# Heavy Metal

Metals are at once essential and unavoidable in our environment. Now a growing body of research at Columbia Mailman School is uncovering their health risks—and exploring state-of-the-art antidotes for overload.

By Carolyn Wilke

Photograph: Unsplash

Present in the Earth's crust since our planet formed, metals are everywhere. They occur in soils and rocky ores. They circulate in the water we drink and the air we breathe. Our food—from vegetables to grains to fish—carries metals too. Our daily activities expose us to metals, in our surroundings and in commercial products. (A new study at the School even found metals in tampons.)

"These are really important environmental exposures," says Ana Navas-Acien, MD, PhD, MPH, Leon Hess Chair and Professor of Environmental Health Sciences. And with its myriad biological interactions, the metallome—the array of metals in our bodies—is crucial to human health.

Many metals are essential for life, such as potassium, calcium, and magnesium. Others, including copper, zinc, and iron, are required in small amounts. As parts of proteins and enzymes, these metals enable the chemical reactions that keep us alive. But the body's relationships with some of these substances can sour if they are present at too high a concentration. Meanwhile, other metals and metalloids are toxic at even low levels. These elements—lead, cadmium, mercury, and arsenic—can wreak havoc on cells and tissues.

Human activities, such as mining or burning fossil fuels, can liberate metals, including toxic ones. As chemical look-alikes of essential metals, harmful metals can interfere with biological processes. For instance, lead mimics calcium while cadmium imitates zinc. "That's one of the key ways in which they induce toxicity," Navas-Acien says.

Metal exposures contribute to manifold health problems. Some metals can cause skin, bladder, or lung cancer. Others play a role in heart disease and diabetes. And some, like lead, are potent neurotoxins. Ten years ago, when lead poisoned the water supply for Flint, Michigan, David Rosner, PhD, MPH, the Ronald H. Lauterstein Professor of Sociomedical Sciences and professor of history, helped bring a spotlight to the situation, writing about the crisis and placing it in a long history of lead contamination from paint and gasoline.

Today, researchers at the School continue to push metals research forward with interdisciplinary work that weaves together strategies from chemical analysis to community partnerships. They are bringing to light exposures from everyday sources, such as water and cannabis. They are tracing the connections between metal exposures and health impacts on individuals and populations. And they're exploring approaches that could remove metals from the body to improve health and treat disease.

**MANY INSIGHTS INTO THE HEALTH EFFECTS OF METAL EXPOSURES HAVE FLOWED FROM LONG-TERM ONGOING PARTNERSHIPS BETWEEN RESEARCHERS AT THE SCHOOL AND INDIGENOUS COMMUNITIES.** Tribal groups are often faced with elevated concentrations of metals in their drinking water and environment. Meanwhile, Indigenous people in the United States shoulder a greater burden of heart disease than the general population. Since the late 1980s, the Strong Heart Study has investigated heart disease, including its mortality and risk factors, by following thousands of tribal members across several states.

Through work with the Strong Heart Study beginning more than 15 years ago, Columbia Mailman School researchers have uncovered links between arsenic exposure and heart disease and between multiple metals and lung disease, as well as certain brain conditions and cancers. Scientists at the School have also unveiled how exposure pathways and the body's metabolism contribute to disease risk, revealing that interventions—from public health to precision medicine—will need to consider environmental exposures, Navas-Acien says.

In its decades-long history, the Strong Heart Study has emphasized community ownership of data and community input into the research, as well as connections—through workshops and visits—between tribal groups and researchers. Columbia Mailman School researchers followed its model when they developed new projects such as the Strong Heart Water Study, which began in 2015. Working with tribal members, the collaboration investigated the efficacy of water filters in reducing arsenic exposures in a Northern Great Plains American Indian nation.

The project, which recently finished, saw a 47 percent decrease in arsenic levels in individuals' urine after a two-year period with use of a mobile health program and a drinking water filter. But not all the lessons were scientific. Navas-Acien recalls wanting to work quickly to achieve water quality improvements. "I learned hard lessons that, as a scientist, you need to be very respectful of the timing, the process," she says. "You need to listen." Science has been slow to recognize the depth of knowledge that rural and Indigenous communities carry. With community feedback, the team altered their experimental approach—favoring a comparison between two groups that both installed water filters but received different types of instruction during the intervention rather than a typical scientific approach using a control group. The tribe had raised concerns about a control group potentially drinking more contaminated water during the study. Navas-Acien's experience with these communities—their deep interest, grasp of scientific topics, and feedback—has underscored how much she and other researchers can learn from them. "It's very humbling."

New directions prompted by findings from the Strong Heart Study have seeded a partnership between researchers across schools at Columbia University and Missouri Breaks, a research organization focused on tribal communities. Beginning in 2022, the Columbia University Northern Plains Partnership for the Superfund Research Program has been searching for environmental health solutions to harmful metals in drinking water sources near abandoned uranium mines and Superfund sites. "There's a huge team of us trying to understand how water consumption, specifically arsenic and uranium [in the water], leads to cardiometabolic diseases such as heart disease and diabetes," says Tiffany Sanchez, PhD, assistant professor of Environmental Health Sciences. And with the possibility of new or renewed mining activity in the Northern Plains, some tribes have approached the researchers to measure metal levels in waterways and learn about potential increases in metals contamination.

**BUT WATER IS FAR FROM THE ONLY WAY IN WHICH PEOPLE TAKE IN METALS,** and researchers at the School have uncovered other metal exposures that have received less attention. In 2021, Sanchez was walking around New York City noticing how many new cannabis shops had cropped up and thinking about how someone needed to figure out what was in these products. After all, the cannabis plant is known to guzzle up metals that are present in water, soil, and chemical treatments as it grows. "I realized it should be me—I should be doing that research," she says. Her realization kicked off work digging through publicly available data collected between 2005 and 2018 on thousands of people in the United States. Sanchez

## ANA NAVAS-ACIEN IS NEW CHAIR OF ENVIRONMENTAL HEALTH SCIENCES

Ana Navas-Acien, MD, PhD, MPH, who joined the School in 2016, has been named Leon Hess Professor and Chair of Environmental Health Sciences. Announcing the appointment, Dean Linda P. Fried, MD, MPH, said: "Ana has distinguished herself as an exemplary and internationally renowned scholar and educator, a champion of environmental justice, and a thoughtful colleague and caring mentor."

Navas-Acien has published more than 350 peer-reviewed publications and leads multiple National Institutes of Health–funded projects and centers. In addition to the Strong Heart Study and the Columbia University Northern Plains Partnership for the Superfund Research Program, she is principal investigator of the VapeScan Study in collaboration with colleagues at the Vagelos College of Physicians and Surgeons and the Chronic Kidney Disease of uncertain origin (CKDu) CURE Consortium. She has served on numerous committees with the National Academies of Sciences, Engineering, and Medicine, and in 2023, was appointed by President Joseph Biden to the National Cancer Advisory Board. From 2013 through 2023, she was the founding editor in chief of *Current Environmental Health Reports*, now a top environmental health journal.

Navas-Acien is faculty director of the Program to Inspire and Mentor Undergraduates in Environmental Health Science Research (PrIMER) and received the 2019 Dean's Excellence in Mentoring Award at Columbia Mailman. She is also a member of the Herbert Irving Comprehensive Cancer Center and an associate member of the Earth Institute. She co-chairs the Columbia Climate School postdoctoral program, helping to ensure a future of strong scholars taking on some of science's most pressing issues.

and her team combined data on cannabis usage with measurements of the levels of five metals in blood and urine.

People who reported using marijuana had elevated levels of cadmium and lead in their blood and urine as compared with people who didn't use the drug. "This is the first study of metals in marijuana users," says Katlyn McGraw, PhD, a postdoc in Environmental Health Sciences who is the lead author on this work. As a federally illegal drug, cannabis was covered by a patchwork of different rules across different states. Such evidence points to a need for federal regulation and more stringent guidelines on contaminants in cannabis products, she says. Sanchez's team now plans to look for links between metals in cannabis and risk factors for heart and lung disease.

**WHEN CERTAIN METALS, SUCH AS LEAD AND CADMIUM, ENTER THE BODY, THEY CAN LODGE THEMSELVES IN THE BONE, WHERE THEY CAN LINGER FOR DECADES, DISPLACING CALCIUM.** Columbia Mailman School researchers wondered if metals could be removed from the body to improve health. They've revived an idea that first gained traction in the 1950s—infusing metal-grabbing molecules into people to pry toxic metals from the body so that they can be excreted in urine. The tactic, called chelation therapy, has shown that it could help some people who had had heart attacks to live longer, but the benefit was inconsistent across studies.

Analytical chemist Kathrin Schilling, PhD, Navas-Acien, and others won a 2023 Precision Medicine Pilot Grant from Columbia's Irving Institute for Clinical and Translational Research to explore the approach. In one pilot study, 20 people above the age of 70 with diabetes received weekly infusions of ethylenediaminetetraacetic acid, or EDTA, over the course of a year. Based on patients' blood and urine samples, the team saw that the molecule was successful at clawing metals out of the body. EDTA removes metals—harmful and essential alike—of a particular charge. So, the researchers gave a supplement to replenish needed metals, such as calcium.

Many of the study participants saw health improvements, Schilling says. Some of these patients had limb ischemia—a condition that hampers blood flow to the limbs, creating a risk of losing fingers, toes, or a limb—and were expecting to have an amputation. "Most of them didn't have to go through with the amputation." That suggests that EDTA can remove the calcium from plaques in the veins, restoring blood flow. Based on chemical signatures of the metals, the researchers can clue in to where in the body the EDTA treatments strip metals from. A second study investigated the potential for chelation therapy to remove metals from younger people. In ten volunteers aged 25 to 40 who received three infusions, the team studied the relationship between EDTA dose and the amount and types of metals removed. The study found that low doses were effective at removing lead. These findings can help clinicians tailor the dose of EDTA to remove lead while preserving other elements.

Metal-removing infusions to prevent disease may take time to reach the clinic. But in the meantime, reducing metals exposures can improve health. Columbia Mailman School researchers documented a decrease in blood lead levels of Indigenous people in Arizona, Oklahoma, North Dakota, and South Dakota over ten years. Over the decade, those same people showed decreases in systolic blood pressure. The improvement was similar to what could be achieved by taking blood pressure medication, starting an exercise regimen, or decreasing salt intake, says recent graduate Wil Lieberman-Cribbin, PhD '24, who led the work while pursuing his PhD, working with Anne Nigra, PhD '20, an assistant professor. "There's a really immediate benefit of lowering the amount of metals in the environment or in the body." Seeing those benefits is motivating to Columbia Mailman School researchers, who will continue uncovering the sources and health impacts of metals so that consumers and policymakers alike can take steps to reduce exposures to these ubiquitous contaminants. ●

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