Lead in bone associated with increased risk of death from cardiovascular disease in men

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Growing evidence shows that exposure to lead in the environment is associated with cardiovascular disease, including increased risk of hypertension. However, those studies have looked at lead concentrations in blood, not bone lead, a better indicator of cumulative lead exposure over time. In a new study, researchers at the Harvard School of Public Health (HSPH) and the University of Michigan School of Public Health found that bone lead was associated with a higher risk of death from all causes, particularly from cardiovascular disease. It is the first study to analyze the association between bone lead and mortality.

The study appears online on September 8, 2009, on the website of the journal *Circulation* and will appear in a later print edition.

"The findings with bone lead are dramatic. It is the first time we have had a biomarker of cumulative exposure to lead and the strong findings suggest that, even in an era when current exposures are low, past exposures to lead represent an important predictor of cardiovascular death, with important public health implications worldwide," said Marc Weisskopf, assistant professor of environmental and occupational epidemiology at HSPH and lead author of the study.

Air pollution was the main source of lead in the environment in recent years, though it has been decreasing since leaded gasoline was banned in the U.S. in the mid-1990s. Most of the lead circulating in the body is deposited in bone and remains there for years, unlike blood lead, which has a half life of about 30 days. Since adverse effects from lead on the

cardiovascular system would be expected to show up over time, the researchers expected that bone lead would be a better marker of chronic toxicity.

The researchers, led by Weisskopf and senior author Howard Hu, professor of environmental health, epidemiology and internal medicine at the University of Michigan School of Public Health, analyzed data from 868 participants in the Department of Veterans Affairs Normative Aging Study, a study of aging in men that began in 1963. Blood lead and bone lead—analyzed using X-ray fluorescence—were measured for each of the participants. The results showed that the risk of death from cardiovascular disease was almost six times higher in men with the highest levels of bone lead compared to men with the lowest levels. The risk of death from all causes was 2.5 times higher in men with the highest levels of lead compared to those with the lowest levels. The results appeared independent of age, smoking, education, race, alcohol, physical activity, BMI, high density lipoprotein or total cholesterol levels, hypertension or diabetes.

There are a number of mechanisms, such as increased oxidative stress, by which lead exposure may result in cardiovascular mortality, say the authors. They also note that, in addition to high blood pressure, exposure to lead has been associated with widened pulse-pressure (an indicator of arterial stiffening) and heart disease.

Given that bone lead may be a better biomarker of cumulative lead exposure than blood lead, it may be the best predictor of chronic disease from exposure to lead in the environment. "In addition to spurring further public health measures to reduce exposure to lead and to begin monitoring for cumulative exposure, mechanistic and clinical research is needed to determine if opportunities exist to conduct targeted screening and treatment that can further reduce the burden of cardiovascular disease for the millions of adults who have had years of elevated lead

exposure in the past," said Hu.

More information: "A Prospective Study of Bone Lead Concentration and Death from All Causes, Cardiovascular Diseases, and Cancer in the VA Normative Aging Study," Marc G. Weisskopf, Nitin Jain, Huiling Nie, David Sparrow, Pantel Vokonas, Joel Schwartz, Howard Hu, *Circulation*, online September 8, 2009.

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