GENERAL PM EXPOSURE AND HEALTH EFFECTS

19) TITLE: Ultrafine Particle Concentrations in Schoolrooms and Homes

PROBLEM: Several studies have implicated ultrafine particles, i.e., those with diameters below about 100 nm, with adverse health effects. They have been specifically implicated in oxidative stress and as a risk factor for cardiovascular events. Yet, knowledge is limited regarding the concentration of ultrafine particles in indoor environments, especially schools and homes.

PREVIOUS WORK: The presence of ultrafine particles in indoor environments may originate from the transport of outdoor air, and from indoor generation processes. Cleaning products and air fresheners contain terpenes that may react with ozone to form ultrafine particles. Cooking is another source of ultrafine particles. Baseline data on the concentrations of ultrafine particles inside schoolrooms and homes is limited because conventional ultrafine particle counters utilize butanol, a malodorous substance. Recently a water-based condensation particle counter has been developed, and shown to efficiently count ambient and vehicular exhaust particles as small as 5 nm. This instrument allows, for the first time, the convenient monitoring of indoor ultrafine particles in occupied environments over an extended period.

OBJECTIVE: The objective is to characterize ultrafine particle concentrations in schoolrooms and homes under conditions of varying proximity to roadways, and for differences in types of activities, such as cleaning and cooking, that may serve as indoor generators of ultrafines.

DESCPRITION: Indoor and outdoor concentrations of ultrafine particles will be measured, together with indoor and outdoor ozone, carbon dioxide (CO_2) and T/RH in approximately eight schoolrooms. These will be selected to provide data near, and distant from heavily traveled roadways, and with, and without the influence of the use of cleaning substances or air fresheners that could provide a source of secondary ultrafines. A single instrument suite, with a manifold that switches between indoors and outdoors, will be utilized to establish indoor/outdoorconcentration relationships. The decay of carbon dioxide once school children leave the room will be used to infer the effective air-exchange rate. Monitors on doors and windows will indicate when these are opened and closed. Data will be collected over a period of one week at each location, and will be logged with a time resolution of approximately 10 seconds.
The first year will focus on data collection schools. In the second year, measurements will be extended to a comparable number of homes. A pilot study will be conducted in one school and home location prior to school and home testing to: verify acceptable accuracy and precision of the instrument in measuring ultrafines in these settings; assure minimal line losses from the toggle approach; and determine the adequacy of the proposed CO_2 decay method for providing a usable air exchange rate measurement.

BENEFITS: This project will provide a survey of ultrafine particle concentrations in schools and homes as a function of traffic proximity, indoor activity and air exchange rate. This is important baseline information that will establish a foundation of future work that could more closely examine the mechanisms of transport and indoor ultrafine formation. The work will also provide a direct empirical basis for improving estimates of inhalation exposure to ultrafine particles.

20) TITLE: Effects of Inhaled Fine and Ultrafine Particles on Lung Growth and Lung Disease

PROBLEM: One of the most provocative and potentially important of the outcomes of the Children's Health Study (CHS), conducted by the University of Southern California, for the ARB, was the finding of reduced lung function growth associated with exposures to NO2, acid vapor, fine ambient particles and elemental carbon (Gauderman et al., 2004 *N Engl J Med*. 351:1057-1067). Pulmonary deficits, measured as the percent of children with clinically significant depression (i.e. <80 percent of age adjusted expected level) of forced expiratory volume at one second (FEV1.0), increased with increasing community pollutant concentration levels. The children were followed to 18 years of age, by which age, most lung growth is complete. One can therefore speculate that any deficits might not be repaired after that time. Because the pollutants in ambient air that were associated with the development of lung function deficits were intercorrelated, it is not possible to definitively attribute the health effects to one or more causal agents. It is also not known whether these deficits will manifest in chronic health effects in adult life.

PREVIOUS WORK: The effects of exposures to concentrated fine and ultrafine aerosols in several communities using mice that were sensitized to chicken egg albumin, OVA (Kleinman et al., 2005 JAWMA in Press) and acute changes in cardiac physiology in geriatric rats have been examined. To perform these studies, a portable particle concentrator (VACES) was installed in a customized van and coupled to an exposure system to allow us to study health effects and physical and chemical properties of particles in close proximity to source and receptor sites. Mice exposed to concentrated ambient particles exhibited elevations of cytokines and OVA-specific immunoglobulin, which are biomarkers of airway allergies. Mice exposed to purified air did not have significant elevations of these biomarkers. In vitro assays determined that concentrated ambient ultrafine particles induce the production of free radicals in a dose-responsive manner and that these particles were taken up by macrophage cells, accumulated in the cells mitochondria, elicited antioxidant defense mechanisms at moderate doses but caused mitochondrial disruption and cell death at high concentrations.

OBJECTIVE: The objective of this proposed study is to test the hypothesis that chronic PM exposures will cause pulmonary function deficits in rodents exposed from birth to adulthood. The hypothesis that these deficits will persist after exposures are terminated will be examined. Analyses of lungs to determine whether pulmonary function deficits are associated with pathological changes in lung structure and whether these changes are dependent on dose will also be performed.

DESCRIPTION: Repeated inhalation studies will be conducted using the VACES in two or more communities and using two concentrations of concentrated fine and ultrafine particles at each site. The low concentration will be proportional to the average concentration at the CHS community location that had the lowest level of pulmonary function deficit. The high concentration will be proportional to the concentration at the CHS site with the greatest degree of pulmonary function deficit. We will dilute the concentrated aerosol with purified air as necessary, to match the concentrations at the two sites. The concentrator will also effectively reduce the concentrations of gaseous co-pollutants (CO, NOX). Acute and chronic cardiopulmonary inflammation and injury will be examined using transgenic mice with specific

knockouts or knockins along the NFkB and NRf2 signaling pathways to test specific mechanistic hypotheses regarding the roles of inflammation and oxidative stress in the development of pulmonary and cardiovascular injury and address the question of whether the differences in adverse human responses were due to particle dose or to qualitative differences in particle composition. Endpoints will include markers of inflammation, histological examinations for evidence of pathology and pulmonary function measurements. The physical and chemical composition of the particles will be determined and collected particles will be tested in vitro for the potential of these particles to produce free radicals and induce cytotoxicity, and heart muscle cell hypertrophy. These experiments will be conducted over a period of three years. Although mice continue to grow throughout their lives, overall growth is very slow after seven weeks of age and there is a marked decrease in the rate of lung growth with age. Thus, the rodent model is a reasonable choice for such studies.

BENEFITS: This study would provide needed information on the effects from long-term exposures to PM on lung development and function. These data will be relevant to ARB's mission to protect children's health.

21) TITLE: Health Effects of Short-Term Particulate Exposures

PROBLEM: California and federal ambient air quality standards have been set for annual and 24-hour averaging periods for particulate matter (PM). However, ambient PM concentrations vary by large factors, often by an order of magnitude over hourly timeframes. These brief excursions may be especially harmful as suggested by cardiac and respiratory outcomes associated with ambient PM. Little relevant health evidence exists to establish health advisories or air standards for short-term fluctuations in PM.

PREVIOUS WORK: Considerable research on the effects of particulate matter has been performed by epidemiologists who employ 24-hour metrics of pollutant concentrations collected at routine air quality monitoring sites. These scientists report associations between PM and cardiovascular and respiratory health outcomes. Some studies have examined shorter-term effects. Los Amigos Research Institute employed two-hour exposures of concentrated ambient particles in human clinical studies and observed changes in the electrical activity of the heart and biochemical markers of inflammation. Researchers at the University of California, Irvine found lung function in asthmatic children varied with one and eight-hour ambient PM levels. Studies of cardiovascular events performed by Peters et. al., in Massachusetts found that hospital admissions followed PM exposures experienced in the hours just prior to the event. In studies conducted at the University of California, San Francisco with mildly asthmatic subjects exposed for ½-hour periods to smoke from rice straw combustion, minor lung function effects were identified.

OBJECTIVE: The objective is to determine the human health impacts of brief (one to eight hour) exposures to ambient PM in California.

DESCRIPTION: Several experimental approaches may be considered to address this issue including: panel, controlled human exposure, or statistical studies. Panel studies could be conducted with people who are likely to suffer from exposures. To increase efficiency and control costs, links to existing cohort/air monitoring projects will be considered. Personal air monitoring could refine personal PM exposures and micro-environmental exposures. Multiple

health outcomes could be studied including: cardiovascular or respiratory outcomes (e.g., heart rate variability, markers of inflammation, lung function, and asthma medication use). Alternate expressions of dose may be employed in statistical analysis. Controlled exposure studies could investigate the nature of dose and dose rate on health outcomes, for example, exposures of an equal dose could be provided over one, two or 8-hours followed by health outcome measures. Statistical studies of effects could include admissions to the hospital for asthma, respiratory illness, stroke, or heart attack with time-resolved data from ambient monitors. Access to health records that contain highly-resolved time information is critical.

BENEFITS: This study would provide critical information on the health effects from short-term exposures to PM. Since PM, as with all pollutants, varies on sub 24-hour time frames, knowledge of the time frame, concentrations, and corresponding health effects of this pollutant are critical to ARB's mission to protect public health.