



Smoke, Dust & Haze

EPA NW Research Center for Particulate Air Pollution and Health Newsletter

Winter 2002



Puget Sound Clean Air Agency

Seattle skyline at increasing levels of particulate matter.

NOW AT THE MIDPOINT OF ITS FIVE-YEAR FUNDING period, the Northwest Research Center for Particulate Air Pollution and Health (PM Center) is beginning to answer some of the questions originally proposed in our application to EPA. Findings from our two-year intensive exposure assessment and health effects panel study of 107 subjects will help guide our future epidemiologic and toxicologic research. Our extensive indoor, outdoor, and personal $PM_{2.5}$ data will be used to assess personal exposure of those 107 subjects and to construct models that predict community-wide exposure to $PM_{2.5}$ in Seattle and perhaps more generally. Combining monitors with others at a central site will provide well-characterized $PM_{2.5}$ for our toxicology studies; these data will be shared with the four other EPA PM Centers.

We have preliminary results to share in four categories: exposure assessment, biological mechanisms, acute health effects, and chronic health effects. In each case, the data represent multidisciplinary efforts nurtured by the NW Center's collaborative atmosphere. We also compare our results with those from the other four EPA PM Centers.

—Jane Q. Koenig, PhD, program director

Research findings

Exposure assessment

Biological mechanisms

Acute health effects

Chronic health effects

Exposure Assessment

Seattle's exposure studies are bringing to light important contrasts to similar studies conducted in the eastern US. Findings from other EPA PM Center-supported studies indicate that most of the $PM_{2.5}$ in northeastern US cities is secondary in origin and exhibits very little spatial variability. However, this is not the case in Seattle and other Pacific Northwest cities where $PM_{2.5}$ is dominated by local, primary sources (Maykut et al., 2001, Kim et al., submitted). In Seattle, $PM_{2.5}$ exhibits modest, yet significant, spatial variability within a radius of 20 km. These spatial differences are likely due to the proximity of major highways and the elevation of the monitoring location (Goswami et al., 2002).

Infiltration

These same exposure studies provide evidence of the impact of indoor PM sources for healthy individuals and susceptible subpopulations. In Seattle, indoor or non-ambient $PM_{2.5}$ sources contributed on average 49% of the total personal $PM_{2.5}$ exposure (Liu and Allen, 2001; Sheppard, 2000). This fraction



UW Photography

Dr. Tim Larson

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varied significantly with subject age, with greater non-ambient PM contributions observed for children. Some types of residences had greater penetration of outdoor particles, and we found significant inter- and intra-home variability (Larson et al., 2001). For the 30 homes monitored, the estimated mean effective penetration efficiency was $56 \pm 8\%$ and the hourly variations in the levels of indoor PM of outdoor origin could be well described by a non-equilibrium model.

We are studying the application of both analytical and statistical methods to the source apportionment of $PM_{2.5}$ exposure. Traditional applications have focused on outdoor particles, with very little attention to indoor and personal samples. Currently, we're analyzing a number of $PM_{2.5}$ samples via x-ray fluorescence (XRF) as a first step in assessing the sources of $PM_{2.5}$ in various microenvironments. The fact that most $PM_{2.5}$ in Seattle, including wood smoke, is primary in origin and rich in combustion-derived organic compounds poses assessment challenges.

New tools

To overcome these challenges, we developed a new assay for methoxyphenols, markers of lignin combustion collected on Teflon filters (Simpson et al., 2001). This enhances our ability to separate the influence of this source from other important combustion sources in our exposure

assessments. It is also an important step in the validation of a urinary biomarker for wood smoke exposure.

We found that the temperature-resolved fractions of particulate carbon collected on quartz filters can be useful in resolving source contributions to outdoor $PM_{2.5}$ (Maykut et al., 2001). However, when we attempted to extend this approach to indoor and personal samples, we found a significant positive sampling artifact associated with the adsorption of organic vapors onto the quartz filter medium (Claiborn et al., 2001).

We eliminated this artifact by developing a new personal sampler that uses carbon-impregnated, open cell foam as an upstream, compact denuder (Pang et al., submitted). This method allows us to more accurately quantify true particulate organic carbon in indoor and personal microenvironments and better resolve the source contributions to both indoor and personal $PM_{2.5}$ samples.

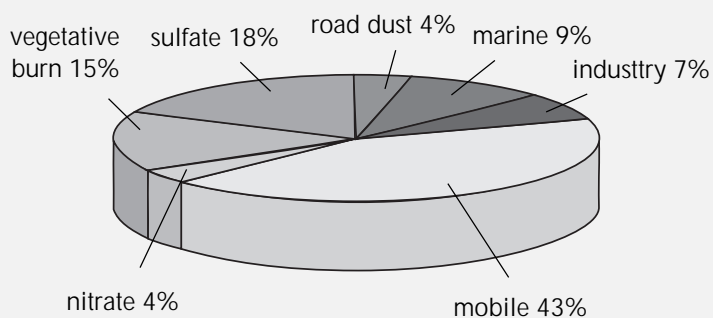
Collaboration

Here are several examples of how the Center has fostered collaborations that allowed us to ask questions that would not be possible as individual investigators.

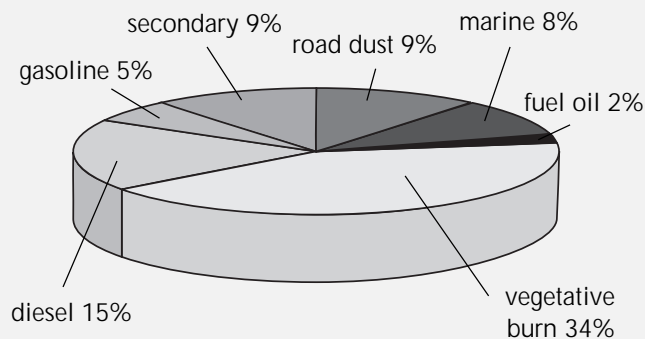
Our panel study of susceptible subjects requires expertise in aerosol measurement and exposure science. Exposure science is a relatively new discipline with

Estimated source contributions to $PM_{2.5}$ at the Beacon Hill monitoring site (1996-1999) from two different receptor models.

Chemical Mass Balance Beacon Hill



Positive Matrix Factor



methods and models unrelated to traditional ambient aerosol science. Investigators in both disciplines are working together to better understand the sources and dynamics of particles as they move from their emission point, through selected microenvironments, to their uptake and passage through the human body.

Two groups that work together are our Center medical professionals, who select susceptible subjects for these exposure studies and guide the protocols to assess acute respiratory and cardiac effects, and laboratory researchers whose toxicological studies involve cardiac effects in susceptible animal models.

Another example of collaboration is the way the exposure group, which collects size-resolved particle samples in microenvironments representative of our panel studies for use in toxicological experiments, is guided by discussions in our weekly science meetings, where we refine our understanding of the sources, exposures, and effects of Northwest particles.

Common to all of the above efforts are Center resources in data management and statistical design and analysis. These components make the information we obtain more accessible to other investigators. The biostatistics group continually analyzes epidemiological information for relevant air quality and health associations.



UW Health Sciences Center for Educational Resources

Dr. Daniel Luchtel, principal investigator, with a laboratory mouse

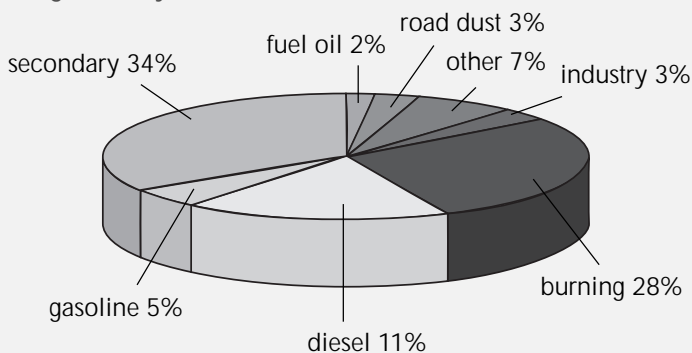
Biological mechanisms

We are testing the hypothesis that inhaled particulate matter causes release of inflammatory mediators from cells in the lung that then become blood borne and target the cardiovascular system. Initial studies have used a mouse model of atherosclerosis; the apolipoprotein E (Apo-E) deficient mouse generated via a targeted disruption of the mouse Apo-E gene. The deficiency of Apo-E leads to spontaneous hypercholesterolemia (an abnormally large amount of cholesterol in the blood) due to the role that Apo-E plays in mediating clearance of cholesterol-rich lipoproteins by the liver. These animals form atherosclerotic lesions throughout the arterial vasculature, which resemble human atherosclerotic lesions. Animals are instrumented and monitored for blood pressure, heart rate, and electrocardiograms using radiotelemetry.

Individual mice were dosed with Washington, DC urban dust aspirated into the lungs. Heart rate was noted to decrease after exposure to PM in normal and in ApoE^{-/-} mice. ApoE^{-/-} mice showed a trend to increased blood pressure and increased variability of blood pressure after PM exposure (Luchtel et al., submitted). Additional experiments are being performed as the control and ApoE^{-/-} mice age, and will include exposure-response

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King County Emissions



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studies using ambient particles from Seattle.

“We have great expectations that the transgenic mouse will tell us the clues for the deciphering pathways of particulate matter toxicity,” said Dr. Daniel Luchtel, principal investigator for this research.

Mechanism

The other centers also are using animal models of compromised health to evaluate the effects of PM. The NYU Center is working with a hypertensive mouse; the Harvard Center is using a dog model with ligated coronary arteries that block blood flow to sections of the heart, and the California Center is developing a mouse model of asthma.

Human clinical studies from other Centers suggest that exposures to either concentrated air particles (CAPS) or ultrafine particles may initiate activation in the endothelium (lining of the heart and blood vessels) and leukocytes (a type of blood cell), with shedding of surface intracellular adhesion molecule-1 (ICAM-1), a key initial step in leukocyte recruitment. To examine the expression of pro-inflammatory and inflammatory mediators such as ICAM-1, microarray-based assays of both lung and heart tissue from exposed mice will be conducted using a mouse array available from the NIEHS-funded UW Center for Ecogenetics and Environmental Health. The Ecogenetics Center has verified an array of 7,500 mouse genes.

Current and future work with this mouse model will involve additional interaction with exposure scientists and aerosol engineers in order to obtain well-characterized ambient particles from Seattle. In addition, results from the microarray assays will generate new hypotheses that can be tested in future field studies with cardiovascular human subjects. These interdisciplinary activities are enhanced by the presence of the NW Center.

Acute health effects

Studies around the world show that PM exposure is associated with both respiratory and cardiac health effects. We measured many of these endpoints in our two-year panel study. One interesting finding is PM-induced changes in heart rate variability in subjects with heart disease.

The study in Seattle involved both patients with and without clinically recognized cardiac disease. Analysis of the EKG recordings is underway, including detailed analyses of heart rate variability and repolarization, using methodology identical to the human clinical studies being conducted at other Centers.

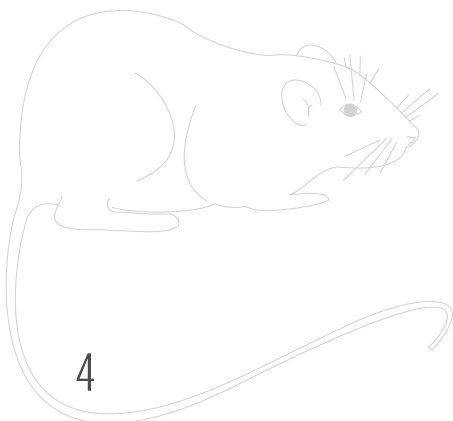
Early results suggest that increased levels of fine particulate air pollution are associated with disturbances in cardiac autonomic control in elderly populations (Sullivan et al., submitted). We investigated whether increases in residence-measured levels of fine PM averaged over 1 hour, 4 hours, and 24 hours prior to heart rate variability (HRV) measures were associated with a decline in high frequency (HF) power in a panel study of 51 elderly individuals with and without cardiac disease (CV).

Methods

To determine this association, we performed daily 20-minute measures of HRV using a Del Mar Dartsan system, including a 5-minute paced breathing protocol, in the subjects' homes over a 10-day exposure period between February 2000 and May 2001. These data were paired with indoor and outdoor calibrated nephelometry measures of fine PM made at the individuals' homes, resulting in 256 measures of HRV in 46 subjects (19 with cardiovascular disease [CV], 17 with chronic obstructive pulmonary disease [COPD], and 10 healthy).

Findings

Multivariate analysis using a linear mixed model with random intercepts that controlled for temperature, relative humidity, and medication use found that a 10 $\mu\text{g}/\text{m}^3$ increase in outdoor fine PM lagged by one hour was associated with a 25% decrease in the median of the



log transformed HF power in those with heart disease during the paced breathing session, which approached statistical significance [95%CI: -45.0%, 0.1%].

We also found borderline significant effects of outdoor measured PM on HF HRV in the CV group at four hours with a 34 percent decline [-58%, 1%] and 24 hours with a 30% decline [-55%, 9%]. We were unable to detect a significant effect of outdoor measures of fine PM on HF power HRV measures in the healthy or COPD participants or an effect of indoor measures of fine PM on HF HRV in individuals with or without heart disease.

Rapid onset

The finding of a decline in HF power with an increase in outdoor levels of fine PM within one hour of HRV measures suggests that fine PM exposure may have a rapid onset of effect on cardiac autonomic modulation in susceptible subgroups. This finding, with a large sample size, confirms an earlier report with seven subjects. The relationship between HRV and personal PM_{2.5} concentrations will be assessed as soon as the air monitoring data are available.

As discussed in the exposure assessment section, Seattle aerosol is predominantly composed of primary particles, rich in organic carbon. In contrast, other reported HRV/PM associations were observed in the eastern US or in a city where a steel mill is the dominant source of PM. Annette Peters is studying a similar cohort of subjects in Erfurt, Germany, as part of the University of Rochester Center.

Blood markers

This panel study also has repeated blood measures on 45 elderly individuals (25 with and 20 without heart disease) to determine the effect of PM_{2.5} and co-pollutant levels on blood coagulation markers (D-dimer and fibrinogen) and an inflammatory marker (C-reactive protein). We are currently examining the relationships between these blood marker levels and various PM exposure metrics. Remaining serum from these individuals has been archived for future analyses.

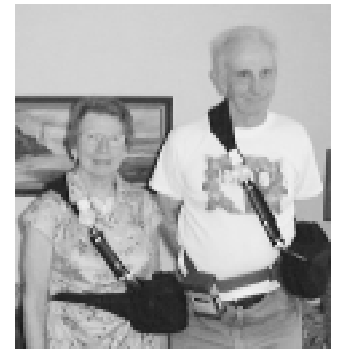
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Outdoor and indoor air quality are compared at a private home

Research subjects wear monitors to measure their personal exposure

Research Technician Christine Sleeman checks the flow rate of air sampling systems



top and middle: Liz Tuttle; bottom: Devon DeLapp

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Children

In addition to examining the inflammatory responses in cardiovascular patients, we are interested in these responses in other populations. We have measured exhaled nitric oxide (eNO) in 16 children aged 6-12 years with mild-to-moderate asthma (Koenig et al., submitted). Exhaled NO is a marker of pulmonary inflammation. Daily samples of exhaled breath were collected for up to 10 consecutive days in the children's homes. A $10 \mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ was associated with a 4.8 (2.26–7.38) ppb increase in eNO. We are currently examining the relationship between this outcome and shorter-term exposure metrics using nephelometry data available for these same subjects.

Heart attacks

The association of particulate matter and ischemia has been supported by recent work on the role of particles as a trigger of myocardial infarctions (heart attacks) (Peters et al., 2001). We intend to replicate the Boston study of myocardial infarctions and short-term $\text{PM}_{2.5}$ exposures in the Seattle area in an attempt to compare the cardiotoxicity of $\text{PM}_{2.5}$ in the two cities (an appropriate cohort of more than 1,000 cases has been identified). We also will apply newly developed case-crossover methodology to this data set (Levy et al., 2000). Collaboration among investigators in the fields of medicine, exposure assessment, and biostatistics in the NW Center make this study possible.

Chronic health effects

The NW PM Center is undertaking an epidemiologic analysis of cardiovascular events and chronic air pollution exposures, based on subject residence, in the Women's Health Initiative Observational Study, which tracks 93,000 women ages 50 through 79 in 40 centers around the country. The Women's Health Initiative is one of the largest studies of its kind, directed by the National Institutes of Health (NIH) and the National Heart, Lung, and Blood Institute (NHLBI). Pollutant exposures will be assessed based on data from the EPA AIRS database.

This study will provide a new cohort of well-characterized subjects (as well as the Harvard Six-City cohort and the American Cancer cohort) for the assessment of long-term PM exposure effects. We anticipate being able to study the effect of chronic exposure to ambient particulate matter on incidence of cardiovascular disease in this cohort using a proportional hazards model approach. The large geographic diversity of the subjects' residences will provide for substantial pollutant contrasts. The study will start early this year.

Since this study involves contemporaneous data, we will have available $\text{PM}_{2.5}$ data from EPA's nationwide federal reference method (FRM) monitoring project. Data analysis in this study requires the combined expertise of epidemiologists, statisticians, and aerosol and exposure scientists. The NW Center's framework of exposure, biostatistical, and health cores provides the essential resources for this newly initiated project.

Data sharing

Examples of sharing data with the other four EPA PM Centers include Dave Kalman sharing archived urine samples; Tim Larson sharing Northwest PM samples with Mitch Cohen at NYU; and Joel Kaufman, Lianne Sheppard, and Thomas Lumley sharing our evaluation of the relationships between hospital admission for myocardial infarction and short-term PM exposure with Annette Peters and Doug Dockery.

Another example is international: four officials from the Taiwan Environmental Protection Agency visited the NW PM Center and the Fresno Supersite in November 2001. While visiting the US, they included a trip to the NW PM Center specifically to obtain ideas on development of PM Centers in Taiwan.

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Participant Comments

from people who participated in the exposure assessment and health effects panel study

"I really missed the Airwatch and diary, the day after everything was taken out. However, I did not miss the rumble of the monitor in the TV room. The study really became a large part of my day. I must tell you, all of the young people that came to my home were so warm and respectful and made me totally comfortable. I looked forward to seeing them every day. I would not hesitate to work with you again if you needed me. Thanks for a good experience."

"Please let the field technicians know how very much I enjoyed seeing them every day. I wish them luck in their endeavors. Thank you for the opportunity to do something worthwhile. I admire all of you."

"Thank you for letting us participate in your study. The young persons who came to our house were very wonderful. We certainly enjoyed the study."

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Smoke, Dust & Haze



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