Final Technical Report

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EPA Grant Number: R827351C004
Center Name: NYU-EPA PM Center: Health Risks of PM Components
Center Director: Morton Lippmann
Title: Health Effects of Ambient Air PM in Controlled Human Exposures
Investigators: T. Gordon, J. Reibman, L.C. Chen
Institution: New York University School of Medicine
EPA Project Officer: Stacey Katz/Gail Robarge
Project Period: June 1, 1999–May 31, 2005 (no-cost extension to May 31, 2006)
Period Covered by the Report: June 1, 1999–May 31, 2006
RFA: Airborne Particulate Matter (PM) Centers (1999)
Research Category: Particulate Matter

Objective(s) of the Research Project: The original hypothesis of this Project was that concentrated ambient particulate matter (PM) will produce acute adverse respiratory and cardiovascular health outcomes in volunteers under controlled exposure conditions. In Year 2, because the project was stopped (with agreement from the External Advisory Committee), we examined whether the stimulation of epithelial cells by ambient particles results in the release of cytokines which can upregulate antigen presentation by dendritic cells. In addition, in Year 5, Dr. Gordon coordinated a multi-Center collaboration which examined the *in vitro* and *in vivo* effects of size-segregated particles collected at geographically diverse sites throughout the U.S.

Summary of Findings:

Technical Aspects

Human Exposure Study. The exposure of human subjects to PM was terminated largely for 2 reasons. First, the centrifugal concentrator that was used in the initial animal studies by Drs. Gordon, Nadziejko, and Chen fell into disrepair. Repeated attempts to salvage the original concentrator were unsuccessful and the concentrator achieved concentration factors of 3 to 5 instead of the original 10-fold concentration factor. A virtual impactor concentrator designed by Sioutas was recently purchased by the New York University (NYU) PM Center and will be used in animal studies, but it has not been established whether this new concentrator would be satisfactory for a human exposure study at NYU. Second, reports from the laboratories at the U.S. Environmental Protection Agency (EPA), Southern California, and the University of Rochester have provided evidence that few, if any, significant effects are observed in normal, healthy subjects exposed to concentrated ambient PM at concentrations greater than those we originally proposed. Thus, our small project, with 10 healthy subjects exposed to concentrated ambient PM, was unlikely to be fruitful. Therefore, with the agreement of the External Advisory Committee, the Project was terminated and the Center resources were made available for research needs.

In Vitro Studies with Airway Epithelial Cells. Due to the fact that human exposure project was not moving forward during Year 2, Drs. Reibman, Chen, and Gordon concentrated their efforts in examining the *in vitro* response of human bronchial epithelial cells to size-fractionated ambient PM. Because of the significant association between ambient PM and exacerbation of allergic asthma, we examined the potential for airway epithelial cells (primary culture) to modulate the immune system. Size-fractionated ambient PM was collected with a MOUDI impactor for 2 week intervals throughout the year and used to treat human bronchial epithelial cells obtained from normal human volunteers. The fraction of particles less than 0.18 μm produced a dose-dependent increase in GM-CSF released from the epithelial cells. GM-CSF is a cytokine that can elicit inflammation in the airways via an effect on eosinophils and can also modulate immune responses via effects on dendritic cells. There was no change in secreted GM-CSF in cells treated with larger size ambient particles or equivalent doses of carbon or Mount St. Helen dust particles, thus suggesting that the human epithelial cell response was not due to a general particle effect. Moreover, treatment of epithelial cells with endotoxin had no effect on GM-CSF. Further experiments with inhibitors demonstrated that MAPK pathways are involved in the ambient particle effects on GM-CSF secretion by epithelial cells. This research has resulted in publication of 2 manuscripts and was used as preliminary data in a successful National Institute of Environmental Health Sciences (NIEHS) grant application by Dr. Reibman in Year 2. These studies have progressed under Dr. Reibman's R0-1 grant.

Multi-Site Ambient PM Study (MAPS). The overall objective of the MAPS study was to collect particles from several different geographical regions, characterize their physical and chemical properties, and make them available to investigators for *in vitro* and animal toxicology studies. The results of these studies would be used to relate health effects with PM components and ultimately sources. Recent studies suggest that PM derived from different sources may differ in toxicity and that specific PM components may serve as markers for different sources, suggesting an alternative, more efficient way of regulating PM. To directly study this issue, airborne particles in the ultrafine, fine, and coarse thoracic size ranges were collected in eight different locations in the U.S. and Europe. The sites were selected to take advantage of regional differences in PM sources and components. Weekly samples were collected for a period of a month in each location, using a 3 stage particle impactor, developed at Harvard's EPA Center, which is capable of collecting 15 to 100 mg of material at 3 size fractions during a weekly sampling interval. The particles have been assayed for a number of chemical components in collaboration with Dr. Devlin (U.S. EPA- National Health and Environmental Effects Research Laboratory (NHEERL) and made available to investigators in several different laboratories. Several studies have been completed and results presented so far demonstrate clear particle size and source dependent differences in toxicity. At least four manuscripts (U.S. EPA, University of Rochester, and NYU) are in preparation for submission.

Supplemental Keywords: NA

Relevant Web Sites: http://www.med.nyu.edu/environmental/
http://es.epa.gov/ncer/science/pm/centers.html