

# UPDATES FROM HEALTH AGENCIES WORLDWIDE

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Recent activity in government and non-government agencies may affect readers of *Ethnicity & Disease* and other healthcare professionals working with ethnic minority and under-served populations. Below are some current items of interest.

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## FROM THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

### People with Diabetes More Sensitive to Cardiovascular Effects from Air Pollution

People with diabetes may be at higher risk for cardiovascular problems when air pollution levels are higher, according to a new study of Boston-area residents. The ability of the blood vessels to control blood flow was impaired in adults with diabetes on days with elevated levels of particles from traffic and coal-burning power plants.

Researchers evaluated several kinds of fine particles found in urban air pollution. These included sulfate particles, which come mainly from coal-burning power plants, as well as ultra-fine particles and black carbon soot, which are generated primarily by

diesel- and gasoline-powered vehicles.

“We don’t really understand why fine particles may cause this decrease in vascular reactivity,” said Marie O’Neill, PhD, lead author of the study. “Further research is needed to confirm this association between air pollution and vascular health and to understand what causes people with diabetes to be especially sensitive.”

Researchers recruited 270 greater Boston metropolitan residents and divided them into two groups. The first group consisted of subjects with a positive diagnosis of type 1 or type 2

diabetes. The second group included subjects who were not diabetic but who had a family history of diabetes or blood sugar levels slightly higher than normal.

The investigators used a technique called brachial artery ultrasound to assess blood vessel response in the study subjects. The measurement was obtained by applying a pressure cuff to the subject’s upper arm and cutting off the blood flow through the arm’s main artery. Researchers then released the cuff, allowing the blood to rush through. The researchers then evaluated changes in the diameter of the main artery as a result of the physical stress placed on the vessel.

“We observed an 11% decrease in diabetics’ vascular reactivity on

days when sulfate particle concentrations were higher than normal,” said O’Neill. “We also noted a 13% decrease in their vascular reactivity on days with higher-than-normal black carbon concentrations.”

“We hope our study will remind people that reducing air pollution is important for everyone’s health, but especially for vulnerable members of our population, including the elderly and people with chronic health problems such as diabetes,” she said.

The funding for the air pollution monitoring was provided by the Environmental Protection Agency’s Particulate Matter Research Center.

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## FROM THE NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

### Genetic Variation Alters Response to Common Anti-Clotting Drug

Millions of people take the anticoagulant drug warfarin to prevent harmful clotting after a heart attack, stroke, or major surgery. But the proper dose of warfarin can vary greatly and can be hard to predict. Some of this variability may boil down to a recently identified gene involved in blood clotting. By

looking at the genetic makeup of people on warfarin, researchers at the University of Washington in Seattle and Washington University in St. Louis learned that variations in a gene involved in blood clotting may explain why certain people require a lower or higher dose of warfarin to get its full benefits.

This line of work ultimately could help doctors determine each patient’s warfarin dose more quickly and precisely.

Warfarin is the most commonly prescribed oral anti-clotting drug. Allan E. Rettie, PhD, University of Washington professor of medicinal chemistry and senior author of the paper, estimated that 2 million people in the United States take warfarin on any given day. Despite its

wide use, physicians find the drug challenging to prescribe. “There is a narrow window between too much and too little effect,” explained Rettie. “A small change in dose can have quite a large effect on blood processes.” For example, too high of a dose can result in excessive bleeding while too little of a dose could allow dangerous blood clots to form.

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Doctors primarily use information about a patient's sex, age, weight, and medical history to set the initial warfarin dose. However, it can take several months of clinic visits and needle pricks to determine an individual's ideal dose. Scientists know that variations in a gene encoding the CYP2C9 enzyme that metabolizes warfarin account for approximately 10% of the difference in people's responses to the drug, but tests for these genetic variations are not routinely performed.

Rettie and his colleague Mark J. Rieder, PhD, an assistant professor in the University of Washington's department of genome sciences and first author of the paper, wanted to better understand the genetic basis for variability in

warfarin response. "If you want to predict dose, you need to know more about the genes that control variability," explained Rieder.

The team focused on another gene: vitamin K epoxide reductase (VKORC1), which makes a protein that helps control clotting and is the key target of warfarin. The researchers analyzed the VKORC1 gene's DNA sequence in 186 patients on a stabilized dose of warfarin. They searched for common DNA variations responsible for changing the gene's activity and the amount of protein it made.

By matching the genetic variations to actual warfarin doses, the scientists discovered that people with a particular variation of the VKORC1 gene generally took similar doses of

warfarin. The genetic variations divided patients into three main groups: low, high, and intermediate dose. The intermediate dose group included people with a combination of the low- and high-dose gene versions. These results, the researchers said, suggest that information about the VKORC1 gene could predict a person's response to the anti-clotting drug.

"We found that 25% of the [overall] variance in warfarin dose is due to this one gene," said Rettie. "This is possibly the single biggest contributor to variability in people's responses to the drug and could be a central factor in setting the initial dose." The team also learned that certain population groups tended to have a higher prevalence of a particular VKORC1 variation.

While Asian Americans generally had the low-dose variation, African Americans had the high-dose version. European Americans fell in the middle.

Although Rettie and Rieder said there's a high probability that genetic screening for the VKORC1 gene could result in better warfarin dosing, they agreed that more studies need to be done first.

"What we've done is the basic science," said Rettie. "This complete genetic analysis of VKORC1 provides the mechanistic framework and impetus for prospective studies in a clinical setting. Such studies could determine if knowledge of genetic variability truly improves patient treatment with this frontline anticoagulant drug."

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## FROM THE WORLD HEALTH ORGANIZATION

### World Health Organization Drives Efforts to Boost Antimalarial Drug Supply

A three-day conference aimed at ensuring a reliable supply of artemisinin-based combination therapies (ACTs), the most effective antimalarial medicines currently available, was held in Arusha, Tanzania, in June 2005. A dependable supply of ACTs is crucial for preventing hundreds of thousands of deaths each year from falciparum malaria, the deadliest form of the disease. Falciparum malaria causes as many as 400 million infections a year and at least a million deaths, some 80% in sub-Saharan Africa.

The meeting, convened by the World Health Organization (WHO), brought together grow-

ers of *Artemisia annua*—the plant containing artemisinin, the raw material needed to manufacture ACT—with representatives of international and non-governmental organizations, government agencies, and companies engaged in making these medicines available to malaria patients and officials from the ministries of health and agriculture of Tanzania, Kenya, and Uganda and the ministry of trade of Tanzania.

Since 2001, 51 countries, 34 of them in Africa, have followed WHO's recommendation that they adopt ACTs as the first-line treatment for malaria. Eighteen countries adopted them in

2004 alone. The resulting surge in demand—from 2 million treatment courses in 2003 to 30 million courses in 2004 and a projected 70 million treatment courses for 2005—led to a shortfall of artemisinin and ACTs, which WHO announced in November 2004. Participants at the meeting sought to develop strategies to avert any future shortage.

One key strategy is stepping up cultivation of *Artemisia annua*, and sights have turned towards East Africa, where it grows well. "Scaling up production of the plant presents an excellent opportunity for economic development in Africa. We are already seeing the first encouraging results here in Tanzania, which started large-scale

cultivation of *Artemisia annua* in 2004.

Participants in the meeting reviewed the status of ACT supply and anticipated demand in the light of experiences over the past two years; pinpointed technical questions that need to be addressed by research; and identified sources of financial, marketing, and technical support for the production of *Artemisia annua*, artemisinin, and WHO-approved ACTs. They also examined strategies to create a sustainable market so as to reduce the price of these vital medicines.

ACTs are at least 10 times more costly than chloroquine and other commonly used malaria drugs, which are no longer effective in many regions because the malaria parasite has

become resistant to them. Twenty-five African countries have received funding for ACT procurement from the Global

Fund to Fight TB, AIDS, and Malaria, which makes it economically feasible at present for them to purchase these medi-

cines for use in public health facilities.

Countries are expected to place orders for at least 130

million treatment courses of ACTs in 2006. It is anticipated supply will be sufficient to meet that demand.

## FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

### African Americans and People Living in Southeastern United States More Likely to Have a Stroke

Two studies issued by the CDC show that racial and regional disparities in stroke prevalence and stroke-related deaths still continue to exist in the United States, particularly among African Americans. In the first study, researchers found that the years of potential life lost from stroke by African Americans before age 75 was more than double that of all other races. The second report provides further evidence that the prevalence of stroke is higher in the Southeast, also known as the "Stroke Belt," and is most significant among African Americans.

The first study titled "Disparities in Deaths from Stroke Among Persons Aged <75 Years—United States, 2002," used national and state mortality data based on death certificate information reported to CDC for 2002. The study found that

approximately 3,400 more stroke deaths than would be expected occurred among African Americans before age 65. Age adjusted stroke death rates before age 65 ranged from 37.4 (per 100,000 population) in New York to 74.3 (per 100,000 population) in Arkansas. Age-adjusted estimates of years of potential life lost before age 75 ranged from 132.7 (per 100,000 population) in Vermont to 361.0 (per 100,000 population) in Mississippi.

The second study, "Regional and Racial Differences in Prevalence of Stroke—23 States and the District of Columbia, 2003," used data from the 2003 Behavioral Risk Factor Surveillance System collected from 23 states and the District of Columbia. The states were divided in two categories—

Southeast states (Alabama, Arkansas, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia) and non-Southeast states (Alaska, Colorado, Connecticut, Hawaii, Maine, Maryland, Minnesota, Montana, Nebraska, New York, North Dakota, Ohio, West Virginia, and the District of Columbia). The study found that the prevalence of stroke was higher in the Southeast than non-Southeast states. Stroke prevalence was highest among African Americans residing in the Southeastern region (3.4%) compared to African Americans in non-Southeastern states (2.8%), White residents of Southeastern states (2.5%), and White residents of non-Southeastern states (1.8%). Differences in demographics, education, uninsured medical care and risk factors for stroke accounted for a substantial proportion of the higher stroke prevalence in the Southeast.

"It is critical that we properly address the risk factors for stroke, such as diabetes, high blood pressure, smoking, and overweight and obesity," said Dr. George A. Mensah, acting director for CDC's National Center for Chronic Disease Prevention and Health Promotion. "We must continue efforts to help people make the kind of lifestyle choices that can help prevent stroke, like eating a healthy diet, getting regular-physical activity, and not smoking. We must also continue to raise awareness of the signs and symptoms of stroke, stress the importance of calling 9-1-1 and improve emergency response and quality of care for stroke victims."

To obtain copies of the two stroke articles, please visit <http://www.cdc.gov/mmwr>. For more information about stroke prevention, visit CDC's Cardiovascular Health Program Web site at <http://www.cdc.gov/cvh>.