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Assessing a Medley of Metals: Combined Exposures and Incident Coronary Heart Disease

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Metals occur naturally in the environment, but they can also be introduced as pollutants. Some exposures to environmental metals occur through air, water, food, and consumer products, whereas other exposures occur on the job.[1] Several previous studies have evaluated associations between heart disease outcomes and exposure to individual metals, including arsenic.[2,3,4] Yet humans are exposed to many metals simultaneously in daily life. A new study in *Environmental Health Perspectives* investigates the associations between exposures to multiple metals and coronary heart disease (CHD) in a large Chinese cohort.[5]

Air and water pollution are major public health concerns in China, where cardiovascular disease is a leading cause of death.[6,7] "Metals are one of the potential components to many of these pollution sources," says coauthor An Pan, an epidemiologist at Huazhong University of Science and Technology in Wuhan.

Study participants were members of the Dongfeng-Tongji cohort, an ongoing prospective study of retired employees of the Chinese auto manufacturer Dongfeng Motor Corporation.[8] Senior author Tangchun Wu, dean of the School of Public Health at Huazhong University, is the principal investigator of the Dongfeng-Tongji cohort. Wu and colleagues measured levels of 23 different metals in blood plasma collected from more than 27,000 retired workers in Shiyan.

Over the course of 3–5 years of follow-up, a total of 1,621 study participants who were free of cardiovascular disease at baseline experienced incident CHD, including events such as heart attacks, stable or unstable angina, and coronary revascularization procedures (e.g., bypass surgery). The researchers matched these individuals with 1,621 controls who were free of CHD at baseline as well as at the end of the follow-up period. Researchers found significant associations between blood concentrations of five metals (titanium, arsenic, selenium, aluminum, and barium) and CHD risk, after adjusting for other cardiovascular risk factors.[5]

When the researchers combined these five metals in the same model, they estimated that participants in the highest quartile of arsenic and titanium exposure were 78% and 32% more likely, respectively, to have experienced a CHD event than participants in the lowest quartile. Conversely, participants in the highest quartile of selenium exposure were estimated to be 33% less

A study of more than 27,000 retired auto manufacturing employees found evidence that titanium exposure may increase the risk of CHD. However, with a median plasma titanium concentration of 30.32 μg/L among participants with CHD, it is unclear how their exposure levels compare with levels in the general population. Image: © STR/AFP/Getty Images.

likely to have experienced incident CHD than those in the lowest quartile.[5]

Wu and colleagues then looked at associations with CHD when people were classified as having low or high selenium levels in combination with low or high levels of arsenic or titanium. Among people with low selenium levels, CHD risk was higher in those who had high arsenic or titanium levels. However, in people with high selenium levels, having high arsenic or titanium levels did not appear to increase the risk of CHD. This finding suggests that having high selenium may offset adverse effects of high exposures to the other metals.[5] Previous studies have found evidence that selenium may be cardioprotective, but only within a narrow range of exposure.[9]

In a separate metals correlation analysis of a subset of 94 individuals,[5] the researchers found a moderate-to-high correlation of plasma levels of arsenic and selenium to urine/whole blood levels, and a moderate correlation of plasma levels of titanium to urine levels. "This provide some confidence [in the use of] plasma concentrations as internal biomarkers to characterize exposures to those metals," says coauthor Pan. They found no significant associations between plasma and urine or whole blood levels of several other metals, including chromium, iron, and cadmium. These metals were excluded from the final analyses.

"The correlation between titanium and heart disease is really novel and needs to be further investigated," says Yu Chen, a chronic disease epidemiologist at New York University School of Medicine who was not involved with the study. Few previous studies have explored sources of titanium exposure, so the researchers do not know how levels of titanium in their study population compare with those of other groups. Titanium, an abundant metal in Earth's crust, is used in many products, including paint and coatings, plastics, pharmaceuticals, and prosthetic joint implants.[1]

The study corroborates previous research[3,4] on the link between arsenic exposure and cardiovascular disease. "It is part of a building case that low-to-moderate levels of arsenic exposure are associated with incident cardiovascular disease," says Katherine Moon, an environmental epidemiologist at the Johns Hopkins Bloomberg School of Public Health. Future studies, she suggests, could look at measures of longer-term arsenic exposure, such as toenail clippings. Moon was not involved with the current research.

Chen points to the Strong Heart Study—a cohort of American Indian men and women—as another population in which levels of arsenic were similarly low yet still associated with CHD.[4] "It is important to see consistent associations across populations with different background risk factors," Chen says. "This gives us some confidence that the association is not due to confounding risk factors."

Lindsey Konkel is a New Jersey–based journalist who reports on science, health, and the environment.

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