Mercury's link to heart disease begins in blood vessel walls

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Heavy metals and other toxins have been linked to many human diseases, but determining exactly how they damage the body remains a mystery in many cases. New research focusing on a relatively obscure, misunderstood protein suggests mercury's link to heart disease can be traced to activation of this enzyme, which triggers a process leading to plaque buildup in blood vessel walls.

The study examined three forms of mercury, matching its characteristics in the environment. Each form of mercury caused changes in the behavior of cells that line the blood vessel walls and that can lead to cardiovascular diseases.

The study also suggests that chelation therapy, a process that removes metals from the body, and antioxidants both show signs of suppressing this activity and might be key to reducing the damage caused by mercury, and possibly other heavy metals.

The research was published in a recent issue of the International Journal of Toxicology.

"Mercury has been implicated as a risk factor in cardiovascular disease because of environmental concerns both from contamination and the atmosphere. But no one has looked at heavy metal regulation of this enzyme," said Narasimham Parinandi, director of the lipidomics and lipid signaling laboratory at Ohio State University Medical Center and senior author of the study. "If we understand this regulation and know

how to block it, we can come up with proper ways to prevent the activity."

Parinandi and colleagues focused on activation of an enzyme called phospholipase D, or PLD, in cells that line arteries in the lung. They exposed the cells to the inorganic, environmental and pharmaceutical forms of mercury, and observed that all three forms activated the enzyme.

The activation of the enzyme involves a complex sequence of events in the cell membranes that in turn releases phosphatidic acid, which can damage cells in the vessel lining – called endothelial cells – and is believed to contribute to vascular disorders.

To further test the enzyme's role in blood vessel lining damage, the scientists then showed that metal chelators and antioxidants lessen the mercury-induced activation of the enzyme in endothelial cells. This portion of the study showed that different types of mercury affect the cells in different ways.

In the three forms of mercury – methylmercury chloride, (environmental form), thimerosal (pharmaceutical form) and mercuric chloride (inorganic form) – the enzyme activation was prevented by metal chelators, which are organic chemicals that bind with and remove free metal ions from substances.

The power of methylmercury chloride to activate the enzyme was also affected by antioxidants, including vitamin C, suggesting that this form of the metal generates free radicals. This is the form of mercury most closely associated with the food supply.

"Chelators overall did a better job than antioxidants at protecting against mercury activation of the enzyme," said Thomas Hagele, first author of

the study and an undergraduate researcher in Parinandi's lab. "This shows that activation of the enzyme is not isolated to one location in the cell. Since we can protect against the enzyme activation with both chelators and antioxidants, that means a few different types of activation are likely to occur, depending on the toxin."

This research is not just about mercury, noted Parinandi, also an assistant professor of pulmonary, critical care and sleep medicine. Mercury in this case acts as a model for other toxins that have similar effects on blood vessel walls, pointing to what happens in the body when toxic substances are a factor in causing diseases.

Source: Ohio State University Medical Center