

Evidence for Mechanisms of Particulate Matter Cardiovascular Mortality Observations

February 26, 2004

Air Resources Board



California Environmental Protection Agency

Good Morning

I am here today to bring you some new information on the health impacts of particles in the air we breathe, especially focused on how these particles may be causing harm following long-term exposures.

Introduction

- **There is clear evidence that brief and prolonged exposures to particles harm people with respiratory and cardiovascular disease**
 - hospitalizations
 - increased deaths
 - suggestions of contributions to disease
- **The mechanisms to explain these effects observations remain elusive**



Over the past several years you have all heard that particles or particulate matter (PM) in the air we breathe can be harmful, especially to people who are at special risk.

We see that people with respiratory and cardiovascular disease who experience brief or more prolonged exposures to elevated PM are likely to seek hospital admission, suffer symptoms of their disease, and are even much more likely to die than people who are not exposed or who do not have these risk factors.

From limited evaluations of prolonged exposures there are suggestions that PM may contribute to disease progression.

A very important and elusive question remains regarding linking PM exposure to adverse health outcomes--What are the “pathophysiological” mechanism that underlie the statistical observations of epidemiological studies. Basically, knowing how pollution impacts human physiology is important in establishing “causal” relationships. Unfortunately epidemiological studies, especially those of long term exposure consequences are often not well suited to provide such information because they do not collect the kinds of data that can establish cause.

Today's Study

“Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution”

Investigators: Arden Pope III, Richard Burnett, George Thurston, Michael Thun, Eugenia Calle, Daniel Krewski and John Godleski

Journal: Circulation, 2004; 109; 71-77

Objective: To determine whether observations of long-term cause - specific mortality suggest mechanisms of PM effect



Today's study was performed by a highly qualified group of epidemiologists, statisticians and and investigators with the specific objective of attempting to evaluate health and PM exposure information to determine whether any statistical outcomes suggest mechanisms or pathophysiological pathways of effect.

Research Protocol

- Epidemiological study based on the American Cancer Society Cancer Prevention Study II
- As many as 500,000 participants US - wide
- Subjects enrolled in 1982 and followed for 16 years
- Subject information gathered at start of study
 - Smoking, race, education, occupation, etc
- Vital status checked periodically, cause of death determined from death certificates
- PM2.5 exposure histories generated for each death
- Protocol imposed limitations



The study was performed using data from an existing, large epidemiological study--assembled by the American Cancer Society

The study group was very large, consisting of ~300- 500K participants from metropolitan areas of all 50 states and Puerto Rico. The specific numbers varied, depending on the availability of data for exposure assignment.

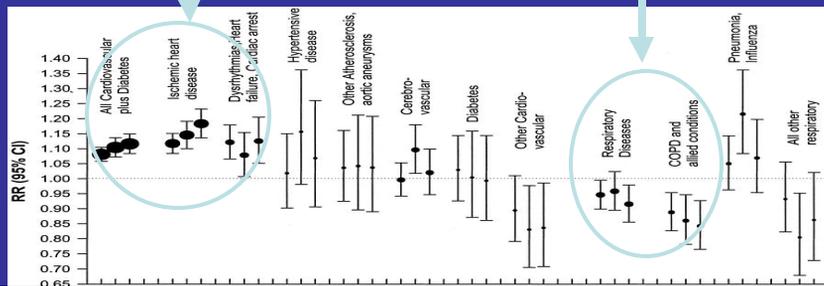
Participants were recruited in 1982 and all participants completed detailed questionnaires to provide important information on factors that characterized their health status and that could influence their health as they aged. Most obvious of these was smoking history, race, age, sex, educational achievement, body mass index, and occupation.

The participants were surveyed during the 16 year study period to determine their vital status (were they alive). If they were found to be dead, death certificates and related documents were obtained. Cause of death was ascertained from these documents.

The investigators of the current study generated PM2.5 exposure profiles for major cities where subjects lived. The basic unit of air quality was quarterly averages of PM2.5. Data estimates were constructed by various means because actual measurements of PM2.5 were not commonly made during the study. These were assembled into annual averages.

Findings

- 23% of participants died during study
 - 45% from cardiovascular disease, 8% from respiratory
- Clear increased risk associations of PM2.5 for cardiovascular diseases -- Not for respiratory disease
 - largest for ischemic heart disease, less for other cardiac causes



Over the 16 years of the American Cancer Society study period approximately 23% of participants died. This presented the investigators with a large study pool.

Of these 45% of these were from cardiovascular disease, 8% of respiratory disease.

The investigators report a clear association of long-term PM2.5 exposure with a increased risk of death from all cardiovascular disease causes.

The largest increased risks were for ischemic heart disease, but other cardiac causes such as dysrhythmia and cardiac arrest also achieved statistically significant elevated relative risk levels.

No increased risks were shown for respiratory causes -- in fact some causes showed an inverse risk in high PM cases.

Findings II

- **Smoking influenced cardiovascular and respiratory death rates, more than PM2.5 alone**
- **PM2.5 and smoking interact to enhance mortality**



Smoking was found to produce (as expected) large impacts on both cardiovascular and respiratory deaths.

An interesting finding was that smokers appeared to be at special risk of various cardiovascular-related deaths in regions of high PM2.5.

Implications and Applications

- Findings of ischemic heart disease deaths suggest inflammatory and atherosclerosis mechanisms
- Findings of dysrhythmia and cardiac failure suggest changes in neural control of heart
- Smokers at special risk when PM 2.5 is high
- Mechanistic information strengthens regulatory utility of epidemiological studies
- Findings are consistent with earlier studies that served as basis for PM Standards adopted by Board in 2002



The investigators end their paper with a lengthy discussion of how the observations of specific causes of cardiovascular deaths that were associated with long-term PM_{2.5} exposures suggest “pathophysiological pathways” of effect. The clear associations of PM with ischemic heart disease suggest that long-term exposures may play a role in inflammatory and atherosclerosis mechanistic pathways.

Findings of dysrhythmia and cardiac failure suggest alterations of the neural/electrical control processes of heart function.

The findings that smokers respond even more strongly to a given level of PM exposures than do non-smokers is quite novel and counters traditional “wisdom” that smokers were somehow less likely to suffer from ambient PM exposures, since they received such high levels of PM from active smoking.

Further studies are needed to confirm and clarify the findings of this study, especially studies where actual ascertainment of physiological status of people exposed to prolonged or repeated PM exposures is included. Studies where direct measures such as circulating factors in the blood are collected and correlated with cardiovascular measures of outcome should be considered.

Finally, these findings are consistent with earlier studies that served as the basis for the annual average PM standards adopted by the Board in 2002.