EPA CENTER FOR AMBIENT PARTICLE HEALTH EFFECTS AT HARVARD SCHOOL OF PUBLIC HEALTH

PROGRESS REPORT : YEAR THREE

THEME I: ASSESSING PARTICLE EXPOSURES FOR HEALTH EFFECTS STUDIES

Project Ia: Assessing Human Exposures to Particulate and Gaseous Air Pollutants

We are currently completing our analysis of data collected in a series of exposure studies that were conducted in several cities located throughout the United States (Boston, MA, Baltimore, MD, Atlanta, GA, Los Angeles, CA, and Steubenville, OH). As part of these studies, we have collected several thousand simultaneous outdoor, indoor, and personal particle and gas samples for several potentially sensitive subgroups, including senior citizens, children, and individuals with chronic obstructive disease (COPD) or recent myocardial infractions (MI). For Atlanta and Steubenville, measurements of cardiovascular health status (heart rate, blood pressure, oxygen saturation, daily symptoms and medication use) were also conducted for each participant. Data collection for the Steubenville and Atlanta studies were co-funded by the Center, while data collection for the remaining studies were supported by other agencies, such as HEI, EPRI, API and EPA (under a separate cooperative agreement).

As part of Project Ia, we are analyzing data from these studies to investigate: (1) the contribution of particles of outdoor and indoor origin to personal PM2.5 exposures; (2) the potential for confounding by gaseous pollutants to affect epidemiological study results and; (3) the ability of particles to penetrate from outdoors to indoor environments. We are currently completing our analyses of data from the Los Angeles, Atlanta and Boston studies and are beginning to examine data from Steubenville, OH. To date, we have published five papers addressing these issues (Sarnat et al., 2000; Long et al., 2000; Long et al., 2001; Sarnat et al., in press a; Sarnat et al, in press, b).

The most recent of these studies investigate the ability of sulfur to act as a tracer of outdoor fine particles. Our results suggest that sulfur compounds are primarily of outdoor origin and behave in a manner that was representative of total PM2.5 in Boston, MA. Thus these findings provide evidence that sulfur can be used as a tracer of outdoor PM2.5. The size composition of outdoor PM2.5 was shown to be an important characteristic affecting the robustness of sulfur-based estimation methods. Sulfur was more representative of particles in the 0.06 and 0.5 m size range as compared to particles in smaller and larger size intervals. The sulfur-tracer method produced consistently accurate results for 0.06-0.5 m particles, however, significantly over-predicted indoor concentration of particles less than 0.06 and greater than 0.7 m in size. These results reflect higher effective penetration efficiencies for sulfur as compared to particles in these smallest and largest size intervals.

Project Ib: Quantifying Exposure Error and its Effect on Epidemiological Studies

During this past year, we have continued our research examining the impact of exposure-related factors on risk estimates from time-series studies of PM10 and hospital admissions. In a paper published last year, we used data from 14 cities located across the US to examine the relationship between air conditioning prevalence and the coefficient for the relationship between ambient PM10 concentrations and cause-specific hospital admissions (Janssen et al, 2002). In addition, we examined whether observed variability in the risk coefficients was specifically related to PM10 emissions from mobile, combustion, and other sources. Results from this study indicate that air conditioning use explains a substantial amount of the variability in the risk coefficients from the different cities. Furthermore, PM10 emissions from mobile and diesel sources were also found to be important determinants of the variability in the risk coefficients, particularly for CVD-related hospital admissions. To validate these findings, we are currently using the same data to examine whether ventilation and source emission profiles explain season-specific risks of PM10 on hospital admissions in each of these 14 cities. This analysis is nearly complete, with a paper expected to be completed for submission this year.

Project Ic: Differentiating Health Effects of Particles from Outdoor and Indoor Sources

We have completed data collection for two field studies conducted in Atlanta and Steubenville, both of which have been co-sponsored by the Center. For the Atlanta study, multi-pollutant exposures and cardiovascular health status were measured repeatedly for two cohorts: individuals with COPD and recent MIs. For the Steubenville study, multi-pollutant exposures and cardiovascular health status were measured for elderly individuals living in government-subsidized housing complexes. The same health protocol was used for each of these studies, with data on heart rate, HRV, blood pressure, oxygen saturation, and daily symptoms obtained for each participant on at least seven days. Twenty-four-hour indoor, outdoor, and personal measurements of particles, ozone, carbon monoxide, nitrogen dioxide were also made on each of the monitoring days. Data analysis from the Atlanta study is nearly complete, with a paper expected to be submitted to a peer-reviewed journal by the end of this year. Laboratory analysis of the ECG data from Steubenville data is currently on-going, with data analysis expected to start early next year.

Our analysis of the toxic effects of indoor and outdoor particles using in vitro bioassays was recently published in Environmental Health Perspectives (Long et al, 2001). In this paper, bioassays were performed using rat alveolar macrophages for 14 paired indoor and outdoor PM2.5 samples collected from nine Boston-area homes. Particle induced pro-inflammatory responses were assessed using tumor necrosis factor (TNF) production in the macrophages. Results from this study indicated that TNF production was significantly higher for indoor as compared to outdoor particles, both before and after normalization for endotoxin concentrations.

THEME II: IDENTIFYING POPULATIONS SUSCEPTIBLE TO THE HEALTH EFFECTS OF PARTICULATE AIR POLLUTION

Project IIa: Examining Conditions which Predispose Towards an Acute Adverse Effects of Particulate Exposures

We have tested the hypothesis that patients with pre-existing respiratory, cardiovascular, or diabetic conditions have an enhanced mortality response to particle exposures. To date, we reported that socio-economic factors are not modifiers of PM associated mortality risk, although there was some increased risk in females (Zanobetti and Schwartz 2000). The same pattern held true for hospital admissions for heart and lung disease (Zanobetti, Schwartz, and Dockery 2000). In contrast, we found (Zanobetti, Schwartz and Gold, 2000) that respiratory illness modified the risk of cardiovascular hospital admissions associated with PM, and that heart failure modified the risk of PM associated COPD admissions.

Last year we examined the association of diabetes as an effect modifier for cardiovascular admissions. We published two studies suggesting that diabetes is an effect modifier (Zanobetti A, Schwartz J 2001 and 2002). Furthermore, we have conducted mortality follow ups of subjects whose potentially predisposing conditions were identified use hospital admissions data. These analyses will use the case-crossover approach. We have recently completed a methodological paper examining the potential for bias and confounding in that approach, and developed new statistical methods, Bateson and Schwartz, currently in review, to overcome this problems. This analysis will be conducted this year.

Mixed models represent an important tool for determining whether persons with certain characteristics are more susceptible to the effects of airborne particles. However, classic mixed regression programs are linear models, whereas we know that season and weather effects on health are often nonlinear. These have often been addressed using nonparametric smoothing. To enhance our ability to assess sensitivity while maintaining good covariate control, we have developed an additive mixed model, which combines the attributes of both approaches Coull et al., 2000).

Furthermore, we have addresses two susceptibility issues: we have clarified that control for influenza and other respiratory epidemics does not change the effect size estimates for PM effects on daily deaths (Braga et al, 2000) and have studied the effects of particulate air pollution on the fetus (Ha et al., 2001).

Finally, we held a workshop (mostly by teleconference) on the role of social condition as a modifier of the effects of air pollution, with an international attendance: Drs. O'Neill, M.S., Jerrett, M., Cohen, A.J., Schwartz, J., Kawachi, I., Levy, J.I., Fletcher, T., Cifuentes, L., Gouveia, N.

Project IIb: Assessing Life-Shortening Associated with Exposure to Particulate Matter

During the first two year we focused on harvesting. Currently, this project deals with the development of statistical methods for investigating confounding, dose-response relationships and other particle health effects issues.

Harvesting: We have examined whether particles advance mortality by a few days (harvesting) or have a more profound impact on public health and have published several papers. The first two used a smoothing approach to examine the association of PM over time with daily deaths in Boston (Schwartz 2000) and Chicago (Schwartz 2001). Hospital admissions were also examined in the second paper. The main conclusions of our analyses were that particle effects on mortality and morbidity become stronger as average time increases.

We also have developed a new methodology (smoothed distributed lag models) to investigate the relationship between pollution and daily deaths in Milan, Italy (Zanobetti et al., 2000). This paper confirmed that far from reduced effects, "harvesting resistant" estimates are higher by a factor of 2. More recently, we extended the distributed lag approach to examine the harvesting effect in 10 cities in Europe. The findings of this study do not provide evidence for harvesting effect (Zanobetti et al., 2002).

Dose-response: To date particle health effects studies suggest a no threshold dose-response relationship. If there are thresholds for the effects of particles on deaths or hospital admissions then health effects may be overstated. We have developed a new methodology that allows combining smoothed dose-response curves from multiple locations and demonstrated its effectiveness using simulation studies. Subsequently, we applied this method to analyze daily deaths in 10 US cities. No deviation from linearity down to the lowest exposure concentrations was observed (Schwartz and Zanobetti, 2000).

We extended this methodology to incorporate heterogeneity in response across cities by developing a smoothed estimate that allows heterogeneity to vary by exposure level. This new methodology was then applied to 8 cities in Spain (Schwartz et al., 2001). We also used this methodology to two-pollutant models and examined the sensitivity of the dose-response curve shape to the way season and weather was controlled. We found a significant linear association between daily deaths and black smoke. This association was little changed by variations in control for weather, season, or SO2. For SO2, the association was implausible (inverted U shape) and disappeared after controlling for black smoke (Schwartz et al., in press). Finally, we have used hierarchical models to identify predictors of heterogeneity in nonlinear dose-response curves. This method was applied to examine the dose-response relationship between PM10 and hospital admissions for heart and lung disease.

Co-pollutant effects: We have investigated the confounding effect of gaseous co-pollutants for both morbidity and mortality. We have developed a hierarchical model to assess confounding, and applied it to examine the association between PM10 and daily deaths (Schwartz, 2000). The results of this analysis suggested that associations were not confounded by gaseous air pollutants.

Timing of the effect: We have found that the PM10 effects on myocardial infarction deaths occur on the same day, while for other cardiovascular deaths the lag is about a day. For respiratory deaths one and two day-lag were observed. These patterns can be explained physiologically and can help to elucidate biological mechanisms (Braga et al., 2001)

Statistical methods: We have demonstrated that it is possible to control for season and analyze mortality and morbidity using the Case Crossover approach (Bateson et al., 1999). During the last year, we showed that there could be a selection bias which can be estimated and corrected (Bateson et al. 2001). Using this approach, we have re-investigated the association between PM10 and daily deaths in 10 US cities (Bateson and Schwartz, in review).

Over the last six months the validity of Generalized Additive Models has being under examination. Our Center has spent a great deal of time to address this issue. Towards this end, we have re-analyzed our 10 city mortality study, the Six City time series study, the Six City Source Apportionment Study, our Hospital Admissions studies, and the long term distributed lag models from the APHEA study. In addition, to re-analyzing these data using different convergence criteria and natural splines, we have developed alternative approaches.

We have shown that mixed models could be used to provide smoothed dose response curves against multiple predictors (Coull et al. 2001). This approach does not have the shortcomings of the GAM in S-plus, since it provides accurate standard errors and does not use back-fitting. We have recently demonstrated that our approach can be used for Poisson data and have applied it to re-examining the association between PM10 and hospital admissions (a manuscript is under preparation).

Project IIc: Investigating Chronic Effects of Exposure to Particulate Matter

We have followed up the Six Cities Study cohort in an effort to assess the cumulative effect of long-term exposures on the incidence of lung cancer, nonmalignant respiratory disease, cardiovascular disease, and cause-specific mortality. More specifically, vital status was determined for the 8111 participants in the Harvard Six Cities adult cohort for an additional nine years of follow-up (1990-1998). We identified 1430 additional deaths brining the total to 2737 deaths. Survival analyses of all-cause mortality shows that life expectancy continues to be reduced in the more polluted cities, with the survival relative ranking be the same to that observed in the original study.

During the follow up-period, 1990-1998, air pollution levels decreased in two of the cities, while remained about the same in the other four. Similarly, the death relative risk decreased in the same two cities as compared to the other four. This suggests that changes in air pollution levels resulted in a fairly immediate drop in mortality (or an increase in life expectancy). A paper is under preparation by Laden et al., and an abstract was presented at the 2002 ISEE meeting.

Project IId: Determining the effects of Particle Characteristics on Respiratory Health of Children

The main objective of this project is to examine the effects of particle composition on the respiratory health of children using particle samples collected as part of the Harvard Twenty-Four Cities study. Due to time constrains and research staff availability this project was initiated just recently. To date, we have analyzed the stored samples for elemental carbon using the reflectance method. Sulfate concentrations were determined by ion chromatography as part of the original Twenty-Four Cities study. Due to the large cost of the XRF elemental analysis, we have decided not to pursuit these measurements as we had originally proposed. The forthcoming statistical analysis will investigate the air pollution-caused respiratory effects in relation to traffic sources (elemental carbon concentrations) and regional sources (sulfate concentrations).

The Principal investigators of this project, Dr. Douglas Dockery, and the Southern California Children's project, Dr. John Peters, are planning to analyze together the data from the Harvard and UCLA children studies. This will make it possible to contrast the effects of the traffic-related particles (Southern California) and power plant-related particles (Northeast).

THEME III: BIOLOGICAL MECHANISMS AND DOSIMETRY

Project IIIa: Differentiating the Roles of Particle Size, Particle Composition and Gaseous Co-Pollutants on Cardiac Ischemia.

The main aim of this study is to investigate the effects of concomitant gaseous co-pollutants, particle size, and particle composition using a dog cardiac ischemia model and our particle concentrator technologies. In a study recently accepted for publication (Wellenius et al 2002a), six mongrel dogs underwent thoracotomy for implantation of a vascular occluder around the left anterior descending coronary artery and tracheostomy to facilitate particulate exposure. After recovery (5-13 weeks), pairs of subjects were exposed for 6 hr/day on 3 or 4 consecutive days. Within each pair, one subject was randomly assigned to breathe concentrated ambient particles (CAPs) on the second exposure day and filtered air otherwise. The second subject breathed CAPs on the third exposure day and filtered air otherwise. Aeorsolized CAPs were produced using the Harvard Ambient Particle Concentrator (HAPC). Immediately following each exposure, subjects underwent 5-min coronary artery occlusion. Peak ST-segment elevation, heart rate, and arrhythmia incidence during occlusion were determined from continuous ECG recordings. Exposure to CAPs (median: 285.7 μg/m3; range: 161.3 - 957.3 μg/m3) significantly ($p<0.01$) enhanced occlusion-induced peak ST-segment elevation in lead V4 (9.4 1.7 vs. 6.2 0.9 mm, CAPs vs. filtered air, respectively) and lead V5 (9.2 1.3 vs. 7.5 0.9 mm). We also observed enhancement of the ST-segment elevation on the day after CAPs exposure, indicating that, although transient, the effects of CAPs exposure persisted for at least 24 hours. ST-segment elevation was significantly correlated with the silicon (Si) concentration of the particles and other crustal elements possibly associated with urban street dust ($p<0.003$ for Si). No associations were found with CAPs mass or number concentrations. Heart rate was not affected by CAPs exposure. These results suggest that exacerbation of myocardial ischemia during coronary artery occlusion may be an important mechanism of environmentally-related acute cardiac events.

In the same group of dogs, we explored the hypothesis that inflammatory responses of the lung result in hematologic changes that influence the systemic coagulation status and cardiac microvasculature (Savage et al 2002a). In these studies, venipuncture was performed immediately post-occlusion for complete blood count and C-reactive protein assay. Acute decreases in platelet counts were observed on the day of exposure. Significant decreases in red cell count, hematocrit, and hemoglobin were associated with CAPs exposure, and continued for 24 hours post exposure. Increases in CRP were significantly associated with CAPs exposure, and this also continued for 24 hours post exposure. There were no aberrations in white blood cell parameters with CAPs exposures (mean 342.5 + 194.0 g/m3). Decreases in red cell count, hematocrit, and hemoglobin were associated with CAPs exposure, and continued for 24 hours post exposure. Increases in CRP were significantly associated with CAPs exposure, and this also continued for 24 hours post exposure. Univariate regression analysis substantiated these findings, and specifically revealed associations with tracer elements and particle mass and numbers. Platelets decreased with sulfur. Hemoglobin decreased with all tested parameters including particle mass, particle number, nickel, sulfur, black carbon, and silicon. Hematocrit followed a similar pattern, and decreased with particle mass, particle number, sulfur and silicon.

Red blood cell counts decreased with particle mass, particle number, sulfur, black carbon, and silicon. C-reactive protein was increased with particle number and nickel. Implications for these decreases in red blood cell parameters other than a localized or microvascular sequestration of red blood cells are not obvious, but have been observed in other studies.

The following table lists a large number of studies using laboratory rodent models that have been carried out by investigators in this Theme. These CAPs exposure studies were completed with funds from various sources including our EPA center. The center has provided funding for continued study of mechanistic questions in relationship to these experiments. The following paragraphs summarize the results of important mechanistic studies with implications for cardiac responses focusing upon components of ambient particles supported in part by our EPA center.

Study	Outcomes	Number of Exposures	Animal Population	Funding Agencies	Publications
Rats CAPs vs. Sham (1997-1998)	BAL Pulmonary Morphology RNA	7	128 Normal 130 CB	EPA, NIEHS	Clarke et al, 1999 Saldiva et al, 2002 Batalha et al, 2002 Godleski et al, 2002
Rats CAPs vs. Sham (1998-1999)	BAL Pulmonary Morphology RNA	3	35 Normal 36 Aged	NIEHS	Clarke et al, 2000
Rats CAPs vs. Sham (1998)	BAL Pulmonary Morphology RNA EKG	1	15 Normal 16 MI	NIEHS	
Rats CAPs vs. CO CAPs vs. Sham (1998-Present)	EKG Morphology	~20	151 CVD	EPA Center	

The objectives of the study by Saldiva et al (2002) were to: 1) determine whether short term exposures to CAPs cause pulmonary inflammation in normal rats and rats with chronic bronchitis; 2) identify the site within the lung parenchyma where CAPs-induced inflammation occurs; and 3) characterize the component(s) of CAPs that are significantly associated with the development of the inflammatory reaction. Four groups of animals were studied: (1) air-treated, filtered air-exposed (air-sham); (2) SO2-treated (chronic bronchitis (CB)), filtered air exposed (CB-sham); (3) air-treated, CAPs-exposed (air-CAPs); and (4) SO2-treated, CAPs exposed (CB-CAPs). Sprague-Dawley male rats were exposed to CAPs, using the HAPC, or to particle-free air (sham) under identical conditions during 3 consecutive days (5h/day) in 6 experimental sets. CB was induced by exposure to 276 + 9 ppm of SO2 (5h/day, 5 days/wk, 6 weeks). Physicochemical characterization of CAPs included measurements of particle mass, size distribution, and composition. Rats were sacrificed at 24 hours after the last CAPs exposure. Pulmonary inflammation was assessed by bronchoalveolar lavage (BAL) and by measuring the numerical density of neutrophils (Nn) in the alveolar walls in the centri-acinar and in the peripheral segments of the pulmonary acinus. CAPs induced a significant increase in BAL neutrophils and in Nn in the lung tissue. Greater Nn was observed in the central compared to peripheral regions of the lung. A significant, dose-dependent association was found between V and Br concentrations and both BAL neutrophils and Nn. BAL neutrophils and protein were also correlated with Pb, SO42-, Si, organic carbon, and elemental carbon concentrations. Results demonstrate that short-term exposures to CAPs from Boston induce a significant inflammatory reaction in rat lungs, with this reaction dependent on particle composition.

In another study, using the same animals as in the study just described, Batalha et al (2002) determined that short term exposures to CAPs altered the morphology of small pulmonary arteries in normal rats and rats with chronic bronchitis (CB). Histologic slides were prepared from random sections of lung lobes and coded for blinded analysis. The lumen/wall area ratio (L/W) was determined morphometrically on transverse sections of small pulmonary arteries. When all animal data (normal and CB) were analyzed together, the L/W ratios decreased as concentrations of fine particle mass, silicon, lead, sulfate, elemental carbon and organic carbon increased. In separate univariate analyses of animal data, the association for sulfate was significant only in normal rats, whereas silicon was significantly associated in both CB and normal rats. In multivariate analyses including all particle factors, the association with silicon remained significant. Our results indicate that short-term CAPs exposures (median 182.7, range 73.5-733.0 µg/m3) can induce vasoconstriction of small pulmonary arteries in normal and CB rats. This effect was correlated with specific particle components, and suggests that the pulmonary vasculature might be an important target for ambient air particle toxicity.

With the repeated finding in both dogs and rats of increased pathologic responses to inhalation of concentrated urban air particles and the identification of silicon (as silicate) as an element associated with some of these responses, we carried out studies to determine whether there is a change in toxicity as silicon containing particles pass through the HAPC (Savage et al 2002b). Using silicate rich Mt. St. Helen's volcanic ash, (MSHA) we exposed 3 groups of Sprague-Dawley rats by inhalation for 6 hours to filtered air, MSHA, or MSHA passed though the HAPC. Twenty four hours following exposure, BAL was performed to assess total cell count, differential cell count, and protein, lactate dehydrogenase, and n-beta glucosaminidase levels. Peripheral blood was examined for packed cell volume, total protein, total white cells, and differential cell count. No significant differences were observed among any of the groups in any parameter measured. Scanning electron microscopy and x-ray analysis was performed to identify particles in the lungs, revealing silicates typical of MSHA throughout the lung. Our findings suggest that particles passing through the HAPC have no change in their toxic potential in an exposure setting where substantial particle deposition has occurred. This study validates the use of the HAPC as a method of creating concentrated aerosol of fine urban air particles without altering their physical properties or potential for toxic insult.

We are continuing to study populations listed in the table above to assess mechanisms of vascular injury. Both the collected RNA and the tissue preserve for immunocytochemical analyses are particularly valuable in this regard. In the coming year, we will continue to exploit this valuable resource.

In the context of this Project, we have started to support and include the innovative work of Dr. Beatriz Gonzales-Flecha's laboratory. Their studies focus on oxidant mechanisms to explain cardiac responses. Dr. Gonzales-Flecha and her collegues have reported rapid increases in the steady-state concentration of reactive oxygen species in the lungs and heart associated with ambient particle exposures Gurgueira et al (2002). More recently, they confirmed the role of oxidants in the inflammatory response to CAPs adult rats. The experimental protocol included exposures to filtered air (Sham) or CAPs aerosols (CAPs, 5 hours exposure, average mass concentration: 1100 ± 300 µg/m3) in the presence or absence of 50 mg/Kg i.p. NAC. BAL, tissue and blood samples were collected 24 hours after exposure. The results of this study suggested a dramatic increase of PMN number in BAL as a result to CAPs exposures. This increase was mediated by oxidants, since pre-administration of NAC effectively prevented PMN influx into the lung. Additional recent data support our hypotheses that CAPs promotes oxidant-mediated inflammation in the lung and that sympathetic activation after CAPs deposition in the lung is critical for CAPs cardiotoxicity. Studies will continue in this important area in the coming year.

Furthermore, we have developed a rat model of acute myocardial infarction (Wellenius et al 2002b) in order to study the effects of particles on ischemia-induced arrhythmias. In these studies, a myocardial infarction (MI) is surgically induced in rats. On the following day, the rats are exposed to CAPs or clean air. Specifically a left-ventricular MI was induced in 31 Sprague-Dawley rats via thermocoagulation of a coronary artery; 32 additional rats served as sham-operated controls. Within 12-18 hours after surgery, diazepam-sedated animals were exposed to room air for 1 hr (baseline period), either residual oil fly ash (ROFA), carbon black, or room air for 1 hr (exposure period), and room air for an additional hour (recovery period). Lead II ECG's were recorded. In the MI group, 41% of rats exhibited one or more premature ventricular complexes (PVC's) during the baseline period. Exposure to ROFA, but not carbon black or room air, increased arrhythmia frequency in a significant number (80%) of animals with pre-existing PVC's. Moreover, in MI rats, heart rate variability (HRV) decreased following ROFA exposure, but increased following carbon black or room air exposure. There was no discernable difference in HRV or arrhythmia frequency among sham-operated animals. These results suggest a link between acute MI and potentiation of the adverse health effects of inhaled PM. We conclude that the rat model of MI is applicable to the study of particulate-related cardiac morbidity and mortality in compromised individuals.

This appears to be a sensitive model of cardiac effects of particle exposure and we are now using this approach to study the influence of gaseous co-pollutants and CAPs. Preliminary results using carbon monoxide indicates that exposure to this gas at 35 ppm for one hour decreases arrhythmias both alone and with CAPs exposure. This rat model also appears to be useful for interventional pharmacologic experiments to determine the pathophysiologic mechanism(s) triggering the observed arrhythmias.

Project IIIb: Assessing Deposition of Ambient Particles in the Lung

We have conducted in situ continuous measurements of ambient particle deposition. The total deposition fraction of fine and ultra-fine aerosols was measured in a group of six healthy adults exposed to Boston ambient particles. During these exposures particle mass and number concentration ranged from 7 and 32 μg/m3 and from 16,100 and 64,100 #/cm3, respectively. Fifteen repeated inhalation-exhalation cycles were conducted during a given exposure session. The deposition efficiency of particles ranging from 40 to 2045 nm was determined using the average concentration of inhaled and exhaled particles measured during these cycles. Deposition efficiencies ranged from 7.3 ± 18.7% (for particles 168 - 195 nm) to 98.6 ± 28.1% (for particles 1545 - 2045 nm). Subjects exhibited similar deposition patterns with a minimum efficiency in the size range of 100 - 200 nm. Results from ANOVA and mixed model regression analyses, suggested that deposition efficiency varied with individual and particle size. Deposition efficiencies varied mostly among subjects for particles in the size range between 100 and 1000 nm. Measured deposition efficiencies were compared to those reported by the International Commission on Radiological Protection (ICRP) model. For this comparison, the ICRP deposition efficiencies for a sitting female subject were used. The minimum deposition estimated by the model was at 400 - 500 nm, while our results show a minimum at about 100 nm. The ICRP model deposition efficiencies were lower for particles <150 nm, about 20%, and higher for particles> 676 nm by about 20%. Inter-subject variability in airway morphology, differences in breathing patterns used in the model and, particle composition may account for the observed differences.

Project IIIc: Relating Changes in Blood Viscosity, Other Clotting Parameters, Heart Rate and Heart Rate Variability to Particulate and Criteria Gas Exposures

The main objective of this Project is to investigate associations of selected inflammatory and blood clotting parameters in free living humans with particle and criteria gas exposures. This project is in collaboration with the Boston Veterans Hospital who is currently conducting the Normative Aging Study (NAS). During the first three years the VA Hospital has been collecting data. Measurements of approximately 650 individuals out of 1200 participants have been completed. Statistical analysis, relationships to ambient pollution levels, and geographical relationships has just commenced.

A new panel study commenced this past summer in St. Louis. Thirty four elderly individuals from three retirement homes were recruited. A mini bus was equipped with a large number of continuous and integrated samplers which were used to determine gaseous and particulate air pollutants inside the bus. Twelve participants took approximately two-hour bus rides during which their cardiac function was continuously measured using holder monitors. The field study was completed last July and statistical analysis is under way. We are planning to investigate relationship between cardiac function and human exposures.

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