EPA

SCIENCE

THE MESA AIR POLLUTION STUDY

Strengthening the Scientific Foundation for Air Quality Management

While it is widely known that factors such as cigarette smoking and high blood pressure are linked to cardiovascular disease, studies indicate that long-term exposure to air pollution also is associated with premature death from this disease.

IN 2004, THE ENVIRONMENTAL PROTECTION AGENCY (EPA) awarded a grant to the University of Washington for the Multi-Ethnic Study of Atherosclerosis (MESA) Air Pollution Study—an unprecedented investigation of the impact of air pollution on hardening of the arteries, or atherosclerosis. This long-term study investigates key questions about the possible effects of fine particles in air pollution on the development of heart disease and mortality.

Air Pollution and Cardiovascular Health

Emissions from power plants, traffic, wood burning, and other combustion processes form airborne particles and liquid droplets of chemicals. While inhaled particulate matter (PM) ranges in size from particles tens of micrometers in diameter (PM_{10}) to minute particles less than 0.1 micrometer in diameter, combustion sources generate fine particles less than 2.5 micrometers in diameter ($PM_{2.5}$), just 1/30 the width of a human hair.

Two landmark studies, originally published in the 1990s with later follow-up reports, indicated that these fine particles pose the greatest mortality risk from air pollution.[1-4] In 1999 and 2006, EPA revised the National Ambient Air Quality Standards for particulate matter to address $PM_{2.5}$ concentrations. Since 1999, EPA also has supported a national $PM_{2.5}$ monitoring network, managed by federal, state and local governments.

Although scientific evidence is accumulating that supports the link between PM exposure and premature mortality and adverse health events, many questions about the health effects of PM remain unanswered. In 2001, the National Research Council highlighted a critical need for further research on the long-term health effects of PM exposure, particularly in two areas: the effects of PM in combination with gaseous pollutants (such as nitrogen dioxide and ozone), and the effects on potentially susceptible groups. The MESA Air Pollution Study addresses these and other research needs.

BUILDING KNOWLEDGE OF PM HEALTH EFFECTS

In accordance with its mission to protect human health, the ultimate goal of EPA's PM research program is to provide information for decision-making. EPA conducts and funds research designed to answer key questions concerning pollution emissions, exposure, health effects and air quality management.

EPA's Science to Achieve Results (STAR) research program, through its competitive grants process, has funded several epidemiological studies investigating long-term exposure to $PM_{2.5}$ in addition to the MESA Air Pollution Study. STAR support of the study will substantially add to this body of research.

IMPROVING OUR KNOWLEDGE BASE

The MESA Air Pollution Study investigates the impact of air pollution on the progression of cardiovascular disease among more than 7000 participants with diverse backgrounds from nine locations in six states for 10 years. The central scientific hypothesis for this study is that long-term exposure to fine particles is associated with a more rapid progression of coronary atherosclerosis and an increased risk of coronary events.

To test this hypothesis, a host of air pollution and participant health measures are being collected and analyzed. Along with measuring PM concentrations and variability at the neighborhood, home and individual levels, the MESA Air Pollution Study is using data from the national $PM_{2.5}$ monitoring system. These environmental data will be integrated into a model to estimate long-term PM exposure for all study participants. The cardiovascular health of each participant also will be tracked, with a subgroup of 3600 participating in additional medical evaluations for subclinical, asymptomatic progression of atherosclerosis.

The MESA Air Pollution Study will address the following critical scientific questions concerning PM-related health effects:

1. **What role does long-term particle exposure play in the progression of coronary artery disease and the onset of clinical cardiovascular disease, including heart failure, heart attacks and mortality?**
2. **Are some ethnic populations more susceptible to the effects of particle exposure?**
3. **Does the presence of gaseous pollutants change the health risks associated with ambient particulate matter?**

COLLABORATING WITH PREEMINENT RESEARCHERS: THE MESA STUDY

The MESA Air Pollution Study is built on the framework of the Multi-Ethnic Study of Atherosclerosis (MESA) which is a 10-year, large-scale epidemiological study of cardiovascular risk factors and atherosclerosis initiated in 1999 by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health. NHLBI-MESA recruited at baseline approximately 1100 participants aged 45-84 years in each of six major metropolitan areas—Los Angeles, CA, St. Paul, MN, Chicago, IL, New York City, NY, Baltimore, MD, and Winston-Salem, NC. MESA researchers continue

RESEARCH COLLABORATION ENCOURAGED

The investigators of the MESA Air Pollution Study invite proposals from other investigators to explore additional research questions. Researchers can gain access to monitoring data or physiological data and samples from both the NHLBI-MESA and MESA Air Pollution Studies. The proposed research must secure independent funding. Further information about research opportunities and the process for proposing collaborative projects can be obtained at the MESA Air Pollution Study Web site or by contacting the principal investigator, Dr. Joel Kaufman. (Please see contact information on the back page.)

BEHIND THE MESA AIR POLLUTION STUDY

The Multi-Ethnic Study of Atherosclerosis (MESA)—the NHLBI epidemiological study—is the foundation of the MESA Air Pollution Study. The collaborating institutions in the NHLBI-MESA also are participating in the MESA Air Pollution Study. These collaborators include the University of California-Los Angeles, Columbia University, Northwestern University, University of Minnesota, Johns Hopkins University, Wake Forest University, University of Vermont, and Tufts-New England Medical Center. The University of Southern California and University of Michigan are also collaborators.

The MESA Air Pollution Study is based at the University of Washington Department of Environmental and Occupational Health Sciences. The study's Principal Investigator is Dr. Joel Kaufman. The study's exposure assessment efforts are directed by Dr. Martin Cohen.

The MESA Air Pollution Study will help determine if cardiac disease is accelerated by exposure to PM in combination with gaseous pollutants.

EXPECTED OUTCOMES

The MESA Air Pollution Study will provide:

- **More precise estimates of the risks for the progression of underlying coronary artery disease and mortality associated with long-term exposure to ambient $PM_{2.5}$.**
- **More information on the role played by traffic-related air pollution and regional air pollution.**
- **Identification of groups especially susceptible to the effects of $PM_{2.5}$ exposure due to racial/ethnic background, poor health status, older age, and other characteristics.**
- **A better understanding of the health risks posed by exposure to gaseous pollutants concurrently with particulate matter.**
- **Opportunities for research collaboration.**

MESA Air Pollution Study: **In Brief**

STUDY POPULATION

- **More than 7000 participants recruited from the NHLBI-MESA Study, the NHLBI-MESA Family Study, and additional participants in New York and southern California**

STUDY SITES (Nine Locations)

- **Six field sites established by the NHLBI-MESA Study in Chicago, Los Angeles County, Baltimore, St. Paul, New York City, and Winston-Salem**
- **An additional area near New York City and two additional areas in and around Los Angeles**

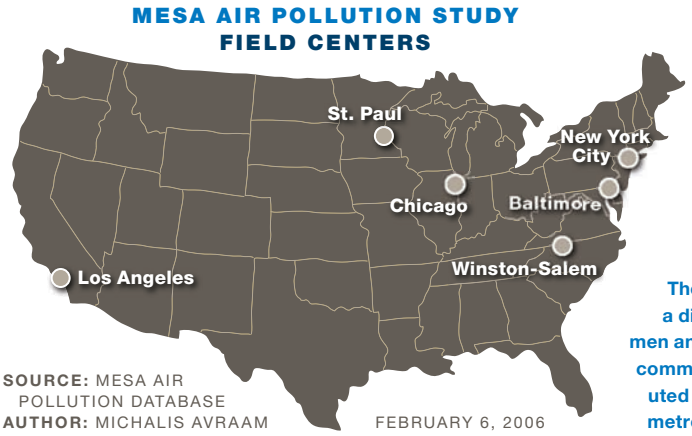
STUDY APPROACH

HEALTH ASSESSMENTS:

- **All participants tracked for clinical cardiovascular events (heart attack, heart failure, death, etc.)**
- **A subgroup of 3600 receive two clinical examinations five years apart to be assessed for pre-symptomatic progression of atherosclerosis**

PM EXPOSURE ASSESSMENTS:

- **Air pollution data collected from existing networks, study-specific outdoor monitors, roughly 330 monitors in homes, and personal monitors (carried by approximately 80 participants)**
- **$PM_{2.5}$ exposure model developed, based on air monitoring and questionnaire data**



SOURCE: MESA AIR POLLUTION DATABASE
AUTHOR: MICHALIS AVRAAM
FEBRUARY 6, 2006

The study follows a diverse group of men and women from communities distributed throughout six metropolitan areas.

to conduct medical evaluations, including collecting detailed health data from participants who will receive a total of four clinical examinations by 2007.

Several academic institutions have secured grant funding to address additional scientific questions in the NHLBI-MESA study population, including measurements of lung function (MESA Lung Study) and genetic markers of susceptibility to disease (MESA Family Study). The University of Washington designed the MESA Air Pollution Study in partnership with the NHLBI-MESA researchers. The investigation of the role of PM in cardiovascular health relies on and adds to the NHLBI-MESA effort. The MESA Air Pollution Study is recruiting several hundred additional study participants and will repeat clinic health assessments in 2010 for the subgroup of 3600 participants undergoing further assessment for asymptomatic evidence of atherosclerosis. The supplemental data collection will contribute to the value of the broader NHLBI-MESA goals.

USING SOPHISTICATED EXPOSURE ASSESSMENTS

The MESA Air Pollution Study team will combine air quality data collected by government agencies with the study's own monitoring effort to develop an exposure model. This model will combine air quality data, meteorological data, traffic information, land

Answering Critical Questions

1 THE PROGRESSION AND ONSET OF HEART DISEASE

In determining associations with PM exposure, the MESA Air Pollution Study is assessing heart disease at three levels:

- **The occurrence of cardiovascular events, such as heart failure, heart attack, stroke, angina, and medical interventions;**
- **Changes in asymptomatic cardiovascular disease; and,**
- **Early indicators of biological stress.**

At the study's inception, participants were free of clinically-recognized (or symptomatic) cardiovascular disease. For the duration of the study, they are being followed for the occurrence of cardiovascular events and cardiovascular death. All participants provided data on individual characteristics, activities and behaviors, medical history and current use of medications, diet and dietary supplements, and social determinants of health. Every year the study participants are contacted to report medical diagnoses made by a physician, significant medical procedures, and to identify deaths that may have occurred. All reports of cardiovascular diagnosis and death are verified by study physicians using hospital medical records and death certificates.

A subgroup of 3600 participants is undergoing additional clinical assessment for the progression of cardiovascular disease in its early, symptom-free stages. To identify underlying heart disease, investigators are using the following advanced noninvasive medical techniques:

- **Computed tomography (CT) scans to determine the presence of coronary artery calcification, a reliable indicator of atherosclerosis.**
- **Ultrasounds to assess the thickness of the arterial wall at specific points on the carotid artery (in the neck). This measurement, referred to as intima-media thickness (IMT), is used to determine the extent of atherosclerosis and the risk of heart attacks and strokes.**

PHOTO CREDIT: CATHY NUN

Noninvasive tests will enable researchers to compare the progression of early, symptom-free heart disease with levels of PM exposure.

PHOTO CREDIT: SARA DUBOWSKY

PHOTO CREDIT: SURESH THURAIRATNAM/MARIA BARNEY

MESA Air Pollution Study researchers are conducting air monitoring at each study location to understand the variation in concentrations of selected pollutants within the communities where participants reside. The monitors on the lamppost in the first photo are two of more than 100 sited periodically throughout each study area measuring NO_2 and NO_x. These monitors are used to determine the spatial variability of air pollution levels and the contribution from vehicular traffic. The monitor in the second photo will remain in place for the duration of the study and is measuring trends over time in $PM_{2.5}$, NO_2 and NO_x as well as the impact of nearby traffic.

use and other geographic data, and individual time activity data to estimate the exposure levels of each study participant.

Recognizing that air pollution varies within metropolitan areas, investigators are characterizing exposure down to the neighborhood level. To supplement the fixed air quality monitors maintained by government agencies, study personnel have conducted monitoring in the communities and outside of about 100 homes in each study area. Within 18 months of joining the study, participants have had $PM_{2.5}$ and gaseous pollutants measured two times for two-week periods using neighborhood monitors. To determine how much outdoor air pollution contributes to indoor PM exposure, some participants' homes have been equipped with indoor monitors for these same two-week periods. Lastly, to get a more precise estimate of individual exposure and to verify the assumptions used in the project's exposure model, some participants from these households are wearing personal monitors.

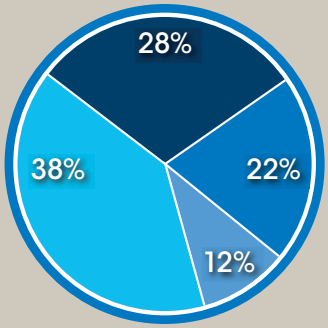
Outdoor monitors also will be used to identify relationships between PM concentrations and factors such as distance to major roads and other PM sources. These relationships will be incorporated into the exposure model in order to estimate exposure concentrations at each participant's residential address.

The University of Washington has leveraged this monitoring effort with the support of the Health Effects Institute to study the role of PM components on health effects associations. ■

To gain insight on how PM could induce atherosclerosis and heart disease, investigators also are assessing a subgroup of 720 subjects for plasma (blood) markers of inflammation, oxidative damage, and impaired blood vessel function. Research has shown that these biological markers may play a role in the development and progression of atherosclerotic plaques in the blood vessel wall.

2 DIFFERENCES IN SUSCEPTIBILITY

The risk of coronary artery disease has been shown to vary by race and ethnicity. NHLBI-MESA and the MESA Air Pollution Study are following a diverse group of older men and women between ages 50-89. Investigators will consider whether individual characteristics, such as age, the presence of subclinical disease or risk factors for diseases, residential location (inner-city or suburban), education level, and race or ethnicity, increase susceptibility to the adverse health effects of long-term exposure to ambient PM. They also will consider the influences of factors that result in a higher exposure burden, such as physical activity levels, differences in outdoor activities, residential proximity to pollution sources, housing characteristics, air conditioner use, and exposure to indoor particle sources, such as wood-burning stoves and cigarette smoke.



RACE/ETHNICITY OF STUDY PARTICIPANTS

The MESA Air Pollution Study population is comprised of the following races and ethnicities: 38% white, 28% African-American, 22% Hispanic, and 12% Asian (predominately of Chinese descent).

3 PM AND GASEOUS POLLUTANTS

Depending on geographic location and season, ambient PM levels can be associated with certain gaseous co-pollutants. Health responses might be stimulated by a mixture of PM components or by the simultaneous or sequential exposure to gaseous pollutants, such as ozone, in ambient air. The comprehensive monitoring and modeling being done in the MESA Air Pollution Study will help researchers and policymakers better understand health effects from PM in combination with other ambient pollutants. ■

REFERENCES

[1] **The Harvard Six-Cities Study:** Dockery, D.W., Pope, C.A. III, Xu, X., et al. (1993). An association between air pollution and mortality in six U.S. cities. N Engl J Med 329:1753-59.

[2] **Follow-up of the Harvard Six Cities Study:** Laden, F., Schwartz, J., Speizer, F.E., Dockery, D.W. (2006). Reduction in fine particulate air pollution and mortality: extended. Am J Respir Crit Care Med 173:667-72.

[3] **American Cancer Society studies:** Pope, C.A. III, Thun, M., Namboodiri, M., et al. (1995). Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. Am J Respir Crit Care Med 151:669-74.

[4] **Pope, C.A. III, Burnett, R.T., Thurston, G.D., Thun, M.J., Calle, E.E., Krewski, D., Godleski, J.J. (2004).** Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. Circulation. 109(1):71-7.

WEB RESOURCES

The MESA Air Pollution Study
www.mesaairpollution.org | This site provides study information, background, and contacts.

EPA National Center for Environmental Research (NCER)
www.epa.gov/ncer | This site describes EPA's extramural research program for exposure, effects, risk assessment, and risk management. NCER supports the STAR (Science to Achieve Results) grants program and graduate and undergraduate fellowships programs. Details regarding the MESA Air Pollution Study can by found by conducting a search for grant number R831697 at www.epa.gov/ncer/grants.

EPA Particulate Matter and Air Pollution
www.epa.gov/air/particlepollution | EPA provides information on PM, including general description, health effects, environmental effects, regulatory actions, monitoring, and links to research.

AIRNow
www.airnow.gov | This cross-agency Web site provides the daily Air Quality Index with maps and information on day-to-day air quality in the United States.

EPA Particulate Matter Research
www.epa.gov/pmresearch | These pages describe the research being done by EPA to better understand particle emissions, transport and atmospheric chemistry, and particle exposure and associated health effects.

DISCLAIMER: The research described in this document has been funded partially by the U.S. Environmental Protection Agency under the STAR Program. The information does not necessarily reflect the views of the Agency, and no official endorsement should be inferred.

Office of Research and Development
Washington DC 20460
EPA/600/S-06/003
December 2006

CONTACTS FOR THE MESA AIR POLLUTION STUDY

Joel Kaufman, M.D., M.P.H.
Principal Investigator
Dept. of Environmental and Occupational Health Sciences
School of Public Health and Community Medicine
University of Washington
Box 354695
Seattle, Washington 98105-4695
(206) 897-1723
mesaair@u.washington.edu

Barbara Glenn, Ph.D.
Physical Scientist
U.S. Environmental Protection Agency
Office of Research Development
National Center for Environmental Research
8723F
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460
(202) 343-9721
glenn.barbara@epa.gov