

## **Final Technical Report**

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**EPA Grant Number:** R827351C006

**Center Name:** NYU-EPA PM Center: Health Risks of PM Components

**Center Director:** Morton Lippmann

**Title:** Effects of Particle-Associated Irritants on the Cardiovascular System

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**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 effect of particulate matter (PM) on the cardiovascular system is an increasingly important public health issue. However, the physical and/or chemical properties of PM responsible for these serious health effects are currently unknown. The questions are: 1) What are the biologically active components of PM? 2) What are the mechanisms by which PM affects the cardiovascular system? and 3) What are the sensitive subpopulations? These three questions are inextricably intertwined. Any hypothesis about a mechanism of cardiovascular effects rests on some assumptions that a certain type of constituent of PM is the culprit.

This research focused on particle-associated irritants based in part on the time course of effects reported in recent epidemiological studies. There is consistent evidence from times-series studies that the lag time between elevated levels of PM<sub>2.5</sub> and increases in cardiovascular-related hospital admissions and death is very short, i.e. one day or less. There is one well-studied physiological mechanism that is consistent with rapid effects of PM on both cardiovascular and pulmonary function, namely stimulation of irritant receptors in the respiratory tract. Irritant receptor activation involves a bimolecular reaction between a protein receptor in the lung and an agonist, which triggers a rapid increase in intracellular calcium (Ca<sup>++</sup>) leading to activation of nerve fibers that send impulses to the central nervous system. Signals from the central nervous system then cause slowing of respiration and changes in blood pressure and heart rate via neural reflex pathways. The stereotypical response to an inhaled irritant is an immediate change in respiratory rate and heart rate, which returns to normal soon after exposure stops.

The objectives of this project were: 1) to examine the time course of effects of concentrated ambient PM (CAPs) on cardiovascular function in sensitive animals to establish the biological plausibility of short lag times between PM exposure and cardiovascular effects; and 2) to expose rats (both normal rats and rat models of cardiac disease) to sulfuric acid aerosols, a known irritant found in PM, to determine whether irritant aerosols cause cardiovascular changes consistent with the adverse health effects of PM. Exposure to carbon black particles was used as a non-irritant control.

## Summary of Findings:

### Technical Aspects

We examined the effects of various PM air pollutants on rats with surgically implanted electrocardiogram (ECG) and blood pressure (BP) transmitters to determine whether inhaled PM causes immediate physiological effects. Spontaneously hypertensive rats (SHR) with BP transmitters (which measure BP, heart rate and respiratory rate) were exposed to CAPs for 4 hrs. The SHR were also exposed to fine and ultrafine sulfuric acid aerosols because acid is one of the components of PM that could potentially activate irritant receptors and cause effects during exposure. Young and old (> 20 months) Sprague Dawley (SD) rats with ECG transmitters (which measure heart rate and core temperature) were exposed to fine and ultrafine acid aerosols and to resuspended carbon black. Inhalation of CAPs by the SHR caused a striking decrease in respiratory rate that was apparent soon after the start of exposure, and that stopped when exposure to CAPs ceased. The decrease in respiratory rate was accompanied by a decrease in heart rate. Exposure of the same SHR to fine particle size sulfuric acid aerosol also caused a significant decrease in respiratory rate similar to the effects of CAPs. Ultrafine acid had the opposite effect on respiratory rate in SHR as CAPs. In both old and young SD rats, inhalation of fine acid aerosol caused an immediate increase in temperature (compared to air-exposed rats) that ceased when exposure stopped. Ultrafine acid caused an immediate decrease in heart rate and temperature during exposure in young SD rats and no significant effect on old SD rats. Carbon black inhalation had no significant effect on heart rate or temperature during exposure in either old or young rats. This study showed that inhalation of ambient PM and acid aerosols have immediate effects on cardiopulmonary function during exposure. The pattern of the response to inhaled PM is consistent with activation of irritant receptors in the respiratory tract.

Overall, we did more than 50 experiments exposing rats to CAPs, irritant aerosols, particulate matter surrogates and even some irritant gases. Every experiment involved monitoring of cardiovascular functional data in an air-exposed and pollutant-exposed group before exposure, during exposure and for 48-72 hrs exposure. We did extensive exploratory data analysis while experiments were being performed and solved a number of issues related to quantifying telemetric data. However, it was apparent that there was no suitable statistical method for determining whether there was a significant difference between the treated and control groups because the onset and duration of the effects were unknown. Drs. Nadziejko and Chen, in collaboration with Dr. Jing-Shiang Hwang, a visiting scientist (and statistician) in the New York University (NYU) PM Center, and Dr. Arthur Nadas, a mathematical statistician in the Department of Environmental Medicine, developed a simple but powerful method of analyzing repeated measures data when the time course of the effect is not known *a priori*. This method, which is called the Fishing License method, has been published and used to analyze all of the telemetry data performed in the PM Center.

**Supplemental Keywords:** NA

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