



STATEMENT

Synopsis of Research Report III

HEALTH
EFFECTS
INSTITUTE

Concentrated Ambient Particles and Blood Coagulation in Rats

INTRODUCTION

Several epidemiologic studies have shown an association between short-term increases in ambient particulate matter and short-term increases in morbidity and mortality, especially in people with cardiovascular disease. The biological mechanisms by which particulate matter may affect cardiovascular events are not well understood, however. Dr Christine Nadziejko of the New York University School of Medicine hypothesized that exposure of healthy rats to ambient particles may cause changes in blood coagulation parameters. The hypothesis that particulate matter may exert its adverse health effects by altering blood coagulation parameters is biologically relevant because clots may precipitate cardiac arrest, especially in people with cardiovascular disease. The Health Effects Institute funded the animal study described in this report to address this hypothesis.

APPROACH

The investigators measured platelet number, blood cells counts, and levels of fibrinogen, thrombin-antithrombin complex, tissue plasminogen activator, plasminogen activator inhibitor, and factor VII. Rats were exposed to concentrated New York City particles or filtered air for 6 hours; blood samples were obtained via an indwelling catheter before and after exposure. A particle concentrator was used to deliver concentrated particulate matter to the animals at a target concentration of 300 $\mu\text{g}/\text{m}^3$, which was reached on 2 of 5 experimental days. The investigators used concentrated particulate matter to increase the likelihood of finding an effect.

RESULTS AND INTERPRETATION

The investigators found no consistent differences in coagulation end points in animals exposed to concentrated particulate matter compared with

animals exposed to filtered air. Due to the limited scope of the study, however, the lack of a consistent effect is difficult to interpret. Factors that may have contributed to the lack of effect in this study include the use of healthy animals, the time points evaluated, the lower than expected concentration of ambient particulate matter on exposure days, and the lack of concentration of smaller particles, where much of the particle mass from mobile sources (a major source of particulate matter) is found. In addition, animal studies generally use small numbers of individuals in comparison with epidemiology studies that investigate large populations, reducing the power to detect small changes.

The blood coagulation system is complex with many positive and negative feedback loops to maintain homeostasis. Thus the particulate matter exposure may have caused changes in parts of the coagulation system that were not investigated in the current study but might be detected with other types of measurements. For example, one could perform functional assays (such as platelet aggregation or clotting time) or investigate endothelial aspects of clot formation. The lack of a consistent effect in the current study as well as other studies does not preclude that particulate matter exposure may affect coagulation under particular circumstances (for example, in individuals with preexisting disease). Animal models that exhibit increased clot formation or vascular plaques may be more likely to show changes in blood coagulation after being challenged with exposure to particulate matter.

Some human controlled exposure and epidemiologic studies have reported changes in blood cell counts, platelet counts, fibrinogen, and factor VII in relation to air pollution, but other human studies and most animal studies have failed to find such changes. No consistent pattern has emerged so far. To complement the current study, it might be worthwhile to perform similar studies with higher concentrations of fine and ultrafine particles, particles

Continued

from specific mobile and stationary sources, or other well-defined particles of known toxicity while using compromised rather than healthy animals.

In summary, this was a well-designed pilot study that will contribute to designing future experiments to address the important topic of particulate matter effects on coagulation. It found no consistent effect of moderate levels of concentrated New York City particulate

matter on six blood coagulation parameters in rats. This does not preclude involvement of the coagulation pathway in adverse health effects of particulate matter on the cardiovascular system, however. In future studies, changes in coagulation may be found in compromised animals with exposure to higher levels of particulate matter or with exposure to particles of different size or composition.

Effect of Concentrated Ambient Particulate Matter on Blood Coagulation Parameters in Rats

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INVESTIGATORS' REPORT

Abstract

Introduction

Particulate Air Pollution and Cardiovascular Morbidity and Mortality
Blood Coagulation and Cardiovascular Disease
Evidence that Particulate Air Pollution Affects Blood Coagulation
Biological Significance of Coagulation Parameters

Specific Aims

Methods and Study Design

Experimental Design
Animal and Blood Sampling Procedures

Exposures and Monitoring
Blood Sample Assays
Statistical Methods and Data Analysis

Results

Blood Sampling Pilot Studies
Control Exposures
Effects of Concentrated PM on Coagulation
Results Summary

Discussion and Conclusions

Appendix A. Detailed Results of Experiments 1 Through 5

HEALTH REVIEW COMMITTEE'S CRITIQUE

Background

Possible Mechanisms Underlying PM Effects
Coagulation Pathway

Technical Evaluation

Aim and Approach

Study Design and Methods
Results and Interpretation
Discussion

Summary and Conclusions

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