

# Air Pollution and Atherosclerosis in the Los Angeles Basin

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Air Resources Board

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California Environmental Protection Agency

Thank you Ms. Witherspoon. Good morning members of the Board. In today's Health Update I will discuss the results of an epidemiologic study that evaluates the possible link between air pollution and heart disease; specifically, atherosclerosis and long-term exposure to ambient PM<sub>2.5</sub> in older subjects living in the Los Angeles Basin.

# Background and Hypothesis

- Cardiovascular disease (heart disease and stroke)
  - Leading cause of death in US
  - Heart disease kills 30% of Californians
- Atherosclerosis is the primary cause of heart disease and stroke
- Atherosclerosis is an inflammatory disease
  - High LDL cholesterol responsible for 50% of the disease risk
  - Other harmful components interact with lipids to create inflammatory response
- Ambient levels of particle pollution (PM<sub>2.5</sub>) may contribute to atherosclerosis through an inflammatory response

Cardiovascular disease (heart disease and stroke) is the leading cause of death in the US. In California, heart disease alone is responsible for nearly 30% of all deaths. Atherosclerosis is the primary cause of cardiovascular disease. Rupture of the arterial lesions created by this disease can lead to acute cardiovascular effects such as heart attacks and strokes.

Atherosclerosis is now considered an inflammatory disease with low density lipoprotein or LDL cholesterol accumulation in the arteries as the primary risk factor. However, 50% of the patients who develop atherosclerosis do not have high cholesterol. Therefore, it is the relationship between the accumulated lipids and other harmful components of inflammation in the arteries that is of concern.

It is this relationship—between the lipids and these other harmful components, in this case, particulate air pollution, that forms the hypothesis for this study.

# Study Design\*

- Baseline health data from two USC clinical trials on atherosclerosis (798 healthy adults >40 years)
- Baseline Carotid Intima-media Thickness (CIMT) and other clinical data (LDL cholesterol, blood pressure)
- Questionnaires on risk factors (lifestyle and demographics)
- Exposure assignment: ambient concentration of PM<sub>2.5</sub> assigned to the ZIP code area of each subject's residential address

\* Kunzli, N.; Jerrett, M.; Mack, W. J.; Beckerman, B.; LaBree, L.; Gilliland, F.; Thomas, D.; Peters, J., and Hodis, H. N. Ambient air pollution and atherosclerosis in Los Angeles. *Environ Health Perspect.* 2005 Feb; 113(2):201-6.

This epidemiologic study is the first to show a relationship between atherosclerosis and air pollution. It was performed by taking advantage of two ongoing clinical trials at the Atherosclerosis Research Unit at the University of Southern California.

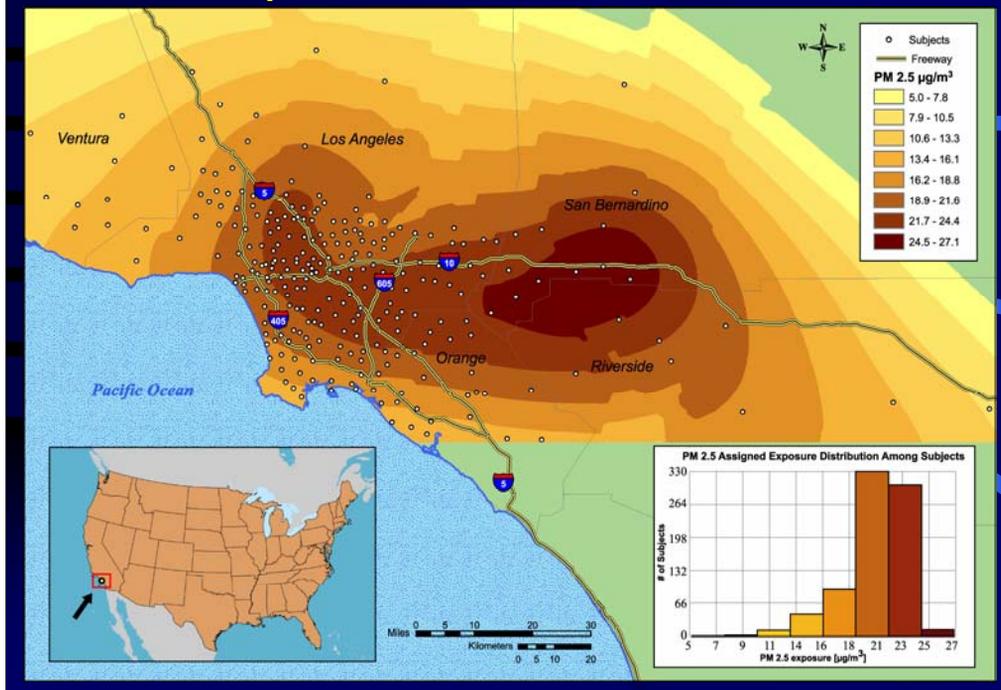
Nearly 800 healthy, middle aged adults with a mean age of 59 years volunteered for these double blind, placebo controlled studies to examine the effects of Vitamin E and Vitamin B on the progression of atherosclerosis, as determined by carotid artery intima-media thickness or CIMT.

Baseline CIMT along with other clinical data was collected at the start of the study. CIMT is measured through ultrasound and is a well-known and well accepted measure of atherosclerosis. It has been used in epidemiologic studies to assess the relationship between environmental tobacco smoke and atherosclerosis.

Questionnaires were used to gather information from the participants on a variety of lifestyle and demographic risk factors including smoking habits, tobacco smoke exposure at home, prescription medication and education.

In order to determine the level of exposure to ambient PM, mean ambient concentration of PM<sub>2.5</sub> was assigned to the ZIP code area of each subject's residential address.

# Exposure Surface PM<sub>2.5</sub>



A geostatistical model was used to create a PM<sub>2.5</sub> surface area map derived from data collected from 23 ambient monitoring stations and averaged for the year 2000. Individually assigned PM<sub>2.5</sub> data had a range from 5.2 to 26.9  $\mu\text{g}/\text{m}^3$ , the mean was 20.3  $\mu\text{g}/\text{m}^3$ . The small dots show the geo-located zip codes for the residences' of study participants. As you can see these locations are scattered throughout the Los Angeles Basin.

The investigators used the participant's residence to capture exposure information since time-activity studies show that people spend most of their time in and around home. In addition, studies have shown there is a strong correlation between long-term outdoor PM concentrations and indoor levels of PM from outdoor origins. One potential problem with this exposure protocol would be the failure to capture ambient concentrations while working and during commute times; with this latter contribution having been shown to be highly relevant in recent studies by the ARB and others.

# Results

## % Difference in CIMT per $10 \mu\text{g}/\text{m}^3$ PM2.5 (95% CI)

Total sample N=798	4.4 (0-9.0)
Lipid lowering medication, N=109	13.3 (0-28.5)
Women >60, N=186	15.7 (5.7-26.6)

## % Difference in CIMT per $20 \mu\text{g}/\text{m}^3$ PM2.5 (95% CI)

Lowest to highest exposure	12.1 (2.0-23.1)*
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Statistically significant increase in CIMT with increasing pollutant levels (dose-response).

\* unadjusted value

Statistical analysis tested the associations between CIMT and ambient PM2.5. The analysis was adjusted for factors that were found to be statistically associated with CIMT and ambient PM2.5. These factors were age, gender, education and income.

The statistical model indicated a 4.4% increase in CIMT per  $10 \mu\text{g}/\text{m}^3$  increase in PM2.5. The numbers in parentheses represent the 95% confidence intervals around the estimated increase. In a subset of patients taking lipid lowering medications the investigators found the response more than doubled to 13.3% per  $10 \mu\text{g}/\text{m}^3$  increase in CIMT. This is particularly significant since animal experiments indicate an increased response for PM exposure based on the tendency to accumulate lipids.

Significant age and gender effects were apparent in the analysis with much larger effects identified for women in the over 60 age category. For this group there was a 15.7% increase in CIMT per  $10 \mu\text{g}/\text{m}^3$  increase in PM2.5. From lowest to highest exposure, a total increase of  $20 \mu\text{g}/\text{m}^3$  PM2.5 concentration, the increase was just over 12%.

The investigators also found a dose-response associated with increased exposure to PM2.5; corresponding increases in CIMT were observed for graduated increases PM2.5 concentrations.

# Research Implications

- Evidence is accumulating that...
  - “air pollution may accelerate the development of coronary atherosclerosis and worsen its sequelae.”
    - (American Heart Association)
- Increase in CIMT corresponds to 3-6% long-term increase risk for heart attack
- To account for short- and long-term effects of PM on health, prospective cohort studies will be needed
- Atherosclerosis results from a complex process and this response may be the result of a combination of various urban pollutants interacting with host factors

In a recent review of the evidence associating air pollution with cardiovascular disease, the American Heart Association stated that “air pollution may accelerate the development of coronary atherosclerosis and worsen its sequelae,” or after effects.

The observed changes in CIMT thickness in this study correspond to a 3-6% increase in the long-term risk for heart attack.

In order to incorporate both the short-term and long-term effects of PM, prospective cohort studies will need to be conducted. These cohort studies should take advantage of long-term outdoor spatially modeled concentrations such as those used in this study.

It should be remembered that atherosclerosis is a complex disease process with a number of host factors including, age, health status, and gender that may be interacting with the urban air pollutants. This study will need to be duplicated with a larger and more representative population in order to truly understand its implications.

Thank you for your attention, and I would be happy to answer questions.