2005 RESEARCH HIGHLIGHTS: HEALTH EFFECTS OF PARTICULATE MATTER AND OZONE AIR POLLUTION

This annotated bibliography presents brief summaries of selected research papers published in 2005 (or in press in January 2006) on the health effects of particulate and ozone air pollution. Some of the highlights of the new studies include:

- A long-term study showing risk of premature death attributable to PM is three times greater than previously reported;
- Studies linking daily exposures in PM with increased hospital admissions for strokes, congestive heart failure, heart attacks, COPD and other respiratory problems;
- A toxicology study showing links between exposure to PM$_{2.5}$ at levels near or below the current standards and development of atherosclerotic plaques;
- Many studies elucidating the biological mechanisms and pathways for cardiovascular effects;
- Studies linking prenatal exposure to air pollution with increased risk of low birth weight, preterm birth, infant mortality, and cancer;
- Research showing that coarse particles exacerbate respiratory disease;
- Three meta-analyses linking ozone air pollution with premature mortality and a multi-city study showing that effects are not due to temperature;
- Intervention studies showing that reductions in air pollution yield measurable improvement in children’s respiratory health and reduction in premature deaths; and
- Policy analyses showing the need for strong annual and daily fine particle standards to protect susceptible populations and provide equivalent levels of protection to different regions of the country.

These summaries are in no way intended to substitute for medical information from a physician, nor are they intended to represent conclusions of the American Lung Association. Citations for all studies are provided.

PARTICULATE MATTER: HEALTH EFFECTS OF SHORT-TERM EXPOSURES

Premature Deaths

Fine Particles Linked to Daily Mortality in California

This multi-city study investigated associations between PM$_{2.5}$ and mortality in nine heavily populated California counties taking advantage of new PM$_{2.5}$ monitoring data collected from 1999 through 2002.
Statistical methods were used to control for effects of season, temperature, and humidity. The nine counties were: Contra Costa, Fresno, Kern, Los Angeles, Orange, Riverside, Sacramento, San Diego, and Santa Clara. Positive associations were observed with all-cause mortality, as well as mortality from respiratory disease, cardiovascular disease, and diabetes, and deaths in persons over age 65. “Overall, this large, multi-county analysis provides evidence of significant associations of fine particles with daily mortality among nearly two-thirds of California’s population,” conclude the authors.


Linear Relationship between PM and Mortality Reported in Multi-City European Study

This study investigated the exposure-response relationship in the 22 European cities participating in the APHEA (Air Pollution and Health--A European Approach) project. The study concludes that the association between ambient particles and mortality can be adequately estimated using the linear model, confirming results previously reported for Europe and the United States. Different statistical models were used to explore the potential for a threshold level at 20 and 10 µg/m$^3$ but the linear models assuming no threshold gave a better fit. Thresholds for effects in individuals and subgroups may differ according to their sensitivity, and cannot be identified with the methodology used in this study. Investigators believe that measures focusing on lowering annual average pollution concentrations will have greater public health benefits than those focusing on a few days with the highest concentrations.


Hospital Admissions and Emergency Room Visits

Air Pollution Linked to Ischemic Strokes

Particulate air pollution (PM$_{10}$) increases the risk for ischemic strokes -- those caused by a blood clot -- according to a study by Harvard University researchers. Hemorrhagic strokes, which occur when a blood vessel ruptures, were not affected by the level of pollution.

Researchers evaluated the link between daily levels of PM$_{10}$ and hospital admission for strokes among Medicare recipients in nine U.S. cities: Birmingham, Chicago, Cleveland, New Haven, Detroit, Minneapolis, Pittsburgh, Salt Lake City, and Seattle. Compared to days with relatively low particulate air pollution levels, the risk of ischemic stroke -- the most common type of stroke -- was 1 percent higher on days with relatively higher air pollution. Similar associations were observed for carbon monoxide, nitrogen dioxide and sulfur dioxide.

“It appears that air pollution has only a small effect on acute ischemic events of either the heart or brain, but everybody in those cities is exposed. So, while the relative risk may be small, the absolute risk in terms of excess number of strokes can be quite high, especially when you realize that someone in the United States has a stroke every 45 seconds,” according to the study authors.

Low Levels of PM Trigger Hospital Admissions for Congestive Heart Failure

PM$_{10}$ concentrations below current EPA standards are associated with an increased rate of hospital admissions for congestive heart failure, in a study of seven U.S. cities. The cities studied were Chicago, Detroit, Cleveland, New Haven, Minneapolis, Birmingham, and Seattle. Researchers evaluated the association between daily levels of PM$_{10}$ and the rate of hospitalization for congestive heart failure in Medicare recipients (aged 65 or older). Overall, a 10 µg/m$^3$ increase in PM$_{10}$ was associated with a 0.72% increase in hospital admissions on the same date. Researchers conclude “these results support the hypothesis that elevated levels of particulate air pollution, below the current limits set by the United States Environmental Protection Agency, are associated with an increase in the rate of hospital admission for exacerbation of CHF [congestive heart failure].”

A related study in Pittsburgh, Pennsylvania evaluated the association between ambient air pollution and the rate of hospitalization for congestive heart failure among Medicare recipients in Allegheny County from 1987 to 1999. The study looked at 55,000 patients admitted with a primary diagnosis of congestive heart failure. PM$_{10}$, carbon monoxide, nitrogen dioxide and sulfur dioxide, but not ozone, were positively and significantly associated with the rate of admission on the same day, with the strongest associations observed with CO, nitrogen dioxide, and PM$_{10}$. The associations with carbon monoxide and nitrogen dioxide were the most robust in two-pollutant models. The results suggest that short-term elevations in air pollution from traffic-related sources may trigger acute cardiac decompensation in heart failure patients.


Particulate Pollution Increases Risk of Heart Attacks in the Elderly

This multi-city study examined the association between PM$_{10}$ and emergency hospitalization for heart attacks among elderly residents of 21 U.S. cities. Researchers obtained Medicare data on hospital admissions for 300,000 heart attacks over a 14-year period. The statistical model was able to control for possible confounding by weather.

The cities studied were Birmingham, AL, Boulder, CO, Canton, OH, Chicago, IL, Cincinnati, OH, Cleveland, OH, Colorado Springs, CO, Columbus, OH, Denver Co, Detroit MI, Honolulu HI, Houston, TX, Minneapolis, MN, Nashville, TN, New Haven, CT, Pittsburgh, PA, Provo/Orem, UT, Salt Lake City, UT, Seattle, WA, Steubenville, OH, and Youngstown, OH.

Overall, there was a small association between daily PM$_{10}$ concentrations and increased risk of hospital admission for heart attack. The risk doubled for those with a previous admission for COPD. The relationship was nearly linear, but risks increased most sharply at daily concentrations less than 50 µg/m$^3$.


Children’s Hospital Admissions Spike with Increases in Outdoor Air Pollution

A large-scale epidemiological study of respiratory hospital admissions in children was carried out in the
largest cities in Australia and New Zealand: Brisbane, Canberra, Melbourne, Perth, Sydney, Auckland and Christchurch. Positive associations were observed for PM$_{2.5}$, PM$_{10}$, nitrogen dioxide and sulfur dioxide, for hospital admissions for pneumonia and acute bronchitis, respiratory disease and asthma. The study found strong and consistent associations between various measures of outdoor air pollution and short-term increases in childhood hospital admissions. These changes were distinct from temperature effects.


**Respiratory Emergency Department Visits Rise with Peaks in Air Pollution**

A time-series study of a very large database of 4 million emergency department visits to 31 hospitals in Atlanta has shown positive relationships between various air pollutants and respiratory disease. In single-pollutant models examining 3-day moving averages of pollutants, visits for upper respiratory infections in infants and children were positively associated with PM$_{10}$, ozone, nitrogen dioxide and carbon monoxide. The association with ozone persisted in multipollutant models. Chronic Obstructive Pulmonary Disease visits were positively associated with nitrogen dioxide and carbon monoxide, while pneumonia was linked to PM$_{2.5}$ and organic carbon.

Peel JL, Tolbert PE, Klein M, Metzger KB, Flanders WD, Todd K, Mulholland JA, Ryan PB, Frumkin H. Ambient Air Pollution and Respiratory Emergency Department Visits. *Epidemiology* 2005; 16:164-174. [http://www.epidem.com/pt/re/epidemiology/abstract.00001648-200503000-00004.htm;jsessionid=DJ9K9yXFRcTxbygYxCIcQ8IF2j6Px8bV2VPwblNhCEAMBDOb6mjRK!400681292!-949856144!9001!-1](http://www.epidem.com/pt/re/epidemiology/abstract.00001648-200503000-00004.htm;jsessionid=DJ9K9yXFRcTxbygYxCIcQ8IF2j6Px8bV2VPwblNhCEAMBDOb6mjRK!400681292!-949856144!9001!-1)

**Respiratory Effects**

**Air Pollution Lowers Lung Function of Asthmatic Children in Detroit**

African-American and Latino children on corticosteroid asthma maintenance medication or with upper respiratory infections are adversely affected by current levels of air pollution, according to a study of primary school age children with asthma in Detroit. The study explored the relationship between lung function and ambient levels of ozone and two measures of particulate matter -- PM$_{10}$ and PM$_{2.5}$.

The study tracked 86 children in six 2-week seasonal assessments from winter 2001 through spring 2002. Two measures of lung function were measured -- peak flow, and forced expiratory volume in 1 second (FEV$_1$). For children on corticosteroids for their asthma, PM$_{10}$ and 8-hour peak ozone were both associated with poorer lung function two days after exposure. For children with symptoms of respiratory infection, PM$_{2.5}$ and PM$_{10}$ were associated with poorer lung function 3-5 days after exposure, while 8-hour peak ozone concentrations were associated with poorer lung function after 1-2 days.

“Our results emphasize the continued need for enforcement of existing standards as well as the importance of considering susceptible subgroups within the population when formulating new standards,” concluded the University of Michigan researchers.

**Cardiovascular Mechanisms and Effects**

**Inflammation and Coagulation Responses May Hold Clues to Mechanisms for PM and Coronary Effects**

A panel study was conducted to measure the early physiological reactions characterized by blood biomarkers of inflammation, endothelial (the cells that line blood vessels) dysfunction, and coagulation in response to daily changes in air pollution in Erfurt, Germany. Blood parameters were measured repeatedly in 57 male patients with heart disease during winter 2000/2001. Hourly measurements were made of ultrafine particles, PM$_{10}$, PM$_{2.5}$, elemental and organic carbon, gaseous pollutants, and meteorological data at a central monitoring site.

Increased levels of C-reactive protein were observed with an increase in various sizes of particle pollution: ultrafine, fine, and PM$_{10}$. Clotting factor levels showed no consistent relationship to air pollution.

“This study adds to the evidence that elevated levels of ambient air pollution may cause systemic inflammatory and coagulation responses. These changes in blood markers could represent additional risk factors which in susceptible individuals such as patients with coronary heart disease, could increase the likelihood of serious arterial vascular thrombotic [blood clots in the arteries] events upon exposure to high levels of air pollutants,” conclude the authors.


**Vehicle Exhaust Contributes to Elevated Blood Pressure**

Researchers exposed 23 healthy nonsmoking adults to concentrated ambient fine particles and fine particles plus ozone during 2-hour exposures. Blood pressure and heart rate were measured at 30-minute intervals during the controlled exposures. A significant increase in diastolic blood pressure was observed with the combined ozone and fine particle exposure. Follow-up investigations revealed that the magnitude of blood pressure change is associated with the PM$_{2.5}$ carbon content, leading investigators to suspect that pollution from vehicular traffic in urban centers may be causing cardiovascular adverse effects.

“Exposure to high ambient concentrations of air pollutants may initiate a rapid hypertensive response, thus promoting acute cardiovascular events in susceptible individuals. In conjunction, if this vasopressor response continues unabated, gradients in personal exposure to air pollution could contribute to long-term differences in interindividual blood pressure levels. Continued exposure to air pollution could thereby increase the risk for developing chronically elevated blood pressure and possibly overt hypertension,” conclude the researchers.


**Diesel Exhaust Impairs Blood Vessels**

Breathing diesel exhaust at levels typically found in large cities for as little as an hour can disrupt important blood vessel functions, suggesting a possible mechanism for increased heart attack rates during periods of high air pollution. A chamber study by cardiologists at the University of Edinburgh used a double-blind, randomized, cross-over design to assess the effects of diesel fumes in two important and complementary aspects of vascular function: the regulation of vascular tone and the ability to remove of small blood clots.
Both functions were impaired and are plausibly related to the cardiovascular effects of air pollution.

The study involved 30 healthy, non-smoking men, aged 20 to 38, who were evaluated during two one-hour tests, two weeks apart. During each test, the men were exposed to either clean air or diesel exhaust from an idling engine, while riding a stationary bicycle for 15-minute stretches inside an exposure chamber. Participants received injections of a vasodilator and researchers measured their blood flow rates during and after exposure. The study found that exposure to diesel exhaust during exercise reduced the blood vessels’ ability to dilate, or expand, and decreased levels on an enzyme that helps prevent clots from forming in the blood.

According to the authors, these findings provide a plausible mechanism linking air pollution to the development of atherothrombosis and heart attacks.


Air Pollution Thickens the Blood

PM$_{10}$ particles thicken the blood and boost inflammation, according to the results of an experimental study. Scientists tested the inflammatory and blood clotting responses of human lung cells, cells taken from the umbilical cord, and immune cells called macrophages. Each was tested six and 24 hours after exposure to particulate matter. The results showed that levels of clotting factors, which thicken the blood, were elevated in several of the cell types. The rate of death in immune cells also increased significantly, and exposure to PM$_{10}$ boosted inflammatory activity.

Researchers concluded that “PM$_{10}$ has the ability to alter macrophage, epithelial, and endothelial cell function to favour blood coagulation via activation of the extrinsic pathway and inhibition of fibrinolysis pathways.” This suggests a mechanism for the adverse cardiovascular effects caused by inhalation of particulate matter.


Susceptible Populations

Diabetics More Vulnerable to Particulate Air Pollution

A study of 270 diabetes patients in Boston used baseline data from earlier clinical trials to compare with 24-hour concentrations for PM$_{2.5}$, sulfates, and black carbon. Pollutant concentrations were evaluated for associations with vascular reactivity. The strongest and most robust finding was the association between sulfate particles, which represent long-range transport from coal-burning power plants, and decreased vascular reactivity.

“Our results link pollution exposure and physiological responses known to be along the pathway of adverse cardiovascular outcomes. We saw significant associations between vascular reactivity and exposure to particulate pollution, especially SO$_4$ [sulfates], and greater responses among people with diabetes. Higher rates of cardiac hospitalization and mortality on high-particulate days among people with diabetes may be partially explained by impairments in endothelial function, vascular smooth muscle function, and subsequent coronary artery vascular responses,” conclude the authors. “Diabetes confers vulnerability to particles associated with coal-burning power plants and traffic.”

**Prenatal Effects**

**Air Pollution Increases Risk of Preterm Births**

Researchers at the University of North Carolina have reported an increased risk of preterm delivery associated with exposure to PM$_{10}$ and sulfur dioxide during the last 6 weeks of pregnancy. The study population consisted of single infants born to mothers from 1997 to 2001 in four Pennsylvania counties: Allegheny, Beaver, Lackawanna, and Philadelphia.

The researchers used a time-series analysis, a study design which eliminates potential confounding by individual risk factors that do not change over short periods of time. The increased risk of preterm birth was small, but researchers note that if the effects are causal, the public health impact could be significant because of the large populations chronically exposed to high concentrations of air pollution.


**Prenatal Exposure to Urban Air Pollutants Can Cause Genetic Alterations Linked to Increased Cancer Risk**

A study of 60 newborns in New York City suggests that prenatal exposure to combustion-related urban air pollutants alters the structure of chromosomes of babies in the womb. Such genetic alterations have been linked to increased risk of cancer in children and adults.

The research involved a sample of infants and their non-smoking mothers in Harlem, Washington Heights, and the South Bronx -- three low-income neighborhoods in New York City. The mothers wore personal monitors to measure their exposure to polycyclic aromatic hydrocarbons (PAH) during the third trimester of their pregnancies. Chromosomal aberrations were measured in the cord blood cells and were found to be associated with PAH exposure. “If confirmed, this finding may open new avenues for prevention,” concluded the Columbia University researchers.


**Maternal Exposure to Environmental Pollutants May Alter Fetal Immune System**

This study examined short-term associations of air pollution exposures with lymphocyte immunophenotypes in cord blood about nearly 1,400 deliveries in two regions of the Czech Republic. Researchers measured daily concentrations of PM$_{2.5}$ and 12 polycyclic aromatic hydrocarbons (PAHs) in the air, and various measures of the immune system in the cord blood at the time of birth. Ambient concentrations of PAHs and PM$_{2.5}$ during the last two weeks of gestation were associated with decreases in the percentages of T-lymphocytes in cord blood. Although the biological relevance of this finding is not
clear, it is significant that the fetal immune system may be altered by maternal exposure to air pollution.


PARTICULATE MATTER: *HEALTH EFFECTS OF LONG-TERM EXPOSURES*

Premature Deaths

Extended Analysis of Harvard Six Cities Study Shows Decline in Pollution Leads to Reduction in Death Rates

In 1993, the results of the landmark Harvard Six Cities cohort study were published reporting an association between long-term exposures to particulate air pollution and premature deaths. Now, researchers have extended the mortality follow-up in this study by eight additional years, during a period of reduced air pollution concentrations. Using estimates of pollution levels derived from ambient monitors, they found that reductions in death rates followed reductions in PM$_{2.5}$ levels, including to concentrations below the current annual average standard of 15 µg/m$^3$. Total mortality and deaths from lung cancer and cardiovascular causes were all positively associated with PM$_{2.5}$ concentrations. Reduction is risk was observed for deaths due to cardiovascular and respiratory disease, and not from lung cancer, a disease with a longer latency period and less reversibility.

Laden F, Schwartz J, Speizer FE, Dockery DW. Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-up of the Harvard Six Cities Study. *Am J Respir Crit Care Med* 2006; Published online January 19, 2006 as doi:10.1164/rccm.200503-443OC. [http://ajrccm.atsjournals.org/cgi/content/abstract/200503-443OCv1](http://ajrccm.atsjournals.org/cgi/content/abstract/200503-443OCv1)

Risk of Premature Death from Chronic Exposure to PM$_{2.5}$ in Los Angeles Three Times Greater than Previously Reported

Earlier studies of long-term health risks of air pollution relied on estimates of community average exposures which may entail measurement error, thus lowering the estimate of health risks attributable to poor air quality. This study used data from 23 PM$_{2.5}$ monitors and 42 ozone monitors to interpolate pollution exposures for nearly 23,000 residents of Los Angeles who are enrolled in the American Cancer Society cohort. After controlling for 44 different factors, the more accurate estimate of PM$_{2.5}$ exposure was associated with an increased relative risk for all cause mortality, deaths from ischemic heart disease, and lung cancer deaths. The results suggest that chronic health effects associated with within city gradients in exposure to PM$_{2.5}$ may be even larger than previously reported across metropolitan areas. Specifically, effects were nearly three times greater than reported in previous studies based on the American Cancer Society cohort.


Long-Term Effects of Air Pollution on Mortality Confirmed in French Study

The long term effects of air pollution on mortality were studied in 14,284 adults who lived in seven French
Daily measurements of sulfur dioxide, total suspended particulate, black smoke, nitrogen dioxide and nitric oxide were available for a three year period. Statistical models controlled for individual confounders such as smoking, educational level, body mass index and occupational exposure. After excluding areas where local traffic pollution dominated, a positive association on the order observed in the long-term U.S. cites was reported for total suspended particulates, black smoke, nitrogen dioxide and nitric oxide and non-accidental mortality. Consistent patterns for lung cancer and cardiopulmonary causes were observed. Researchers conclude that “urban air pollution assessed in the 1970s was associated with increased mortality over 25 years in France.”


**Particle Pollution Increases Women’s Risk of Developing and Dying from Coronary Heart Disease**

A multi-decade study published in *Environmental Health Perspectives* reports that women who live in areas with greater coarse and fine particle concentrations have a higher risk of developing and dying from coronary heart disease. In this long-term follow-up of the Adventist Health Study (ASHMOG), a cohort of non-smokers in California, PM$_{10}$, PM$_{10-2.5}$, and PM$_{2.5}$ were associated with increased risk of fatal heart disease in women, especially older women, with the effect strongest for fine particles. No associations were found in males. This study is important because it explores the long-term effects of three different size fractions of particles.


**Long-Term Fine Particle Exposure in California Linked to Lower Birth Weight and Infant Mortality**

A study of California infants who were born full term has shown a small but consistent effect of PM$_{2.5}$ on birth weight. Researchers matched air pollution monitoring data with California birth records. The pollution measurements were collected within 5 miles of the mother’s residence, and were averaged for the time period corresponding to the pregnancy. California mothers who lived in areas with the highest PM$_{2.5}$ exposures during their pregnancy delivered slightly smaller babies, by 30 grams, compared to those with lower exposures, after controlling for demographic factors and carbon monoxide. No associations were observed between carbon monoxide and birth weight.

The authors noted several limitations of their study including difficulty in deciding on an appropriate time period for exposure measurements, and in assigning exposures to each mother based on residence, as well as the lack of data on maternal smoking.

“These findings have important implications for infant health because of the ubiquitous exposure to fine particulate air pollution across the United States,” conclude the authors.

Particulate air pollution has been associated with infant mortality, particularly for respiratory causes and sudden infant death syndrome. A follow-up study by the same research group linked PM$_{2.5}$ monitoring data to infants born in California in 1999 and 2000 using the addresses of mothers who lived within five miles of a monitor. Each infant who died was matched to 4 infants who lived to age 1 by birth weight category and date of birth. For each matched set, researchers calculated exposure as the average PM$_{2.5}$ concentration
Respiratory Effects

Researchers Link Childhood Asthma to Exposure to Traffic-Related Pollution

Living near a freeway may bring an increased risk of asthma according to researchers at the Keck School of Medicine of the University of Southern California. Scientists studying air pollution levels in ten Southern California communities found that the closer children live to a freeway, the greater their chance of having been diagnosed with asthma. Researchers also found that children who had higher levels of nitrogen dioxide -- commonly emitted by internal combustion engines -- in the air around their homes were more likely to have developed asthma. Researchers looked at the pollution-asthma link in 208 children who were part of the Children’s Health Study, the longest running investigation into air pollution and kids’ health. Investigators concluded that the results “strengthen an emerging body of evidence that air pollution can cause asthma and that traffic-related pollutants that vary within communities are partly responsible for this association.”


Cardiovascular Mechanisms and Effects

Air Pollution, High-Fat Diet Cause Atherosclerosis in Laboratory Mice

Test results with laboratory mice show a direct cause-and-effect link between exposure to fine particle air pollution and development of atherosclerosis, commonly known as hardening of the arteries. Mice that were fed a high-fat diet and exposed to air with fine particles had 1.5 more times plaque production than mice fed the same diet and exposed to clean air. Plaque, a fatty deposit on the inner lining of the blood vessels, can predispose individuals to conditions such as heart attacks and strokes. The fine particle exposure also led to increased inflammation of the artery walls and reduced function of the artery wall’s inner lining.

The findings of the study may explain why people who live in polluted areas have a higher risk of heart disease. The findings are also important because the fine particle concentrations used in the study were well within the range of concentrations found in the air in the Northeastern U.S.. The average particle concentration over the course of the study was below the current 24-hour standard of 65 µg/m³ and close to the annual average standard of 15 µg/m³. “These results suggest that repeated periods of short-term (eg, several hours) exposures to high particulate matter levels, such that may occur during rush hour traffic, is potentially capable of promoting progression of atherosclerosis, although the mean daytime particulate matter exposure concentration is within national recommendations. This may potentially have implications for the relevance of both the 24-hour and annual average National Ambient Air Quality Standards,” concluded the study authors.
Long-Term Exposure to Air Pollution Implicated in Clogging of the Arteries

Two large clinical trials in Southern California have been following the progression of atherosclerosis in participants by measuring the thickness of the carotid artery. Researchers compared this data with the subjects’ annual ambient PM$_{2.5}$ exposures. After adjusting for age and other factors, an association was observed between a measure of hardening of the arteries and PM$_{2.5}$ exposures, suggesting a biological pathway for the relationship between particle exposure and premature death from heart disease. Researchers caution that PM$_{2.5}$ may be serving as a surrogate for the mixture of urban air pollution and constituents of PM and that follow-up studies are needed to confirm these findings.


Prenatal Effects

Child Cancers Linked to Pollutants

Researchers collected information on childhood deaths from leukemia or other cancers in Great Britain between 1953 and 1980. Children born near industrial emissions hotspots for carbon monoxide, PM$_{10}$, volatile organic compounds, nitrogen oxides, benzene, dioxins, 1,3-butadiene, and benz(a)pyrene had increased relative risk of dying from cancer. The study suggests that childhood cancers may be initiated in the womb, by industrial pollutants that have been inhaled by the mother.


COARSE PARTICLE HEALTH EFFECTS

Mortality

Particle Pollution Increases Women’s Risk of Developing and Dying from Coronary Heart Disease

A multi-decade study published in Environmental Health Perspectives reports that women who live in areas with greater coarse particle concentrations have a higher risk of developing and dying from coronary heart disease. In this long-term follow-up of the Adventist Health Study (ASHMOG), a cohort of non-smokers in California, PM$_{10}$, PM$_{10-2.5}$, and PM$_{2.5}$ were associated with increased risk of fatal heart disease in women, especially older women, with the effect strongest for fine particles. No associations were found in males. This study is important because it adds to our understanding of the long-term effects of inhaling particulate air pollution.

Hospital Admissions

Coarse Particles Increase Hospitalization for Respiratory Infection in Children

A study published online in Pediatrics reported a detrimental effect of relatively low levels of coarse particulate matter on hospitalizations for respiratory infections in children. This study used a case-crossover design to examine the relationship between various air pollutants and hospitalization for respiratory infections among children younger than 15 years in Toronto over a 4-year period. When PM and gaseous pollutants were both taken into account, the effect remained pronounced for PM$_{10-2.5}$ in both boys and girls.

http://pediatrics.aappublications.org/cgi/reprint/116/2/e235

Coarse Particles in Vancouver had Larger Effect on Elderly Hospital Admissions than Fine

A time-series study of nearly 9,000 adults over age 65 in Vancouver, Canada examined the relationship between hospital admissions for respiratory disease and daily measures of PM$_{10}$, PM$_{2.5}$, and PM$_{10-2.5}$. After adjustment for gaseous copollutants and meteorological variables, the study found that coarse particles have a larger effect on respiratory hospital admissions in the elderly than PM$_{2.5}$.

Chen Y, Qiuying Y, Krewski D, Burnett RT, Shi Y, McGrail KM. The Effect of Coarse Ambient Particulate Matter on First, Second, and Overall Hospital Admissions for Respiratory Disease Among the Elderly. Inhalation Toxicology 2005; 17:649-655.  

Systematic Review Supports Regulation of Coarse Particles

A systematic review of the epidemiological literature published in the European Respiratory Journal examined studies that have investigated the effects of both fine and coarse particles, and found that for some health endpoints, the effects are even stronger for coarse particles than for fine. Specifically, the paper finds that “in studies of chronic obstructive pulmonary disease, asthma and respiratory admissions, coarse PM has a stronger or as strong short-term effect as fine PM, suggesting that coarse PM may lead to adverse responses in the lungs triggering processes leading to hospital admissions.” The review also found support for an association between coarse PM and cardiovascular hospital admissions.

With respect to the toxicology of coarse particles, the review concluded that “studies clearly show that coarse PM exerts toxic effects in laboratory experiments, and that such effects are at least as potent as those observed in experiments using fine PM, when expressed on a mass basis,” while cautioning that fine particles may deliver a higher dose of toxic material to the lungs.

Researchers concluded that the coarse particle fraction is of importance in the regulatory process as well as for control measures.

In an accompanying editorial, Swedish, German, and Dutch researchers argued that systematic review offers evidence for the separate regulation of the coarse particle fraction.

http://erj.ersjournals.com/cgi/content/abstract/26/2/309
http://erj.ersjournals.com/cgi/content/full/26/2/187

**Toxicological Mechanisms**

**Mechanisms for Coarse Particle Toxicity Developed**

The results of a laboratory toxicology study which exposed human alveolar macrophages and airway epithelial cells to particles in vitro and followed them for endpoints of inflammation and oxidant stress were reported in *Toxicology and Applied Pharmacology*. These are the two main airway cell types likely to interact with inhaled particles. This study found that the proinflammatory response in alveolar macrophages was driven by material present in the coarse PM. Cultures of bronchial epithelial cells also responded to the coarse fraction with higher levels of certain markers of inflammation than induced by fine or ultrafine PM. These epithelial cells also showed evidence of oxidant stress in response to coarse particle exposure, as well as to other size fractions of PM. This study adds to our understanding of potential mechanisms.

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WXH-4GJK857-1&_coverDate=09%2F01%2F2005&_cdi=7159&_user=10&_orig=search&_sort=d&_docanchor=toc&_version=1&_origin=search&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=bc7620603a455138eba195ebda74dac4

**MISCELLANEOUS**

**Intervention Studies**

**Two Studies Report Children’s Respiratory Health Improves When Pollution Declines**

Before reunification of Germany in 1989, outdoor concentrations of total suspended particles were higher in East Germany than in West Germany due to emissions from industrial and domestic sources. Traffic-related air pollution was higher in West Germany than in East Germany. During the initial years after reunification, total suspended particulates (TSP) levels declined in East German and reached West German levels, but emissions from traffic increased. A German study compared two measures of lung function -- lung capacity and airway resistance in six year old East and West German children during this time of decreasing concentrations of TSP in East Germany.

Total lung capacity showed a clear association with long-term concentrations of TSP, while resistance was affected by short-term concentrations. Reduction in TSP was associated with better lung function when comparing repeated cross sections in six-year-old children. However, for children living near busy roads, this improvement was counteracted by increased air pollution associated with traffic during this period.

Reduction in air pollution exposures contributes to improved respiratory health in children, according to a new cross-sectional study of children in nine communities in Switzerland. Researchers investigated a moderate decline of PM$_{10}$ air pollution in the 1990s in Switzerland. Some 9,600 children tracked their respiratory symptoms over a 9 year period.

After adjusting for socioeconomic, health-related, and indoor air factors, declines in PM$_{10}$ were associated with declining prevalence of chronic cough, bronchitis, common cold, nocturnal dry cough, and conjunctivitis symptoms. Changes in prevalence of sneezing during pollen season, asthma, and hay fever
were not associated with the PM$_{10}$ reduction.

No threshold with adverse effects of PM$_{10}$ was apparent, because researchers observed the beneficial effects for relatively small changes of rather moderate air pollution levels.

“The larger reduction in symptom rates in areas with a stronger decrease in PM$_{10}$ levels supports the causality of observed associations between air pollution and respiratory health in children,” conclude the researchers.


**Biological Mechanisms**

**Biological Pathway for PM Damage Similar to Cigarette Smoking**

This review article explores potential mechanisms of vascular disease induced by lung inflammation. Ambient particles and inhaled cigarette smoke are processed by alveolar macrophages and lung epithelial cells. These cells produce proinflammatory mediators such as cytokines that promote a local inflammatory response in the lung that are thought to contribute to the exacerbation of Chronic Obstructive Pulmonary Disease (COPD) and asthma and promote lung infection. These inflammatory mediators may also translocate into the circulation and induce a systemic inflammatory response. This response can include stimulation of the marrow to release leukocytes and platelets, activation of proteins such as C-reactive protein and fibrinogen that may increase coagulability, and activation of the vascular endothelium, the layer of cells that line the blood vessels and are in direct contact with the blood.

Together, researchers surmise, these effects could cause progression and instability of atherosclerotic plaques, precipitating or aggravating cardiovascular events.

http://pats.atsjournals.org/cgi/content/abstract/2/1/61

**Ultrafine Particles**

**Ultrafine Particles and PM Health Effects -- A Review**

Heart disease is the leading cause of death and hospitalization among older adults. Numerous community health studies have reported positive and consistent associations between cardiovascular hospital admissions and mortality with outdoor air pollution, particularly measures of PM$_{2.5}$ and PM$_{10}$. Panel studies have also reported positive associations between PM and risk of cardiac ischemia and arrhythmias, increased blood pressure, decreased heart rate variability, and increased markers of inflammation and clotting in the blood.

This review study focuses on ultrafine particles, those less than 0.1 microns, which dominate particle number concentrations and surface area, and are therefore capable of carrying large concentrations of adsorbed toxic air pollutants to cardiovascular target sites. The article reviews epidemiologic, panel, and
experimental studies of cardiovascular effects. Though most of these studies used measures of PM$_{2.5}$ or PM$_{10}$, reviewers hypothesize that it is the ultrafine fraction that may be the causal agent leading to a cascade of acute cardiovascular responses.

“High UFP [ultrafine particle] exposures may lead to systemic inflammation through oxidative stress responses to reactive oxygen species, and thereby promote the progression of atherosclerosis and precipitate acute cardiovascular responses ranging from increased blood pressure to myocardial infarction,” state the authors.

They propose that components in ultrafine particles from fossil fuel combustion reach target sites in the lungs, veins, and heart to induce inflammation and oxidative stress, and suggest that future research focus on PM causal components and size fractions.


### Policy Analyses

#### Benefits of an Annual Average PM$_{2.5}$ Standard in California

Analysts used the BENMAP model developed for U.S. EPA to assist in preparation of air pollution control policies to compare the impact of a the current annual average PM$_{2.5}$ NAAQS of 15 µg/m$^3$ with a more stringent standard of 12 µg/m$^3$ in California. The model estimates that achieving the current standard would avert approximately 4,000 premature deaths in California each year, and that approximately 2,000 additional fewer deaths would occur in California each year as a result of attainment of the more stringent standard.


#### Stringent Annual and Daily Standards Are Needed to Provide Uniform Protection Across the U.S.

An analysis of air quality monitoring data found that 78 percent of the U.S. population could be protected if EPA lowers both the daily and annual average air quality standards for fine particles. This level of protection would be achieved if the daily standard were lowered from 65 µg/m$^3$ to 30 µg/m$^3$, in conjunction with a lowering of the annual average standard of 15 µg/m$^3$ to a level of 12 µg/m$^3$.

The analysis found that the 30/12 µg/m$^3$ suite of standards provides nearly equivalent 24-hour and annual control of PM$_{2.5}$ distributions across the U.S., thus ensuring a more uniform and consistent level of protection than achieved by lowering only the daily standard.


#### 38 Percent of Northeasterners are Especially Susceptible to Particulate Air Pollution

Using susceptibility criteria compiled from major regulatory and research reports, this study found that within the New England, New Jersey, and New York study areas, 38 percent of the population is under age 18 or over age 65 -- age groups considered especially sensitive to PM pollution effects. Four to eighteen
percent of the adults in the region have cardiopulmonary conditions or diabetes, while 12-15 percent of the children have respiratory allergies or lifetime asthma.

The study finds that more protective air quality standards are needed to protect these sensitive populations.


**OZONE: HEALTH EFFECTS**

**Premature Deaths**

**Ozone Deaths Not Due to Changes in Temperature**

Ozone air pollution has been associated with changes in daily mortality, but because high ozone days are generally quite hot, researchers seek to separate out the effect of temperature. The case-crossover approach allows each person to serve as his own control, by comparing the day of death with a day when the person did not die. This controls for season as well as individual risk factors by matching the control day with the day of the event.

This technique was used in a study of over one million deaths in 14 U.S. cities: Birmingham, Boulder, Canton, Chicago, Cincinnati, Colorado Springs, Columbus, Detroit, Houston, New Haven, Pittsburgh, Provo, Seattle and Spokane.

The study found that during the summer months, after controlling for temperature, a 10 ppb increase in maximum hourly ozone concentrations was associated with a small increase in the risk of death. Researchers concluded that "the association between ozone and mortality risk is unlikely to be caused by confounding by temperature.”


http://ajrccm.atsjournals.org/cgi/content/abstract/171/6/627

**Three Meta-Analyses Find Short-Term Ozone Exposures Increase the Risk of Death**

The U.S. Environmental Protection Agency commissioned 3 meta-analyses of studies of ozone and mortality. Three separate research groups were asked to conduct a meta-analysis, using their own methods and study selection criteria. All three studies report a small but substantial association between daily ozone levels and total mortality.

Researchers from Johns Hopkins University looked at 144 effect estimates from 39 time-series studies and estimated pooled effects by lags, age groups, cause-specific morality, and concentration metrics. They compared the results with pooled estimates from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) a time-series study of 95 large U.S. urban centers from 1987 to 2000. They found that the meta-analysis and NMMAPS results provided strong evidence of a short-term association between ozone and mortality, with large effects for cardiovascular and respiratory deaths, the elderly, and current-day ozone exposure.

Harvard University scientists gathered 71 time-series studies relating ozone to all-cause mortality, and selected 48 estimates from 28 studies for the analysis. They found a greater effect in the summer, and concluded that the “relationship between ozone and mortality should be considered for future regulatory impact analyses.”
New York University researchers conducted a review of 43 short-term ozone mortality studies from around the world and conducted an additional time-series analysis for 7 U.S. cities: **Chicago, Detroit, Houston, Minneapolis-St. Paul, New York City, Philadelphia, and St. Louis.** Their results suggest short-term associations between ozone and mortality, although the estimates vary from city to city.

A commentary on the meta-analyses by Dr. David Bates concludes: “The 2 new meta-analyses ... along with the recent European study, each have unique features and appear to resolve the question of whether ambient ozone levels are associated with increased mortality. It seems unlikely that \( PM_{2.5} \) is an important confounder, and the effect of ozone appears to be independent of temperature. A final question -- that of biologic plausibility -- is in some ways the easiest to answer. Ozone is capable of causing inflammation in the lung at lower concentrations than any other gas. Such an effect would be a hazard to anyone with heart failure and pulmonary congestion, and would worsen the function of anyone with advanced lung disease.”


Levy JI, Chemerynski SM, Sarnat JA. Ozone Exposure and Mortality: An Empiric Bayes Metaregression Analysis. *Epidemiology* 2005; 16:458-468. [http://www.epidem.com/pt/re/epidemiology/abstract.00001648-200507000-00006.htm;jsessionid=DJt0tmArXh4FIlwECoaYRYSpm35YoJ4KOMtraA1ta4u0XatHlQg!693302636!-949856145!90011-1](http://www.epidem.com/pt/re/epidemiology/abstract.00001648-200507000-00006.htm;jsessionid=DJt0tmArXh4FIlwECoaYRYSpm35YoJ4KOMtraA1ta4u0XatHlQg!693302636!-949856145!90011-1)


**Respiratory Effects**

**Infants at Risk of Respiratory Symptoms at Ozone Levels at or Near EPA Standards**

Young children may be particularly sensitive to ozone because significant lung development continues after birth. This study followed close to 700 infants born in southwestern Virginia during the summer months in 1995 and 1996. Air quality levels were monitored in Vinton, Virginia, near Roanoke. Mothers were interviewed at enrollment and biweekly to report infants’ daily respiratory symptoms.

Maximum 8-hour ozone and peak 1-hour ozone were associated with difficulty breathing, but not wheeze, in infants of asthmatic others. Ozone was not associated with cough in this study. The mean concentrations in this study (55 ppb 8-hour average, and 61 ppb peak 1-hour concentration) were below the EPA standards of 80 ppb and 120 ppb, respectively.
Infants of mothers who have asthma were found to have consistently higher risk of respiratory symptoms with increasing ozone exposure.

“At levels of ozone exposure near or below current EPA standards, infants are at increased risk of respiratory symptoms,” concludes a study by Yale University medical researchers.


Mail Carriers Exposed to Ozone Below Current Standards Show Declines in Acute Lung Function

Outdoor workers are considered populations at risk of ozone exposure, because of the time they spend out of doors and the increased dose they receive due to exercise. A study in *Taichung City, Taiwan* has demonstrated that mail carriers exposed to daily ozone concentrations below the current 8-hour air quality standard experienced declines in lung function.

Ozone is a powerful oxidant that can induce pulmonary function impairment at low levels via several toxicological mechanisms. This study measured peak expiratory flow rates in 43 mail carriers twice daily for 6 weeks. A central monitoring station measured ozone, PM$_{10}$ and nitrogen dioxide concentrations.

After working for 8 hours on a day with elevated ozone concentrations, the workers lost respiratory function in nighttime measurements for the same day and on the two following days.


Lifetime Exposure to Ozone Stunts Lung Function in Young Adults

This study assessed effects of chronic exposure to air pollutants in University of California, Berkeley freshmen who were lifelong residents of the Los Angeles or San Francisco Bay areas. Students in the study had never smoked. Air pollution exposure was estimated based on spatial interpolation of PM$_{10}$, nitrogen dioxide, and ozone monitors to the students residences. Lung function measurements were gathered between February and May, when the students had not had recent exposure to increased levels of ozone.

The study found that lifetime exposure to ozone in adolescents 18-20 years old is associated with reduced levels of lung function measures that reflect the function of the small airways. The associations are independent of any effects related to PM and nitrogen dioxide.


Cardiovascular Effects

Ozone Air Pollution Implicated in Heart Arrhythmias
This study evaluated cardiac arrhythmias in patients with implanted cardioverter defibrillators in association with various measures of community air pollution.

Breathing increased ambient ozone concentrations during the previous hour was associated with increased risk of episodes of a particular type of cardiac arrhythmia, suggesting that community air pollution may be a precipitant of these events. Associations with PM$_{2.5}$, nitrogen dioxide, and black carbon were positive, but not statistically significant. These episodes, known as atrial fibrillation, are not generally considered lethal, but are tied to an increased risk of premature death. People with this condition have a 5-fold increased risk of stroke if their episodes are not controlled by medication.


**New Evidence of Ozone and Pollution and Heart Attacks**

French researchers have reported that short-term ozone exposure within a period of 1 to 2 days is related to acute coronary events in middle-aged adults without heart disease, and that nitrogen dioxide and sulfur dioxide are not. The study design allowed for control of long-term seasonal trends, and adjusted for temperature, relative humidity, and influenza epidemics.


**Prenatal Effects**

**Prenatal Exposure to Ozone Linked to Reduced Birth Weight**

This study investigated the effects of air pollutants on birth weight among term infants who were born in California during 1975-1987 and who participated in the Children’s Health Study. Birth certificates provided material reproductive history and residence at time of birth. Information on sociodemographic factors and maternal smoking during pregnancy were collected by questionnaire. Monthly average air pollutant levels were interpolated from monitors to the zip code of the mother’s residence at childbirth.

The researchers observed an association between lower birth weight and intrauterine growth retardation with ozone concentrations. Second- and third-trimester ozone levels were most strongly associated with deficits in birth weight, followed by carbon monoxide exposures during the first trimester. They reported a clear pattern of increasing deficits in birth weight with increasing levels of ozone for 24-hour ozone levels above 30 ppb.

Although the differences in birth weight were small on average, those in the highest ozone exposure group had deficits of a magnitude equivalent to those observed after exposure to cigarette smoke.

“Because exposures to the levels of ambient air pollutants observed in this study are common, and fetal growth is an important determinant for childhood and adult morbidity and mortality, or findings are likely to have important public health and regulatory implications,” conclude the researchers.