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For nearly 100 years, the American Lung Association and Lung Association affiliates throughout the United States have worked together in the fight against lung disease.



January 16, 2004

2003 SELECTED AIR POLLUTION HEALTH STUDIES OF NOTE: OZONE AND PARTICULATE MATTER

Periodically, the American Lung Association summarizes selected studies from current research in the published literature on outdoor air pollution. These summaries are grouped below by major topic. 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.

ADVERSE BIRTH OUTCOMES

L.A. Women Who Live Near Busy Roads Have Increased Risk of Premature Births

Researchers at UCLA have previously reported that increases in ambient air pollution in the Los Angeles basin increase the risk of low birth weight babies and premature births. This follow-up study examined mothers' differential exposure to air pollutants resulting from living near roadways with heavy traffic.

Researchers examined data on low birth weight and/or preterm birth in Los Angeles County between 1994-1996. They mapped the home locations at birth, and estimated exposure to traffic-related air pollution using a measure that takes into account residential proximity to and level of traffic on roadways surrounding homes.

The study reported a 10-20 percent increase in the risk of preterm births and low birth weight in infants born to women potentially exposed to high levels of traffic-related air pollution. Women whose third trimester fell during the fall or winter, when atmospheric stability tends to limit dispersion of pollutants, experienced the greatest effects.

Willhelm, M., and Ritz, B. Residential Proximity to Traffic and Adverse Birth Outcomes in Los Angeles County, California, 1994-1996. *Environmental Health Perspectives*, Vol. 111, No. 2, pp. 207-216, February 2003.

Maternal Exposure to Air Pollution May Lower Birth Weight of Babies

A study in Kaohsiung, Taiwan has reported a significant exposure-response relationship between maternal exposures to sulfur dioxide and PM₁₀ during the first trimester of pregnancy and lowered birth weight. The study of 54,000 deliveries in Taiwan's second largest city correlated mothers' residences with data from air quality monitoring stations less than 2 kilometers away.

Maternal exposures were estimated for the different gestational stages of each child. Various confounders including maternal age, season, marital status, maternal education and infant gender were controlled for.

Another study on the relationship between low birth weight and air pollution exposure in **Seoul, Korea** found that **exposure to carbon monoxide, PM₁₀, sulfur dioxide, and nitrogen dioxide during early to mid pregnancy contributes to risks or low birth weight babies.**

Yang, C.Y., Tseng, Y.T., Chang, C.C. Effects of Air Pollution on Birth Weight Among Children Born Between 1995 and 1997 in Kaohsiung, Taiwan. J Toxicol Environ Health A. Vol. 65, No. 9, pp. 6070816, May 9, 2003.

Lee, B.E., Ha, E.H., Park, H.S., Kim, Y.J., Hong, Y.C., Kim, H., and Lee, J.T. Exposure to Air Pollution During Different Gestational Phases Contributes to Risks of Low Birth Weight. Human Reproduction. Vol. 3, pp. 638-643, March 2003.

Low Concentrations of Gaseous Air Pollutants and Adverse Birth Outcomes

Recent studies in China, the Czech Republic, and the United States have related ambient air pollution to adverse pregnancy outcomes. This study examines relationships between preterm birth, low birth weight, and intrauterine growth retardation and ambient concentrations of sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone in **Vancouver, Canada**, a relatively clean city.

Researchers conclude that, overall, the associations among SO₂ and low birth weight, preterm birth, and intrauterine growth retardation “appear to be the most robust against copollutant adjustment,” **but that the effects of air pollutants on birth outcomes are likely related to more than one component of the complex mix of air pollutants present in urban environments.**

Siu, S., Krewski, D., Shi, Y., Chen, Y., and Burnett, R.T. Association between Gaseous Ambient Air Pollutants and Adverse Pregnancy Outcomes in Vancouver, Canada. Environmental Health Perspectives., Vol. 111, No. 14, pp. 1773-1778, November 2003.

EFFECTS ON INFANTS AND CHILDREN

Infants are Most Susceptible Age Group to Mortality from Air Pollution

This is the first study to determine that infants are more susceptible to mortality from air pollution than other age groups. Researchers tracked daily counts of total and respiratory death in **Seoul, Korea** relative to PM₁₀ and other air pollutant concentrations for three age groups: infants aged 1 month to 1 year old, those from 2 years to 64 years old, and those over 65 years of age. Newborns were not included in the study.

For all age groups, the number of total deaths and particularly respiratory deaths increased on days when PM₁₀ air pollution was the worst, but the effect was most pronounced in infants. The elderly were second in increased susceptibility.

Researchers hypothesize that *“infants are more vulnerable to respiratory disease leading to death from particulate air pollution, because the infant lung and immune system is immature and unable to control adequately the inflammation resulting from exposure to ambient particles.”*

The researchers conclude that the results of their study have “*serious implications on the air pollution criteria, which should be based on the effects on infant health rather than on adult health.*”

Ha, E.-H., Lee, J.-T., Kim, H., Hong, Y.-C., Lee, B.-E., Park, H.-S., and Christiani, D. Infant Susceptibility of Mortality to Air Pollution in Seoul, South Korea. *Pediatrics*. Vol. 111, pp. 284-290, February 2003.

Ozone Alters Development of Trachea in Infant Rhesus Monkeys

This study examined the development of the “basement membrane zone” in the trachea of infant rhesus monkeys exposed to ozone, filtered air, and ozone plus allergen from house dust mites. In monkeys, this structure develops after birth, allowing studies of the effects of environmental exposures.

The study found significant differences, including irregular width, in the tracheal “basement membrane zone” in monkeys exposed to either ozone, or ozone plus allergens, during the developmental period. This resulted in altered regulation of proteins that may explain the atypical development of the lung observed in rhesus monkeys after exposure to ozone.

Evans, M.J., Fanucchi, M.V., Baker, G.L., Van Winkle, L.S., Pantle, L.M., Nishio, S.J., Schelegle, E.S., Gershwin, L.J., Miller, L.A., Hyde, D.M., Sannes, P.L., and Plopper, C.G. Atypical Development of the Tracheal Basement Membrane Zone of Infant Rhesus Monkeys Exposed to Ozone and Allergen. *American Journal of Physiology - Lung Cellular and Molecular Physiology*. Vol. 285, pp. 931-939, June 27, 2003

Diesel Exposure Increases Susceptibility to RSV Infection

Researchers studied the impact of inhaled diesel engine emissions in mice, to investigate the potential mechanisms for inhaled pollutants in modulating susceptibility to respiratory infection. **Prior exposure to diesel particulate pollution was shown to increase lung inflammation in response to respiratory syncytial virus (RSV), a common respiratory pathogen in young children.**

The lungs of the mice were flushed, and inflammatory cells in the fluid were found to increase in a dose-dependent manner with the diesel exhaust exposure. Changes in the mucous cells increased markedly in the diesel exposed mice following RSV infection. Researchers suggest that diesel exhaust exposure “*modulates the lung host defense to respiratory viral infections and may alter the susceptibility to respiratory infections leading to increased lung disease.*”

Harrod, K.S., Jaramillo, R.J., Rosenberger, C.L., Wang, S.-Z., Berger, J.A., McDonald, J.D., and Reed, M.D. Increased Susceptibility to RSV Infection by Exposure to Inhaled Diesel Engine Emissions. *American Journal of Respiratory Cell and Molecular Biology*. Vol. 28, pp. 451-463, 2003.

Particle Pollution Worsens Asthma in School-Aged Children

A large number of epidemiologic studies have found that short-term increases in particulate matter levels can trigger lung function decrements, use of asthma medications, emergency department visits, hospital admissions, and symptoms in people with asthma. A group of researchers at the University

of Washington sought to investigate the severity of asthma symptoms in relationship to air pollution. The researchers recruited a panel of 133 children with mild to moderate asthma, ages 5 to 13 years old, who were enrolled in a clinical asthma management program in **Seattle**. The children completed daily diary cards for an average of 58 days to indicate their medication use and asthma severity.

Researchers found that daily increases PM_{2.5} and PM₁₀ increased the risk of having a more severe asthma attack, and increased the use of rescue inhaler medication in the children.

Specifically, a 10 µ/m³ rise in PM_{2.5} concentrations increased the risk of having a more serious asthma attack the next day by 20 percent.

Increases in carbon monoxide were also associated with more severe asthma attacks, but researchers believe that this pollutant is a marker for exposure to combustion byproducts.

Slaughter, J.C, Lumley, T., Sheppard, L., Koenig, J.Q. and Shapiro, G.G. Effects of Ambient Air Pollution on Symptom Severity and Medication Use in Children with Asthma. *Ann. Allergy Asthma Immunol.* Oct. 1, 2003, Vol. 91, No. 4, pp. 346-53.

Air Pollution Triggers Bronchitis in Children with Asthma

The Children's Health Study has followed a cohort of children with asthma in 12 **Southern California** communities for over a decade. This study explored the role that different components of the air pollution mix can have on various symptoms of bronchitis, such as cough, congestion, and phlegm, in children with asthma. The study found that effects varied in relation to changes in yearly concentrations of air pollutants within each community. **The authors found associations of bronchitic symptoms with yearly changes in PM_{2.5} and organic carbon particles (from gasoline and diesel exhaust), and with gaseous nitrogen dioxide and ozone.**

Researchers suggest that previous cross-sectional studies may have underestimated air pollution risks and conclude that *“the yearly variability in bronchitic symptoms in association with changes in air pollution provides indirect evidence that even modest reductions in air pollution could result in improved respiratory health in children.”*

McConnell, R., Berhane, K., Gilliland, F., Molitor, J., Thomas, D., Lurmann, F., Avol, E., Gauderman, W.J., and Peters, J.M. Prospective Study of Air Pollution and Bronchitic Symptoms in Children with Asthma. *American Journal of Respiratory and Critical Care Medicine.* Vol. 168. pp. 790-797, 2003.

Low Levels of Ozone Increase Respiratory Risk in Asthmatic Kids

Yale University researchers studied a group of 271 asthmatic children under age 12, living in **Connecticut and Springfield, Massachusetts** involved in a prospective study of asthma severity. The children's mothers tracked their asthma symptoms such as wheeze, persistent cough, chest tightness, and shortness of breath, and their medication use, on a daily basis.

The study published in the *Journal of the American Medical Association*, reported that a 50 ppb increase in 1-hour ozone concentrations dramatically increased the likelihood of wheeze (by 35%) and chest tightness (by 47%). **The study found that asthmatic children using maintenance medication were particularly vulnerable to ozone even after controlling for co-exposure to fine particles, and even at pollution levels below EPA's current air quality standards for ozone.** The

highest levels of ozone on a one-hour and eight-hour average basis were associated with increased shortness of breath and rescue medication use. $PM_{2.5}$ was not significantly associated with a worsening of asthma when both ozone and fine particles were co-analyzed.

In an accompanying editorial, Dr. George Thurston and Dr. David Bates write that “air pollution is one of the most under-appreciated contributors to asthma exacerbations.”

Gent, J.F., Triche, E.W., Holford, T.R., Belanger, K., Bracken, M.B., Beckett, W.S. and Leaderer, B.P. Association of Low-Level Ozone and Fine Particles with Respiratory Symptoms in Children with Asthma. *Journal of the American Medical Association*. Vol. 290, No. 14, pp. 1859-1867, October 8, 2003.

Thurston, G.D. and Bates, D.V. Air Pollution as an Underappreciated Cause of Asthma Symptoms. *Journal of the American Medical Association*. Vol. 290, No. 14, pp. 1915-1917, October 8, 2003.

Air Pollution and Asthmatic Symptoms in Panel of Hispanic Children

Researchers conducted a panel study of 22 Hispanic children aged 10-16 years old with asthma living in a **Los Angeles** community with high traffic density. Subjects kept daily diaries of their symptoms for three months. Air quality measurements were collected for ozone, nitrogen dioxide, sulfur dioxide, carbon monoxide, PM_{10} , as well as for the elemental and organic carbon fractions of PM_{10} and for numerous toxic volatile organic compounds. $PM_{2.5}$ data was not available.

Researchers presented new evidence that particle composition is important to adverse respiratory effects. **There were positive associations reported between asthma symptoms and organic carbon, elemental carbon and PM_{10} , but the evidence was stronger for organic carbon and elemental carbon in the two-pollutant models.** Elemental carbon is a marker for diesel emissions. Positive associations were also reported for selected volatile organic compounds associated with motor vehicles, including benzene, formaldehyde, toluene and xylene.

Delfino, R.J., Gong Jr., H., Linn, W.S., Pellizzari, E.D., and Hu, Y. Asthma Symptoms in Hispanic Children and Daily Ambient Exposures to Toxic and Criteria Air Pollutants. *Environmental Health Perspectives*, Vol. 111, No. 4, April 2003.

Poor Children in U.S. - Mexico Border City Suffer Effects of Air Pollution

The Commission for Environmental Cooperation of North America commissioned a study of the health impacts of air pollution on the children of **Ciudad Juárez, Mexico** a city where children may be more vulnerable because of poor living conditions. **The study found significant associations between ambient levels of ozone, and respiratory-related emergency visits by children, for upper respiratory infections and asthma.** No association was observed with ambient concentrations of PM_{10} .

Overall, ambient air pollutants were not related to respiratory deaths, but when data were stratified by socioeconomic status, an increase in respiratory mortality was observed among infants in the poorest group.

Romieu, I., Ramirez Aguilar, M., Moreno Macias, H., Barraza Villarreal, A., Hernandez Cadena, L., Carbajal Arroyo, L. Health Impacts of Air Pollution on Morbidity and Mortality Among Children of

Ciudad Juárez, Chihuahua, Mexico. Working Paper prepared for the Commission for Environmental Cooperation, November 10, 2003 available online at:
http://www.cec.org/files/PDF/POLLUTANTS/cdjuarez_en.pdf.

Urban Air Pollution Damages Children's Lungs

Children in **Mexico City** are chronically exposed to a complex mixture of air pollutants, including hydrocarbons, ozone concentrations well above the NAAQS, and significant concentrations of metal-containing PM. Researchers followed 174 children aged 5-17, and compared them to 27 control children living in low-polluted areas. Researchers assessed several measures of respiratory damage in the children, including nasal abnormalities, hyperinflation and interstitial markings in the lungs observed by chest X-ray, lung function changes, and blood concentrations of proteins that are indicative of the health of the immune system.

Researchers found that the air pollution exposure produces significant chest X-ray abnormalities in the exposed children, depressed lung function, and an imbalance of blood proteins important to immune response. They found that 22 percent of the exposed children had grossly abnormal nasal mucosa, which can impair nasal defense mechanisms against inhaled gases and particles. The lung damage observed is similar to the chronic inflammatory damage observed in an earlier study of dogs in Mexico City. Researchers report that the x-ray and lung function changes they found in the exposed children could be due to pollution-associated chronic bronchiolitis, which could put the children at greater risk of developing chronic obstructive airway disease later in life.

They conclude that lifelong exposure to urban air pollution causes respiratory damage in children and may predispose them to development of chronic lung disease and other problems due to suppression of the immune system.

Calderón-Garcidueñas, L., Mora-Tiscareño, A., Fordham, L.A., Valencia-Salazar, G., Chung, C.J., Rodríguez-Alcaraz, A., Paredes, R., Variakojis, D., Villarreal-Calderón, A., Flores-Camacho, L., Antunez-Solis, A., Henríquez-Roldán, and Hazucha, M.J. Respiratory Damage in Children Exposed to Urban Pollution. *Pediatric Pulmonology*. Vol. 36, No. 2, pp. 148-61, August 2003.

More Ozone "Responders" Among Children and Asthmatics

Large differences in the sensitivity of individuals to ozone have been well documented. Those that are particularly sensitive are known as "responders." This study sought to establish the prevalence of "responders" in four different population subgroups: children, asthmatics, the elderly, and athletes, by assessing symptoms and measuring respiratory function.

The study found higher rates of ozone responders in asthmatics (21%) and children (18%), as compared to the elderly and athletes (both 5%). **This means that children and asthmatics have a higher risk of being ozone sensitive and experiencing more acute lung function decrements than other population groups.**

Höppe, P. Peters, A., Rabe, G., Praml, G., Lindner, J., Jakobi, G., Fruhmann, G., and Nowak, D. Environmental Ozone Effects in Different Population Subgroups. *International Journal of Hygiene and Environmental Health*. Vol. 206, pp. 505-516, 2003.

CARDIOVASCULAR EFFECTS IN ADULTS

Air Pollution Boosts Stroke Risk

Higher levels of air pollution increase the risk of hospitalization for stroke, especially in warmer weather, according to a study in **Kaohsiung, Taiwan**. Researchers tracked data on multiple air pollutants and 23,000 hospital admissions for stroke over a 4-year period in Taiwan's second largest city. They compared air pollution levels of the dates of admissions with the levels one week before and after admission. They found that PM₁₀ and nitrogen dioxide were the most important pollutants and that their effects were greatest on warmer days.

Another recent study in **England and Wales** reported that **road traffic pollution is associated with excess risk of mortality from stroke**. Researchers reported that stroke deaths were 7 percent higher in men living within 200 meters of a main road, compared with men living more than 1,000 meters away.

Tsai, S.-S., Goggins, W.B., Chiu, H.-F., and Yang, C.-Y. Evidence for an Association Between Air Pollution and Daily Stroke Admissions in Kaohsiung, Taiwan. *Stroke*. Published online before print October 9, 2003, doi:10.1161/01.STR.0000095564.33543.64

Maheswaran, R., and Elliott, P. Stroke Mortality Associated with Living Near Main Roads in England and Wales, A Geographical Study. *Stroke*. Vol. 34, pp. 2776-2780, 2003.

Ozone Pollution Sends Elderly to Hospitals in Denver

A large number of epidemiologic studies from around the world have reported an association between various air pollutants and hospital admissions for cardiovascular causes. Extremes in weather have also been associated with adverse health effects, including mortality.

This study tracked hospital admissions for cardiovascular diseases at all 11 **Denver** County hospitals during July and August, two extreme temperature months, for a four year period. The study focused on men and women older than 65 years of age.

Researchers found that ozone increases the risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease. Sulfur dioxide was related to increased hospital stays for cardiac dysrhythmias, and carbon monoxide was significantly associated with congestive heart failure hospitalization. No associations were found between particulate matter or nitrogen dioxide and hospitalizations. Higher temperatures were an important factor in increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure, but were associated with a decrease in the frequency of visits for the other heart conditions studied.

Researchers conclude that "*exposures to higher air pollutant concentrations (except for particulate matter and NO₂), even at levels that meet federal air quality standards, appear to have an effect of increasing the number of hospital admissions for cardiovascular diseases as a whole.*"

Koken, P.J.M., Piver, W.T., Ye, F. Elixhauser, A., Olsen, L.M., and Portier, C.J. Temperature, Air Pollution, and Hospitalization for Cardiovascular Diseases among Elderly People in Denver. *Environmental Health Perspectives*. Vol. 111, No. 10, pp. 1312-1317, August 2003.

Particulates Linked to Hospital Stays for Heart Attacks

A study in **Rome, Italy**, used a “case-crossover” design to evaluate the relation between daily indicators of air quality and hospitalizations for acute myocardial infarctions, or heart attacks. Individual data on patients was considered as possible effect modifiers. The study period was over two years and included over 6,000 patients.

The strongest and most consistent positive effects were found for total suspended particulates, with positive associations also reported for nitrogen dioxide and carbon monoxide.

The study suggests that traffic-derived air pollutants increase the risk of heart attacks, especially during the warm season, among the elderly, and in people with heart conduction disturbances.

D’Ippoliti, D., Forastiere, F., Ancona, C., Agabity, N., Fusco, D., Michelozzi, P., Perucci, C.A. Air Pollution and Myocardial Infarction in Rome: A Case-Crossover Analysis. *Epidemiology*, Vol. 14, No. 5, pp. 528-535, 2003.

Air Pollution Particles Lower Heart Rate Variability in Elderly Humans

Investigations of cardiovascular health effects are being carried out to better explain the mechanisms responsible for mortality attributable to particulate air pollution. For instance, recent studies have reported associations between elevated PM levels and serious ventricular arrhythmias and myocardial infarctions.

Several recent panel studies have investigated heart rate variability in relationship to particle air pollution. Heart rate variability reflects the autonomic function of the heart. In this study, a small panel of healthy elderly volunteers aged 60 to 80, were exposed to concentrated particles derived from the ambient air in **Chapel Hill, North Carolina**, and to clean air. Changes in heart rate variability were measured before, immediately following, and 24-hours after exposure.

The study found that a 2-hour exposure of healthy elderly subjects to moderate levels of particulate pollution -- comparable to levels seen in many metropolitan areas -- resulted in alterations in heart rate variability. Lowered heart rate variability has been associated with increased risk for developing coronary heart disease and to sudden cardiac death.

These results are in contrast to the findings of the same researchers in a similar study of healthy young adults, suggesting that elderly people are more responsive to particulate matter pollution.

Devlin, R.B., Ghio, A.J., Kehrl, H., Sanders, G., and Cascio, W. Elderly Humans Exposed to Concentrated Air Pollution Particles Have Decreased Heart Rate Variability. *The European Respiratory Journal*. Vol. 21, Suppl. 40, pp. 76s-80s, 2003.

Fine Particles and Ozone Suppress Heart Rate Variability in Nursing Home Residents

Thirty-four residents of a nursing home in **Mexico City** underwent 5-minute electrocardiograms every other day for a 3-month period. Ambient ozone measurements were obtained, as well as indoor and outdoor PM_{2.5} concentrations. **After adjusting for age and heart rate, investigators observed a decline in heart rate variability in association with air pollutants, particularly among those**

with high blood pressure. Reductions in heart rate variability are correlated with increased rates of cardiovascular morbidity and mortality in the high-risk and general population, but the clinical significance of minor, transient changes such as observed in this study are uncertain.

Holguin, F., Tellez-Rojo, M.M., Hernandez, M., Cortez, M., Chow, J.C., Watson, J.G., Mannino, D., and Romieu, I. Air Pollution and Heart Rate Variability Among the Elderly in Mexico City. *Epidemiology*. Vol. 14, No. 5, pp. 521-527, 2003.

Mittleman, M.A. and Verrier, R.L. Air Pollution: Small Particles, Big Problems? Commentary. *Epidemiology*. Vol. 14. No. 5. pp. 512-513, September 2003.

Fine Particles and Gaseous Air Pollutants Increase Risk of Hospitalization

This time-series study in **Atlanta, Georgia** funded by the Electric Power Research Institute used data on more than 4 million emergency department visits from 331 hospitals, and detailed air quality data on criteria air pollutants. For the last two years of the study, detailed data on several chemical characteristics of PM were available.

Researchers found evidence for an association between hospitalization for cardiovascular disease and PM_{2.5}, nitrogen dioxide, carbon monoxide, and components of PM_{2.5} including organic carbon, elemental carbon, and oxygenated hydrocarbons.

The effect of ambient pollution on cardiovascular conditions tended to be rapid, with the strongest associations observed with pollution levels on the same day as emergency department visits.

Metzger, K.B., Tolbert, P.E., Klein, M., Peel, J.L., Flanders, W.D., Todd, K., Mulholland, J.A., Ryan, P.B., and Frumkin, H. Ambient Air Pollution and Cardiovascular Emergency Department Visits in Atlanta, Georgia, 1993-2000. *Epidemiology*, Vol. 15, No. 1, pp. 46-56, January 2004.

RESPIRATORY EFFECTS IN ADULTS

Living Near a Major Road Exacerbates Respiratory Symptoms in U.S. Veterans

There have been numerous population-based studies investigating the health effects of exposure to traffic, many focusing specifically on the effects on children, and most undertaken in other countries.

This study focused on effects in over 5,000 veterans -- adult males -- living in **southeastern Massachusetts**. Participants completed questionnaires on their chronic illnesses and respiratory symptoms, and a Geographic Information System was used to estimate the distance of their residence from a major road.

The results of this study point to increased risk for persistent wheeze and possibly chronic phlegm for people living within 50 meters of heavily trafficked roads. The authors conclude that *“exposure to vehicular emissions by living near busy roadways might contribute to symptoms of chronic respiratory disease in adults.”*

Garshick, E., Laden, F., Hart, J.E., and Caron, A. Residence Near a Major Road and Respiratory Symptoms in U.S. Veterans. *Epidemiology*. Vol. 14. No. 6, pp. 728-736.

Hospitalizations and Emergency Room Visits Increase Following High Particulate Matter Episodes

A study of half a million Kaiser Permanente members living in the **San Joaquin Valley of California** has reported that **following wintertime episodes of high PM_{2.5} and PM₁₀ concentrations, and to a lesser extent carbon monoxide and nitrogen oxides, hospital admission rates and emergency room visits increased for patients who suffer from acute respiratory ailments such as asthma and bronchitis.** Admissions for chronic respiratory ailments such as emphysema were similarly elevated, particularly during the winter. The study followed patients over a four-year period. Effects estimates were consistently greater for PM_{2.5} than for PM₁₀. Investigators did not find convincing evidence of associations with coarse particles or with ozone.

Van Den Eeden, S.K., Quesenberry, C.P., Jr., Shan, J., and Lurmann, F. Particulate Air Pollution and Morbidity in the California Central Valley: A High Particulate Pollution Region. Final Report to the California Air Resources Board, Contract 97-303, July 12, 2002. Available at: <ftp://ftp.arb.ca.gov/carbis/research/apr/past/97-303.pdf>

Fine Particles Induce Symptoms in Elderly Heart Patients

This is the first study in recent years to explore the relationship between cardiovascular symptoms and air pollution. Researchers followed a panel of non-smoking elderly subjects with coronary heart disease in three cities during the winter of 1998-1999: **Amsterdam, the Netherlands; Erfurt, Germany; and Helsinki, Finland.** Participants recorded occurrence of selected cardiovascular and respiratory symptoms in a daily diary. Air quality measurements were made for PM₁₀, PM_{2.5}, ultrafine particles, nitrogen oxide, carbon monoxide, sulfur dioxide and ozone. Information on potential confounding factors such as weather variables and influenza data was also collected.

Researchers reported consistent positive associations of PM_{2.5} with shortness of breath and phlegm, and weak positive associations between PM_{2.5} and being awakened by breathing problems and avoidance of activities. Associations were more consistent with PM_{2.5} than with other pollutants, including ultrafine particles. There was no association between chest pain and air pollution.

de Hartog, J.J., Hoek, G., Peters, A., Timonen, K.L., Ibaldo-Mulli, A., Brunekreef, B., Heinrich, J., Tittanen, P., van Wijnen, J.H., Kreyling, W., Kulmala, M., and Pekkanen, J. Effects of Fine and Ultrafine Particles on Cardiorespiratory Symptoms in Elderly Subjects with Coronary Heart Disease. *American Journal of Epidemiology*. Vol. 157, No. 7, pp. 613-623, 2003.

Ozone Exacerbates Symptoms in COPD Patients

Thirty-nine senior adults with severe chronic obstructive pulmonary disease (COPD) were followed by their physicians in **Paris, France**, during a 14-month period. Daily levels of PM₁₀, ozone, sulfur dioxide and nitrogen dioxide were monitored.

No evidence of symptom exacerbation and PM₁₀, SO₂, or NO₂ was observed. **However, the 8-hour average ozone concentration was associated with exacerbation of COPD symptoms.**

According to the researchers, *“our results are consistent with those of toxicological studies that have shown the inflammatory mechanisms of O₃. The recruitment of inflammatory cells into the lung presents a risk of tissue damage through the release of toxic mediators by activated inflammatory cells. Perhaps this phenomenon would be more serious among patients suffering from COPD, in whom a pre-existent inflammation of the small or large airways would be constant.”*

Desqueyroux, H., Pujet, J.C., Prosper, M., Le Moullec, Y., Momas, I. Effects of Air Pollution on Adults With Chronic Obstructive Pulmonary Disease. *Archives of Environmental Health*, Vol. 57, No. 6, pp. 554-560, Nov.- Dec. 2002.

Autopsies Show Evidence of Particle Damage to Small Airways

Researchers evaluated a series of autopsied lungs from **Mexico City**, a city with high PM levels, and compared them by formal grading analysis to lungs from **Vancouver**, a region of generally low air pollution. The small airways in the Mexico City lungs showed markedly higher levels of fibrous tissue and muscle, and microscopic evidence of particle accumulation in the respiratory bronchioles. **The study demonstrates that particle pollution penetrates into and is retained in the walls of the small airways.** The type of airway wall remodeling found here is the same as that associated with chronic airflow obstruction in cigarette smokers and in asthmatics, and may have a similar effect in those exposed to PM.

A related laboratory study has demonstrated that air pollution particles produce airway wall remodeling in rat tracheal tissue maintained in culture. Researchers exposed the tissue to two types of particles -- **Ottawa** urban air particles, and diesel exhaust particles. **The study found that exposure to these particles can induce expression of genes involved in fibrogenesis and airway wall fibrosis**, suggesting an explanation for the fibrosis and increased muscle observed in human airways subject to chronic exposure to high levels of PM.

Researchers conclude that *“PM-induced airway wall remodeling may play an important role in producing airflow obstruction in individuals living in high PM regions.”*

Churg, A. Brauer, M., Avila-Casado, M.d.C., Fortoul, T.I., and Wright, J.L. Chronic Exposure to High Levels of Particulate Air Pollution and Small Airway Remodeling. *Environmental Health Perspectives*. Vol. 111, No. 5, pp. 714-718, May 2003.

Dai, J., Xie, C., Vincent, R., and Churg, A. Air Pollution Particles Produce Airway Wall Remodeling in Rat Tracheal Explants. *American Journal of Respiratory Cell Molecular Biology*. Vol. 29, pp. 352-358, 2003.

SARS Deaths Higher in More Polluted Regions

High levels of air pollution may increase the risk of dying from SARS -- severe acute respiratory syndrome. A study in China found that patients with SARS who were living in areas with high air pollution were more than twice as likely to die from the illness than those living in cleaner areas.

Researchers developed an air pollution index from data on ambient concentrations on ozone, particulate matter, sulfur dioxide, nitrogen dioxide and carbon monoxide, to compare with data on

SARS illnesses and fatalities. There have been over 5,000 cases of SARS reported in China since November 2002, with 349 fatalities.

The study authors suggest that air pollution might compromise lung function, predisposing SARS patients to illness and death.

Cui, Y., Zhang, Z.-F., Froines, J., Zhao, J., Want, H., Yu, S.-Z., and Detels, R. Air Pollution and Case Fatality of SARS in the People's Republic of China: An Ecologic Study. *Environmental Health: A Global Access Science Source*. Vol. 2, No. 15, November 20, 2003. Available online at: <http://www.ehjournal.net/content/pdf/1476-069X-2-15.pdf>.

Prior Exposure to Fuel Oil Combustion Particulates Enhances Allergic Response

Experimental studies have shown that diesel exhaust and gaseous pollutants may enhance the allergic response.

In this human experimental study, researchers sought to determine whether pre-exposure to combustion particles would enhance the response to subsequent exposure to pollen. The combustion particles used in the study were residual oil fly ash from a Boston power plant. Nasal cells were examined following exposure for evidence of inflammation and allergic response.

Researchers reported evidence of a greater than additive interaction between particulate exposure and allergen challenge. Specifically, they found an increase in certain inflammatory cells and cytokines that are measures of irritant or allergic response, relative to subjects pre-exposed to clean air.

Hauser, R., Rice, T.M., Krishna Murthy, G.G., Wand, M. P., Lewis, D., Bledsoe, T., and Paulauskis, J. The Upper Airway Response to Pollen is Enhanced by Exposure to Combustion Particulates: A Pilot Human Experimental Challenge Study. *Environmental Health Perspectives*, Vol. 111, No. 4, pp. 472-477, April 2003.

Diesel Exhaust Emissions Causes Chronic Damage to Nasal Mucous Membrane

Diesel exhaust contains numerous toxic substances such as sulfur dioxide, acrolein, formaldehyde, metals, and particulate matter. Many of these combustion byproducts are known to be genotoxic, cytotoxic, fibrogenic, and carcinogenic. Uncontrolled diesel emissions from heavy equipment constitute a major public health concern.

Researchers in Switzerland studied some 200 male, non-smoking customs officers over a five year period. Some of the officers were engaged in the clearing of diesel trucks over 8 hours per day during the workweek, while the control group worked in the office. Researchers measured concentrations of diesel exhaust in the ambient air and collected nasal swabs from the workers during the summer and winter.

In humans, the nose is the initial site of injury by inhaled irritants, and it is a common site for particle deposition and for the absorption of potentially toxic gases.

Researchers found increased abnormalities in the nasal skin cells and an increase in white blood cells, in the workers chronically exposed to diesel exhaust. They describe the changes as a chronic

inflammation of the nasal mucous membrane. In addition, **researchers report that the cell changes may be indicative of a genotoxic effect (capable of causing damage to DNA) of chronic diesel exposures in humans.**

Glück, U., Schütz, R., Gebbers, J.-O. Cytopathology of the Nasal Mucosa in Chronic Exposure to Diesel Engine Emission: A Five-Year Survey of Swiss Customs Officers. *Environmental Health Perspectives*, Vol. 111, No. 7, pp. 925-929, June 2003.

LONG- AND SHORT-TERM STUDIES OF PREMATURE MORTALITY

Soot's Impact on Heart Comparable to Risk for Former Smokers

In a follow-up analysis to the American Cancer Society cohort study, researchers have reported a striking link between chronic exposure to fine particle air pollution and increased risk of death from cardiovascular disease in the United States. The increased risk was comparable to that associated with being a former smoker. The new analysis is based on data collected by the American Cancer Society on the cause of death of 500,000 adults over a 16-year period, and on data on air pollution levels in cities nationwide. Data on other risk factors such as body mass, smoking, occupational exposures, and diet were also considered.

The study identifies a strong link between particulate air pollution and ischemic heart disease (which causes heart attacks), and also a link between pollution and irregular heart rhythms, heart failure, and cardiac arrest. It also suggests general biological pathways through which pollution might cause these diseases that lead to death -- increased inflammation and nervous system aberrations that change heart rhythm. Mortality attributable to respiratory disease had relatively weak associations in this study.

Researchers conclude that “the results of this analysis are largely consistent with the proposition that the general pathophysiological pathways that link long-term PM exposure and cardiopulmonary mortality risk include pulmonary and systemic inflammation, accelerated atherosclerosis, and altered cardiac autonomic function.”

Pope, C.A. III, Burnett, R.T., Thurston, G.D., Thun, M.J., Calle, E.E., Krewski, D., and Godleski, J.J. Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution: Epidemiological Evidence of General Pathophysiological Pathways of Disease. *Circulation*. Vol. 109, pp. 71-77, 2004. Published online before print at: <http://www.circulationaha.org>, DOI: 10.1161/01.CIR.0000108927.80044.7F.

Short-Term Studies Underestimate Premature Deaths

The APHEA-2 project was a major study of the health effects of air pollution in 30 cities across Europe and in adjacent countries. That and many other studies have reported that short-term changes in PM₁₀ lead to short-term fluctuations in sickness and death. This study uses a statistical model-- known as the distributed lag model -- to explore whether those deaths are advanced by just a few days or a few weeks, or more.

The researchers found that the adverse effects of short-term increases in air pollution persist for more than a month after exposure. They estimate that the size of the effect of exposure to PM₁₀ doubles for cardiovascular deaths when looking at effects 40 days after exposure, and

increases five-fold for respiratory deaths. These results are consistent with higher risk estimates found in cohort studies such as the Harvard Six Cities Study, and strongly suggest that estimates of the effects of short-term exposures to air pollution seriously underestimate the impact of particle exposure.

Researchers conclude that *“risk assessment based on the short-term associations likely underestimate the number of early deaths that are advanced by a significant amount, and that estimates based on the cohort studies, or studies such as this one, would more accurately assess the public health impact.”*

Another research group took a different approach to evaluate the extent of life-shortening implied by short-term estimates of particulate air pollution on mortality. They sought to establish a separate relative rate of mortality for different time scales. They applied this method of a database on particulate air pollution, daily mortality, and weather in four cities: **Pittsburgh, Minneapolis, Seattle, and Chicago.**

The authors found that the mortality rates during periods from 14 days to two months after exposure were larger than the rates from one to four days after the exposure. This refutes the “harvesting hypothesis”: that is the argument that any increase in mortality associated with increased particle concentrations stems entirely from the death of very frail persons who die a few days early. If “harvesting” were the case, the rate of mortality would not continue to be higher for these extended periods of time.

Zanobetti, A., Schwartz, J., Samoli, E., Gryparis, A., Tuoloumi, G., Peacock, J., Anderson, R.H., Le Tertre, A., Bobros, J., Celko, M., Goren, A., Forsberg B., Michelozzi, P., Rabczenko, D., Perez Hoyos, S., Wichmann, H.E., and Katsouyanni, K. The Temporal Pattern of Respiratory and Heart Disease Mortality in Response to Air Pollution. *Environmental Health Perspectives*. Vol. 111, No. 9, pp. 1188-1193, July 2003.

Dominici, F., McDermott, A., Zeger, S.L., and Samet, J.M. Airborne Particulate Matter and Mortality: Timescale Effects in Four US Cities. *American Journal of Epidemiology*. Vol. 157, No. 12, pp. 1055-1065, June 15, 2003.

Dutch Study Confirms that Long-Term Exposures to Particulate Matter are Deadly

This long-term cohort study confirms the findings of the Harvard Six Cities Study and the study of the American Cancer Society Cohort that found an association between chronic exposure to particulate air pollution and shortened life expectancy.

Investigators assessed the association between long-term exposure to traffic-related air pollution and cause-specific mortality in a cohort of 4,500 elderly people, participants in the ongoing Netherlands Cohort study on Diet and Cancer. **People who lived near major roads had a 95 percent greater risk of dying early from cardiopulmonary causes than people living in cleaner air areas.**

Hoek, G., Brunekreef, B., Goldbohm, S., Fischer, P., and van den Brandt, P. A. Association Between Mortality and Indicators of Traffic-Related Air Pollution in the Netherlands: A Cohort Study. *The Lancet*. Vol. 360, pp. 1203-1209, October 19, 2002.

INTERVENTION STUDIES

Control of PM Substantially Diminishes Daily Deaths

Air quality in **Dublin, Ireland** deteriorated in the 1980s after a switch from oil to bituminous coal for domestic heating. In 1990, the Irish Government banned the marketing and sale of bituminous coals within the city of Dublin. A dramatic improvement in air quality ensued. This study investigates the effect of a ban on coal sales.

Concentrations of air pollution, measured as “black smoke” and death rates were compared for 72 months before and after the ban. The analysis was adjusted to reflect age, weather, respiratory epidemics, and other factors. **Respiratory and cardiovascular death rates fell markedly following the ban on soft coal.**

The authors conclude: *“Our findings suggest that control of particulate air pollution in Dublin led to an immediate reduction in cardiovascular and respiratory deaths. These data lend support to a relation between cause and the reported increase in acute mortality associated with daily particulate air pollution. Moreover, our data suggest time-series studies could be underestimating the benefits of particulate air pollution controls.”*

A follow up study presented an analysis of the medium term (weeks to months) exposure effects of particulate pollution, measured as “black smoke” and temperature, over a period of 17 years in **Dublin. Investigators found that the effects of particulate air pollution are strongest on the day of and the few days following exposure, but extend out over 40 days following exposure.** This was especially noticeable for respiratory causes of death. *“These extended follow-up effects were two to three times greater than the acute effects reported in other studies, and approach the effects reported in longer term survival studies. This analysis suggests that the studies on the acute effects of air pollution have underestimated the total effects of temperature and particulate air pollution on mortality,”* report the investigators.

Clancy, L., Goodman, P., Sinclair, H., and Dockery, D.W. Effect of Air-Pollution Control on Death Rates in Dublin, Ireland: An Intervention Study. *The Lancet*. Vol. 360, pp. 1210-14, October 19, 2002.

Goodman, P.G., Dockery, D.W., and Clancy, L. Cause Specific Mortality and the Extended Effects of Particulate Pollution and Temperature Exposure. *Environmental Health Perspectives*, In Press. Available online November 12, 2003, doi: 1289/ehp.6451, available at <http://dx.doi.org/>.

Improvement in Air Quality Benefits Children’s Health

Following German reunification in 1990, there was a tremendous decline in combustion-derived emissions of sulfur dioxide and total suspended particulate (TSP) in Eastern Germany. This provided a unique opportunity to study trends in the prevalence of respiratory illness along with the improvement in air quality.

This review focused on the results of two repeated surveys of nonallergic respiratory disease of children living in East Germany. **The surveys found that declines in chronic bronchitis were associated with the decline in TSP.**

Another study of three communities in East Germany measured lung function in 2,500 children. **Lung function increased as TSP and sulfur dioxide pollution declined.** Researchers concluded that “a reduction of air pollution in a short time period may improve children’s lung function.”

Heinrich, J. Nonallergic Respiratory Morbidity Improved Along With a Decline of Traditional Air Pollution Levels: A Review. *European Respiratory Journal*. Vol. 21, Suppl. 40, pp. 1s-6s, 2003.

Frye, C., Hoelscher, B., Cyrus, J., Wjst, M., Wichmann, H.-E., and Heinrich, J. Association of Lung Function Declining Ambient Air Pollution. *Environmental Health Perspectives*. Vol. 111, No. 3, pp. 383-387, March 2003.

Reductions in Pollution Particles Linked to Reductions in Infant Mortality

Economists at the University of Chicago and the University of California, Berkeley have reported new evidence of an association between particles in the air, and infant health. They examined the sharp reduction in manufacturing, and in turn, reductions in particulate air pollution (measured as Total Suspended Particulates (TSP)) during the 1981-1982 recession, in relation to county-specific data on infant deaths.

In Chicago, for instance, researchers estimated that the decline in air pollution lowered the infant mortality rate by 5 percent between 1980 and 1982.

Their research suggests that 2,500 fewer infants died during this period than would have, absent the reductions in air pollution. The majority of the infant deaths occurred within one month of birth, suggesting a possible impact of air pollution on fetal development.

Another study by these same researchers examined the relationship between implementation of the 1970 Clean Air Act Amendments and infant mortality. They documented sharp reductions in TSP pollution between 1971 and 1972, when the Clean Air Act took effect, and a corresponding reduction in infant death rates.

Chay, K.Y., and Greenstone, M. The Impact of Air Pollution on Infant Mortality: Evidence From Geographic Variation in Pollution Shocks Induced by a Recession. *Quarterly Journal of Economics*. Vol. CXVIII, pp. 279-300, August 2003. (Available online at: <http://www-news.uchicago.edu/releases/03/particles/chay-greenstone.pdf>.)

Chay, K.Y., and Greenstone, M. Air Quality, Infant Mortality, and the Clean Air Act of 1970. National Bureau of Economic Research, Working Paper No. w10053, October 2003. (Available online at: http://www.nber.org/cgi-bin/author_papers.pl?author=kenneth+chay).

MISCELLANEOUS

Air Pollution Hits Poor People the Hardest

This study investigated mortality in relation to neighborhood levels of income and air pollution in a cohort of 5,000 people who had been referred for pulmonary function testing in the urban area of **Hamilton-Burlington in southern Ontario**. Income was estimated using census data, and average neighborhood levels of total suspended particulates and sulfur dioxide were estimated by interpolating data from the monitoring network.

Mean pollution levels tended to be higher in the lower-income neighborhoods, and these neighborhoods also had higher mortality rates. While biologic risk factors were not controlled for, investigators reported that ***“two of the broader determinants of health -- income and air pollution levels -- were important correlates of mortality in this population.”***

Finkelstein, M.M., Jerrett, M. DeLuca, P., Finkelstein, N., Verma, D.K., Chapman, K., and Sears, M.R. Relation between Income, Air Pollution and Mortality: A Cohort Study. Canadian Medical Association Journal, Vol. 169, No. 5, September 2, 2003.

PM Research Centers Report Progress

In 1988, Congress directed the U.S. EPA to substantially increase its level of funding on PM health effects research. It also mandated that a National Research Council (NRC) committee be established to provide scientific oversight for PM research. In its first report, the NRC Committee on Research Priorities for Airborne Particulate Matter recommended the establishment of interdisciplinary research centers to be funded on a multi-year basis to foster comprehensive and integrated research on particle health effects. In a competitive process, EPA awarded grants to five centers: A California consortium headquartered at the University of California Los Angeles, Harvard University, New York University, the University of Rochester, and the University of Washington.

This review article reports on the substantial accomplishments of the PM centers in their first two and a half years of operation, and lays out short- and longer-term research goals. Six topics are discussed: biological mechanisms, acute effects, chronic effects, dosimetry, and exposure assessment.

Lippmann, M., Frampton, M., Schwartz, J., Dockery, D., Schlesinger R., Koutrakis, P., Froines, J., Nel, A., Finkelstein, J., Godleski, J., Kaufman, J., Koenig, J., Larson, T., Luchtel, D., Liu, L-J., S., Oberdörster, G., Peters, A., Sarnat, J., Sioutas S., Suh, H., Sullivan J., Utell, M., Wichmann, E., and Zelikoff, J. The U.S. Environmental Protection Agency Particulate Matter Health Effects Research Centers Program: A Midcourse Report of Status, Progress and Plans. Environmental Health Perspectives. Vol. 111, No. 8, pp. 1074-1092, June 2003.

Autopsy Evidence Points to Diesel’s Role in 1952 London Smog Episode

Researchers obtained archived lung tissue from autopsies of 16 victims of the London smog disaster over 50 years ago. This provided a unique opportunity to examine the form and composition of the particulate matter found in the lungs of those known to have died from exposure to the smog. Pathologists examined samples from different compartments of the lungs: for instance the airway, airspace, interstitium, and lymph node. This allowed researchers to see what people had been exposed to just before their deaths and over the longer term.

The study found high volumes of ultrafine carbon particles and various metals including lead. But most significant was the evidence of particles associated with diesel fuel, given that London had made a switch from electric trams to diesel buses early in 1952.

Hunt, A., Abraham, J.L., Judson, B., and Berry, C.L. Toxicologic and Epidemiologic Clues from the Characterization of the 1952 London Smog Fine Particulate Matter in Archival Autopsy Lung Tissues. Environmental Health Perspectives. Vol. 111, No. 9, pp. 1209-1214, July 2003.