Risk Factor for Heart Attacks

Particulate air pollution has been linked to cardiovascular mortality in a number of studies, but the mechanisms for this effect are not well understood. Recent research centers on the effect of pollution on heart rate and heart rate variability. Low heart rate variability is a marker of poor cardiac control by the autonomic nervous system, and is associated with a higher risk of heart attacks and sudden cardiac death. One hypothesis is that inhalation of particle air pollution may trigger an inflammatory response in the lung, followed by the release of chemical mediators that affect autonomic nervous system control of the heart beat.

Pope, et al. measured oxygen saturation and pulse rate in a panel of 90 elderly residents of the Utah Valley, using a small medical device known as an oximeter. The experiment was conducted during the winter months, when PM concentrations are highest. Researchers found little evidence of pollution effects on the oxygen carrying capacity of the blood, but observed that a small elevation in pulse rate was associated with a rise in PM\textsubscript{10 levels. The medical and biological relevance of this effect is unclear.

Dr. Duanping Liao, of the University of North Carolina, and co-investigators, conducted daily electrocardiogram measurements on elderly nursing home residents outside Baltimore, Maryland. Harvard physician Dr. Diane Gold et al. studied 53- to 87- year old active residents of Boston. 25 minutes of electrocardiogram measurements during different exercise states were taken on a weekly basis. Both the Baltimore and Boston studies found that elevated concentrations of fine particulate matter were associated with lower heart rate variability, and that the association was stronger for people with pre-existing cardiovascular conditions.


Increased Heart Rate and Plasma Viscosity During an Air Pollution Episode Suggest Possible Mechanisms

The World Health Organization Monitoring Survey of Trends and Determinants in Cardiovascular Disease (the “MONICA” survey) took place in Augsburg, in Southern Germany during the winter of 1984-1985. Over 4,000 randomly selected adults participated, and received electrocardiograms to measure their resting heart rate, and donated blood samples to measure plasma viscosity. Electrocardiograms were administered again in 1987-1988.

In January 1985, an air pollution episode occurred throughout central Europe, with elevated concentrations of sulfur dioxide, total suspended particulates, and carbon monoxide. During the air pollution episode, higher heart rates were observed for men and women, after adjusting for cardiovascular risk factors and weather. An elevated resting heart rate is a risk factor for death and fatal heart disease, and may signal changes in the autonomic control of the heart, that might partially account for the adverse health effects observed in association with air pollution.

One hypothesis is that increased plasma viscosity might lead to constricted blood flow in the heart (ischemia), which can be fatal in people with severe coronary heart disease. During the air pollution episode, increases in plasma viscosity were observed, and persisted after adjusting for other cardiovascular risk factors and weather. German researcher Annette Peters, et al. conclude that “the increased plasma viscosity observed in these analyses of a cross-sectional survey might therefore represent a part of the pathophysiological chain linking high ambient air pollution to increased mortality and hospital admissions for cardiovascular diseases.”

An alternate hypothesis is proposed by Professor Anthony Seaton of the University of Aberdeen Medical School. He collected blood samples from 112 elderly people in two cities in the U.K. over an 18-month period, and examined various blood values in comparison to PM10 concentrations. Based on the analysis, Seaton suggests that inhalation of some component of PM10 may cause sequestration of red blood cells, which may explain the cardiovascular effects reported in other studies.


Heart Patients Vulnerability to Potentially Fatal Arrhythmias Increases After Exposure to Air Pollution
A pilot study was designed to test the hypothesis that heart patients with a history of serious arrhythmia requiring implanted cardiac defibrillators experience potentially life-threatening arrhythmias following short term increases in air pollution. Defibrillators monitor electrical activity of the heart and initiate interventions such as pacing or shock therapy to restore a normal heartbeat. The devices record information on arrhythmic events.

One hundred heart patients in eastern Massachusetts were followed for a three-year period. The study found that a subgroup of these patients -- those with more than ten defibrillator events -- were most susceptible to pollution, with effects occurring one to two days after exposure. Among these patients, the strongest associations were with nitrogen dioxide, but positive associations were reported for PM$_{10}$ and PM$_{2.5}$ exposures as well.


Combustion Source Metals May Trigger Biologic Responses to Ambient Particulate Matter

Researchers have been trying to determine whether one component of particulate matter -- such as metals -- is responsible for the toxic effects. U.S. EPA investigators led by Dr. Daniel Costa obtained samples of particulate matter from oil and coal fly ash and ambient air from St. Louis, MO, Washington, DC, Dusseldorf, Germany, and Ottawa, Canada. The fly ash is rich in metal components such as iron, copper, nickel, vanadium, and zinc, as well as sulfate. Laboratory rats were instilled with PM samples from these sources, and lung cells were obtained via bronchoalveolar lavage and analyzed for signs of cell injury. Investigators found that the constituent metals and their bioavailability determine the acute inflammatory response of PM samples in lung tissue.

In a second experiment, rats were pretreated with a chemical intended to model certain disease conditions, namely inflammation of blood vessels and high blood pressure in the lungs. These animals were instilled with the fly ash samples, and lung cells were obtained for laboratory examination. After 96 hours of exposure, there was clear evidence of lung inflammation, however many of the test animals had died, apparently due to altered cardiac function. Survivors had increased electrocardiographic changes. Investigators hypothesize that soluble metals from PM mediate an array of injuries to the cardiopulmonary system of healthy and at-risk subjects.


Laboratory Research on Dogs Suggests that PM May Harm People with Heart Disease
This toxicology study by Harvard pathologist Dr. John Godleski is one of the first to test whether exposure to particulate matter can change heart function in laboratory animals. Two groups of dogs were tested—healthy dogs, and dogs with an induced coronary occlusion intended to simulate human coronary artery disease. Researchers exposed dogs to concentrated particles from the ambient Boston air. Both the normal and the compromised animals showed effects, but the clearest sign of PM effects was found in the dogs with the induced heart condition. The occluded animals were more susceptible to serious arrhythmias when exposed to air pollution. The electrocardiogram signals for these dogs indicated more rapid development of ischemia, an inadequate flow of blood through the heart that can lead to a heart attack. Study reviewers concluded: "this is a plausible and important mechanism to explain the association of increased cardiopulmonary mortality and exposure to particle pollution."


**Concentrated Air Particles Induce Pulmonary Inflammation and Blood Changes in Humans**

Effects of particles are showing up not only in laboratory animals, but also in a chamber study with human subjects performed by EPA research physician Dr. Andrew Chio and colleagues. This controlled exposure study of young, healthy volunteers examined the effect of exposure to concentrated ambient particles from Chapel Hill, North Carolina. Volunteers alternated between moderate exercise and rest over a two-hour period in a chamber with high particle concentrations. No symptoms or decrements in pulmonary function were noted. However, eighteen hours after exposure, lung tissue had a higher concentration of neutrophils, a marker of inflammation. Blood work indicated a higher concentration of fibrinogen, which is a risk factor for clotting and heart attacks.

Chio, A.J., Kim, C., and Devin, R.B. Concentrated Ambient Air Particles Induce Mild Pulmonary Inflammation in Healthy Human Volunteers. In Press.

**HOSPITAL AND EMERGENCY ROOM VISITS**

**Air Pollution May Account for Five Percent of Cardiac Hospital Admissions**

Numerous studies have focused on mortality because it is an easy to measure effect for which data is readily available. It is important to note that early deaths represent just the tip of the iceberg of particulate related health effects. For each death, there are many more people admitted to the hospital, and for each hospital admission, many more visits to emergency departments and doctors offices. Similarly, for each patient who visits an emergency clinic, many more experience uncomfortable respiratory symptoms or days when they must restrict their activity, increase their use of medication, or remain indoors.
Increased hospital admission rates represent one of the most serious effects of air pollution. This study examined the association between \( PM_{10} \), carbon monoxide, and hospital admissions of the elderly for heart disease across eight urban counties with different pollution and weather profiles. The eight locations are: Chicago; Colorado Springs; New Haven; Minneapolis; St. Paul; Seattle; Spokane; and Tacoma. The study design was intended to minimize confounding by weather or other pollutants. Associations of both \( PM_{10} \) and CO with cardiovascular hospital admissions were observed in areas with widely varying correlations between these pollutants and weather factors or other air pollutants. Overall, the results suggest that air pollution may be responsible for five percent of hospital admissions for heart disease, representing an enormous public health impact.


**Emergency Room Visits for the Respiratory Illness in the Elderly Linked to Air Pollution**

Consistent with reports of aggravated symptoms in those with chronic respiratory conditions, a study in Montreal, Canada found strong associations between air pollution and emergency room visits for patients over 64 years of age during 1993, when more data were available. Positive associations were reported for ozone, \( PM_{10} \), \( PM_{2.5} \), and sulfate, at air pollution levels well below the U.S. air quality standards. The elderly are especially susceptible to the effects of air pollution.

The NMMAPS study, discussed above, reported strong and consistent associations between particulate air pollution and hospital admissions among the elderly for cardiovascular disease, pneumonia, and chronic obstructive pulmonary disease.


**Pre-Existing Cardiovascular Disease Increases the Risk of PM-Related Hospital Admissions for Respiratory Causes**

This ten-year study of Medicare patients in Chicago was designed to identify subgroups that are especially susceptible to particulate pollutions. Researchers examined records of previous hospital admissions and secondary diagnoses to determine whether people with certain conditions were predisposed to having a greater risk from air pollution. Investigators found that people with asthma had double the risk of a \( PM_{10} \)-associated hospital admission, and that people with heart failure had double the risk a \( PM_{10} \)-induced COPD admission. The authors conclude, *"the results suggest that patients with acute respiratory infections or defects in the electrical control of the heart are a risk group for particulate matter effects."*
INFANT MORTALITY AND EFFECTS ON CHILDREN

Growth in Children’s Lung Function is Slowed by Air Pollution

Researchers with the Children’s Health Study led by the University of Southern California have monitored levels of major air pollutants in a dozen southern California communities since 1993, while tracking the respiratory health of more than 3,000 school age children. The twelve communities, which fell along a gradient of air pollution levels, were all within a 200-mile radius of Los Angeles. The California towns studied were Alpine, Atascadero, Lake Arrowhead, Lake Elsinore, Lancaster, Lompoc, Long Beach, Mira Loma, Riverside, San Dimas, Santa Maria, and Upland.

In fourth-graders, significant deficits in growth of lung function were associated with various measures of fine particles (PM$_{10}$, PM$_{2.5}$, and PM$_{10-2.5}$), nitrogen dioxide, and inorganic acid vapor, but not with ozone. The deficits were larger for children that spent more time outdoors. "This is the best evidence yet of a chronic effect of air pollution in children," said Dr. John Peters, University of Southern California professor of preventative medicine and one of the study authors. The study concluded that "the results suggest that exposure to air pollution may lead to a reduction in maximal attained lung function, which occurs early in adult life, and ultimately to increased risk of chronic respiratory illness in adulthood."


Doctor Visits Climb In Relation to Air Pollution

In Paris, France, doctors still make house calls, and public records on the reason for the visits are available through the French national health insurance program. This enabled investigators to examine a significant but understudied health endpoint, doctor visits, that affects a much larger number of patients than those admitted to hospitals or treated in emergency departments of hospitals. The statistical model of daily air pollution effects used in this study controlled for season, pollen counts, influenza epidemics and weather. Medina et al. report that house calls for asthma for children 0-14 years old showed the strongest association with air pollution.

Air Pollution May Contribute to Infant Mortality

A small but growing body of literature suggests that air pollution may contribute to infant mortality. British scientists Bobak and Leon analyzed infant mortality and several measures of long-term exposure to air pollutants in highly polluted regions of the Czech Republic. They found a consistent, positive association between PM\textsubscript{10} levels and post neonatal infant mortality from respiratory causes, after controlling for socioeconomic factors and other pollutants.

Dr. Dana Loomis, of the University of North Carolina, and co-workers found that air pollution is associated with acute increases in infant mortality in Mexico City after controlling for temperature and other factors. Increases in fine particles, ozone and nitrogen dioxide resulted in an increased number of infant deaths 3 to 5 days later. The effect of particles was the most consistent and the least sensitive to the presence of other pollutants.

A study by EPA scientist Dr. Tracey Woodruff et al., of 86 cities in the United States reported an association between infant mortality and the level of inhalable particles in the first two months of life.


Air Pollution In Highly Polluted Regions May Cause Low Birth Weight Infants

Low birth weight is the most important predictor for neonatal mortality in developed and developing countries, and is a significant determinant of infant health and survival. A large study in Beijing, China looked at maternal exposure to air pollution during pregnancy and subsequent birth weight of infants. Coal stoves used for heating and cooking are a major source of indoor and outdoor air pollution in the study region. Xiaobin Wang of the Boston University School of Medicine and colleagues found a significant exposure-response relationship between maternal exposure to sulfur dioxide and total suspended particles during the third trimester of pregnancy and low birth weight.


ASTHMA EXACERBATION

001503
Children’s Emergency Room Visits for Asthma Increase on High Air Pollution Days

“Asthma is the most common chronic illness in children and the cause of most school absences,” state Norris et al., in their study of children’s emergency department visits for asthma. University of Washington investigators found significant associations between pediatric hospital visits for asthma and increased daily concentrations of PM and carbon monoxide in Seattle. Significantly, exacerbation of asthma was evident even when daily PM_{2.5} concentrations were substantially below the level of the newly adopted National Ambient Air Quality Standard of 15 ug/m^3 annually.

In perhaps the largest study of pediatric asthma visits to date, Dr. Paige Tolbert, of the Rollins School of Public Health at Emory University, and co-investigators, obtained data on emergency department visits for three summers from seven large Atlanta area hospitals. The study included information on a variety of pollutants including spatial resolution of ozone data, a broad range of exposure levels, and a balanced distribution of socioeconomic status in the study population.

Increases in both ozone and particulate matter were found to heighten the risk of pediatric emergency room visits for acute asthma. According to the authors, “the study suggests continuing health risks at pollution levels that commonly occur in many U.S. cities,” and “supports accumulating evidence regarding the relation of air pollution to childhood asthma exacerbation.”


Children with Asthma are More Susceptible to Respiratory Effects

Increased particle concentrations have been associated with acute reductions in lung function and increased symptom reporting in children, including children with asthma. Dr. Sverre Vedal, Professor of Medicine at the University of British Columbia, and co-workers followed a group of 2,200 elementary school children in a pulp mill community on Vancouver Island, in Canada. Concentrations of potentially important copollutants such as sulfur dioxide, ozone, and acid aerosol were very low in the study community.

Vedal et al. found that children experience declines in peak expiratory flow, a measure of respiratory function, and increased symptoms such as cough, phlegm production, and sore throat, after increases in relatively low 24-hour PM_{10} concentrations. Children with asthma were found to be more susceptible to these effects than other children.
Children's Asthma Symptoms Increase on High Pollution Days

This study followed a group of 133 children with mild to moderate asthma, ages 5-13, in the Seattle, Washington area. Daily reports of asthma symptoms were obtained from study diaries and compared with daily air pollution levels during 1994 and 1995. Researchers found that a 30 percent increase in symptoms for each 10 μg/m³ increase in PM$_{10}$ and an 18 percent increase in symptoms for a 10 μg/m³ increase in PM$_{10}$. Effects were also increased with carbon monoxide increases, which authors assume serves as a marker for vehicle exhaust. Study authors conclude: "These results for daily symptoms complement the other Seattle-area studies that found air pollution health effects for emergency department visits and hospital admissions. Taken together, these studies suggest that the health effects among asthmatics from short-term changes in air pollution levels are an important public health problem."


Particulate Pollution Worsens Bronchitis in Asthmatic Children

A University of Southern California School of Medicine study of more than 3,600 fourth, seventh and tenth grade children relied on parent questionnaires to identify children with pre-existing asthma or wheeze, and to assess their bronchitic symptoms. The students lived in 12 communities in Southern California with a broad range of air pollution levels: Alpine; Atascadero; Lake Elsinore; Lake Gregory; Lancaster; Lompoc; Long Beach; Mira Loma; Riverside; San Dimas; Santa Maria; and Upland, California. Children with asthma were much more likely than other children to experience bronchitis and phlegm in relation to PM$_{10}$ exposures.


Cleaning Up Air Pollution Improves the Respiratory Health of Children
A rather dramatic improvement in air quality in East Germany occurred following the German reunification in 1990. Researchers wanted to study if the declines in air pollution had produced a corresponding improvement in health, and they focused in on a cohort of first-, third-, and sixth-grade children in three East German communities. During the study period, bronchitis, ear infections, and frequent colds were dramatically reduced. Authors found that “the prevalence of nonasthmatic respiratory symptoms and diseases was higher in children living in more polluted communities, especially with respect to TSP and SO2, suggesting that disease occurrence may be reduced within a short period by improvement in air quality.”


RECENT RISK ASSESSMENTS

Air Pollution from Power Plants Responsible for 30,000 Premature Deaths Each Year in U.S.

This analysis by Abt Associates used EPA-approved emissions and air quality modeling techniques to forecast ambient air quality in 2007, assuming full implementation of the Clean Air Act’s acid rain control program, and the EPA’s 1999 “NOx State Implementation Plan (SIP) call.” Analysts then applied risk functions derived from epidemiological studies to estimate health impacts of power plant emissions in the U.S. The focus of the study was on gaseous emissions of sulfur dioxide and nitrogen oxides that are converted in the atmosphere to fine particle sulfates and nitrates. The analysis estimated that 30,100 deaths may be attributed to power plant emissions each year. In addition, power plant emissions causes 20,100 hospitalizations for respiratory and cardiovascular causes, more than 7,000 asthma-related emergency room visits, 18,600 cases of chronic bronchitis, 600,000 asthma attacks, over 5 million lost work days, and over 26 million minor restricted activity days. Reductions in emissions from uncontrolled power plants could substantially reduce the adverse health effects.

In addition, analysis used a simpler model to estimate the impacts of emissions from on- and off-road diesel engines. The analysis reported that 15,400 premature deaths each year are attributable to the diesel contribution to fine particle concentrations. In addition, there are an estimated 11,100 cases of chronic bronchitis due to diesel emissions, thousands of hospitalizations due to chronic obstructive pulmonary disease, pneumonia, asthma, and cardiovascular causes, and over a million cases of minor illness such as acute bronchitis, upper and lower respiratory symptoms, and asthma attacks. Because of the use of different models, these results are not directly comparable to the power plant estimates.

Air Pollution Causes 40,000 Premature Deaths Each Year in Alpine Countries

As part of an assessment prepared for the World Health Organization, Nino Künzli and coauthors estimated health risk attributable to PM_{10} pollution in three European countries, Austria, France, and Switzerland. Using functions of health risk obtained from epidemiological studies, the authors estimate that air pollution caused six percent of total mortality, or more than 40,000 cases each year, with about half associated with motor vehicle pollution. In addition, the study estimated that 47,000 new cases of chronic bronchitis in adults, more than 500,000 episodes of bronchitis in children, and more than a million asthma attacks are attributable to air pollution each year. Despite uncertainties inherent in risk assessment, this analysis highlights the magnitude of the public health burden attributable to current levels of air pollution.