STATEMENT

Synopsis of Research Report 120

HEALTH EFFECTS INSTITUTE

Effects of Exposure to Concentrated Ambient Particles from Detroit Air on Healthy Rats and Rats with Features of Asthma or Mild Bronchitis

INTRODUCTION

Epidemiologic studies in diverse locations have reported that short-term increases in low levels of particulate matter (PM) are associated with short-term increases in morbidity and mortality. These associations are particularly evident in some groups of people, including those with compromised airway function. For people with asthma, a chronic disease of the lower airways, short-term exposure to PM appears to exacerbate symptoms and decrease lung function. Based on this and other evidence, the US Environmental Protection Agency in 1997 promulgated National Ambient Air Quality Standards for particles 2.5 µm or smaller in aerodynamic diameter ($PM_{2.5}$ or "fine" particles).

Despite the existing evidence, a number of questions remained about these effects. The Health Effects Institute issued Request for Applications 98-1, "Characterization of Exposure to and Health Effects of Particulate Matter," to address critical questions about the effects of particles. A key component of that RFA was to evaluate the health effects of ambient particles in humans and in animals that mimic relevant human conditions. One area of interest involved controlled exposures to concentrated ambient particles (CAPs) because such exposures might better reflect actual exposures to the particle mixture and because a technology to concentrate fine particles and expose humans and other species to them had recently become available.

APPROACH

HEI funded Dr Jack Harkema and colleagues to conduct a 2-year study with rats to evaluate the short-term effects of inhaling CAPs derived from the air in an area of Detroit, Michigan that has a high incidence of childhood asthma. They would assess CAPs effects on two key features of asthma: airway inflammation and hypersecretion of mucus. The investigators evaluated CAPs-associated airway effects in healthy BN and F344 rats; in BN rats that had been sensitized with the allergen ovalbumin to induce some features of asthma; and in F344 rats pretreated with endotoxin to have some features of mild bronchitis, which is also characterized by hypersecretion of mucus. Animals were exposed to CAPs for 10 hours/day for 1 day or for 4 or 5 consecutive days in July or September, times of the year when the researchers thought mass concentrations of PM would be high. To conduct the study, HEI provided the investigators with the instrument to concentrate fine particles from ambient air. The investigators used non-HEI funds to build a mobile air research laboratory, a trailer that could be moved to the study site and contained equipment for monitoring ambient air, inhalation exposure chambers, and animal laboratory facilities.

Harkema and colleagues also explored whether the metal elements in the particles had toxic effects. First, the investigators determined whether metals were retained in the lungs of animals after inhaling CAPs. Second, they collected particles on filters during the exposure period and resuspended them in an aqueous solution. Using intratracheal instillation with a different set of healthy and ovalbumin-sensitized rats, the investigators compared the ability of different fractions of resuspended particles to induce airway inflammation: the soluble fraction, considered to be the fraction rich in metals; the insoluble fraction; and the total particles.

RESULTS

As expected, during the exposures ambient PM characteristics varied over the course of a day, from day to day, and in different seasons. The investigators concentrated ambient fine particles

Continued

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Jack R Harkema at Michigan State University, East Lansing MI. The complete report, *Effects of Concentrated Ambient Particles on Normal and Hypersecretory Airways in Rats*, can be obtained from HEI or our website (see reverse side). HARKEMA 120

by an average of 19-fold, varying between 10-fold and 30-fold depending on weather conditions and ambient PM levels. Particles in the range 0.6 µm to 1 µm were preferentially concentrated. Several major PM components—including sulfate, nitrate, ammonium, and crustal elements—were found in the same proportions in CAPs as in ambient PM. In addition, the trace elements iron, vanadium, and antimony were all concentrated to the same extent in CAPs compared with ambient levels. Mass concentrations of CAPs were similar during the July and September series of exposures.

At 24 hours after exposure to CAPs, no CAPs-associated inflammatory effects were found in the airways of healthy rats or of rats with mild bronchitis (the bronchitis had resolved by 4 days after endotoxin pretreatment). In CAPs-exposed rats with features of asthma, levels of some measures of mucus secretion and other markers of airway inflammation were higher than in control animals. These increases were modest, however (range 20% to 50%). Inflammatory responses to the instilled, water-soluble fraction of resuspended particles were small and variable. Some trace metals—lanthanum and vanadium in particular—were found in the lungs of rats exposed to CAPs in September. This finding is interesting because it indicates that some elements contained in PM may be retained in the lungs immediately after exposure, although it is not clear for how long. These findings are difficult to interpret: Trace metals were retained in the lungs of animals exposed in September but not those exposed in July, although the levels of trace metals in the CAPs during the two different exposure protocols appeared to be similar.

CONCLUSIONS

This study was the first to examine the effects of inhaled CAPs on the airways of rats conditioned to model asthma. In those animals, few inflammatory endpoints were affected and the changes that were detected were small in magnitude. The study found no inflammatory responses in healthy rats or rats with features of mild bronchitis. Some earlier CAPs exposure studies had detected airway inflammatory effects in healthy rats and in rats with a different, longer-lasting model of bronchitis. Differences in exposure protocols, strains of rats, models of bronchitis, and characteristics of the concentrated particles at the various study sites make comparing the results of these different studies challenging. The results of the current study did not find clear evidence of the toxicity of metal components in $PM_{2.5}$.

Harkema and colleagues showed that they could concentrate and characterize fine particles under different weather conditions in a mobile laboratory, expose rats to the concentrated aerosol, and evaluate many of the CAPs-associated responses on site. Thus, the mobile laboratory can be used to conduct similar studies of the effects of fresh, real-world, fine particles in many different locations.

However, the current study also underscores some of the limitations of the CAPs exposure approach: First, the fact that the composition of fine PM varies over the course of a single exposure day and from day to day makes identifying a potentially toxic PM component difficult. Second, a particular size range of fine particles is preferentially concentrated, which limits the conclusions that can be drawn about the characteristics of particles responsible for toxicity. In addition, because of this preferential concentration of particles based on size, some elements or compounds in the particles may be preferentially concentrated and others not.

Carefully designed epidemiologic studies and controlled exposures with consistent animal models and endpoints are needed in this and other locations to assess the health effects of particles outside the size range concentrated in this study.

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