HEALTH EFFECTS INSTITUTE

STATEMENT

Synopsis of Research Report Number 91

Effects of Concentrated Ambient Particles on the Cardiac and Pulmonary Systems of Dogs

INTRODUCTION

Epidemiology studies have indicated that short-term exposure to low-level increases in particulate matter is associated with an increase in morbidity and daily mortality, particularly in individuals with cardiopulmonary conditions. A plausible biologic mechanism linking low-level particle exposure and pathophysiologic effects has not been established, however. Assessing the effects of particulate matter in appropriate animal models is important to learning how particulate matter may exert adverse health effects. The Health Effects Institute funded the study described in this report as part of a research program to reduce this information gap.

APPROACH

Dr John Godleski and colleagues at Harvard School of Public Health conducted an exploratory study to test the effects of particulate matter exposure in dogs, which share many features of the human cardiovascular system. The investigators hypothesized that particulate matter might affect the animals' cardiac function, leading to arrhythmia, and might induce inflammatory responses and changes in pulmonary mechanical measurements. To maximize possible effects, they used a device to concentrate particles up to 30 times their level in ambient Boston air and exposed dogs to these concentrated ambient particles (CAPs) via inhalation. The investigators physically and chemically identified components of the CAPs and tested their effects in 12 dogs, in 6 of which they also induced a coronary occlusion to simulate human coronary artery disease. They evaluated the effects of CAPs on electrocardiographic (ECG) wave patterns and performed a sophisticated analysis of each dog's ECG to measure possible effects of particulate matter on other electrical properties of the heart: heart rate variability, which is influenced by the involuntary nervous system, and T wave alternans, a change in the heart beat pattern. These two are among the measures currently used to predict further heart problems in humans with cardiovascular disease, but they have not been established as predictive parameters in normal humans or other species. The investigators also assessed whether changes in respiratory parameters or inflammatory responses were associated with CAPs exposure.

RESULTS AND INTERPRETATION

The most biologically and clinically significant finding was that in dogs with induced coronary occlusion, CAPs affected one of the major ECG signs of myocardial ischemia in humans, known as elevation of the ST segment. CAPs-exposed animals showed a shortened time to ST segment elevation and an increased magnitude of the ST segment compared to controls. These findings suggest what may be a plausible mechanism to explain PM's effects on individuals with cardiopulmonary conditions: exposure to particulate pollution may make patients with ischemic heart disease more susceptible to developing serious cardiac effects. If substantiated in larger groups of animals, the evidence may help to explain the previously described association between increased particulate pollution and cardiopulmonary morbidity and mortality. Animals with an induced coronary occlusion also showed other changes in cardiac and respiratory parameters after exposure to CAPs.

The investigators also reported that normal dogs showed CAPs-induced changes in heart rate variability and average heart rate (which fluctuated widely from day to day during the course of the study), decreases in T wave alternans, and changes in respiratory parameters such as breathing rates and air flow rates. They did not identify whether the variability in responses was due to day-to-day fluctuation of a specific component of the particulate mixture. In addition, the investigators reported that CAPs had little or no effect on inflammatory mediators, suggesting that changes in cardiac and pulmonary responses occurred in the absence of significant airway inflammation.

The investigators interpreted their findings to indicate that CAPs influenced the nervous system's control of the normal dog's heart but did not necessarily induce arrhythmia. This interpretation may be reasonable, but the statistical approach the investigators used to identify changes in heart rate variability is not clearly applicable to the small number of dogs tested. In addition, it is not apparent whether it is appropriate to extrapolate these results to humans because the human and dog cardiovascular

This Statement, prepared by the Health Effects Institute, is a summary of a research project conducted by Dr John J Godleski at Harvard School of Public Health. The complete report, *Mechanisms of Morbidity and Mortality from Exposure to Ambient Air Particles,* can be requested from HEI by phone, fax or e-mail (see reverse side)

systems differ in some critical features. Furthermore, the clinical significance of changes in heart rate variability or T wave alternans in normal dogs, or in humans who do not have preexisting heart disease, is currently unknown.

Because Godleski and colleagues tested only a small number of animals, confirmation of the findings both in animals with impaired cardiac function and in normal animals is required in larger studies. Studies of effects in humans, such as those currently underway at HEI, are also expected to provide information about the possible effects of particulate matter on the heart.

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