



# STATEMENT

Synopsis of Research Report 118

HEALTH  
EFFECTS  
INSTITUTE

## Effects of Exposure to Concentrated Ambient Particles from Los Angeles Air on Healthy and Asthmatic Volunteers

### INTRODUCTION

Ambient particulate matter (PM) is a complex mixture of particles suspended in the air. The size, chemical composition, and other physical and biological properties of these particles vary with location and time. Although the characteristics of PM vary in different places, epidemiologic studies in many diverse locations have reported that short-term increases in levels of PM are associated with short-term increases in illness and death. These studies have raised several critical questions, including: (1) What are the characteristics—especially size and chemical composition—of particles that may cause harmful human health effects? (2) What biologic mechanisms may explain the reported epidemiologic associations? and (3) Which groups of people are particularly sensitive to the effects of PM?

In 1998, the Health Effects Institute issued Request for Applications 98-1, *Characterization of Exposure to and Health Effects of Particulate Matter*. A key component of RFA 98-1 was to evaluate the health effects of ambient particles in healthy and sensitive persons. Preliminary studies had indicated that nonhuman species exposed to CAPs showed certain changes in electrocardiogram (ECG) readings and differences in cell counts of peripheral blood leukocyte subsets. The relevance of these findings to humans was not clear, however. Thus, one area of interest was studies that would use a technology designed to concentrate ambient particles (CAPs) and expose human volunteers to CAPs using a controlled laboratory protocol.

HEI funded two studies to address the effects of controlled human exposure to CAPs. The first, described here, was led by Dr Henry Gong of Los Amigos Research and Education Institute, Downey CA. The second was led by Dr Mark Frampton,

University of Rochester School of Medicine and Dentistry, Rochester NY, and will be published in 2004. Before both studies began, Gong and Frampton participated in an HEI-sponsored workshop and decided to use similar exposure levels and evaluate a similar set of endpoints so that the results of their studies could more easily be compared with each other and with CAPs studies being performed at the US Environmental Protection Agency research facility in Chapel Hill NC.

### APPROACH

HEI commissioned Dr Petros Koutrakis, one of the developers of the concentrator that had been used in studies at the Harvard School of Public Health, to provide Gong and colleagues with an ambient particle concentrator. Gong and colleagues recruited 12 healthy individuals and 12 individuals with mild asthma—a group thought to be particularly sensitive to PM. During a 2-hour exposure to either filtered air or CAPs derived from air in the Los Angeles region, participants exercised intermittently on a stationary bicycle. The investigators' target CAPs exposure level was 200  $\mu\text{g}/\text{m}^3$ , considered to be a "worst-case" ambient PM exposure scenario for metropolitan Los Angeles.

Gong and colleagues hypothesized that CAPs exposure would cause cardiopulmonary effects, mediated by local and systemic inflammation, and that responses to CAPs would differ among individuals depending on their health status. They measured pulmonary function and cardiac electrophysiologic and blood parameters in an ordered sequential manner at multiple time points before, during, and after CAPs or air exposures; the day after exposure, they also collected sputum.

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### RESULTS AND INTERPRETATION

Gong and colleagues found few airway, systemic, or cardiac electrophysiologic changes at different times after exposing 12 healthy and 12 mildly asthmatic volunteers for 2 hours to approximately 200  $\mu\text{g}/\text{m}^3$  CAPs derived from air in the Los Angeles Basin. For example, they found no changes in lung function, blood leukocyte differential cell counts, or the blood levels of fibrinogen or serum amyloid A—both of which are acute-phase reactants that participate in the inflammatory response. The largest CAPs-associated change in both healthy and asthmatic participants was a 50% decrease in the number of columnar epithelial cells in sputum acquired from participants 24 hours after exposure; this may indicate that the particles stimulated an irritant or toxic response in the airways that removed these cells before sputum was collected.

Both healthy and asthmatic participants showed small changes in a few parameters. These included modest changes in (1) heart rate variability (normal fluctuations in heart rate) that are unlikely to have clinical significance or prognostic value for people who do not have heart disease; (2) blood levels of factor VII (involved in coagulation); and (3) blood levels of soluble intercellular adhesion molecule (ICAM) 1 (a marker of endothelial cell activation

and an independent risk factor for coronary heart disease). As the investigators appropriately note, when evaluating many endpoints and finding only a few that changed, it is always possible that those few changed by chance.

The clinical significance of any of the CAPs-associated changes is not clear; but the results suggest that in this small set of healthy and mildly asthmatic participants, the effects from approximately 200  $\mu\text{g}/\text{m}^3$  CAPs for 2 hours are not large. The paucity of effects in the current study is consistent with the types of effects reported in human CAPs exposures conducted on the East Coast of the US, predominantly in the studies reported by the US Environmental Protection Agency. It will be interesting to compare the effects reported in these studies with those reported in the forthcoming report by Frampton and colleagues.

Conducting controlled exposures to CAPs with different susceptible populations (such as those with cardiovascular disease); using a larger number of participants, longer exposure durations, and higher CAPs concentrations; involving other types of particles; and measuring different endpoints would be important next steps in determining whether PM effects are limited or whether they can be larger and more distinct.

## Controlled Exposures of Healthy and Asthmatic Volunteers to Concentrated Ambient Particles in Metropolitan Los Angeles

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