



Heavy Metal?

THE LATEST EVIDENCE ON ALZHEIMER'S

DISEASE AND METAL EXPOSURE

Recently, a study by Consumer Reports found lead and cadmium in several popular dark chocolate bars, leading many of us to give up our favourite treat. The study found that for 23 of 28 bars tested, consuming the very modest serving size of just one ounce daily would exceed levels considered harmful to health for at least one of these metals, according to limits established by the California Office of Environmental Health Hazard Assessment.

METALS ARE WIDESPREAD IN OUR ENVIRONMENT. ONCE INHALED, INGESTED, OR ABSORBED, THEY CAN REACH THE BRAIN AND MAY HARM BRAIN HEALTH, DEPENDING ON THE DEGREE OF EXPOSURE.

Mind Over Matter® rounded up the latest evidence and spoke to experts about common metals and their potential links to Alzheimer's disease (AD). This article summarizes what's known about lead, cadmium, aluminum, manganese, and iron relative to AD, plus some surprising facts about exposure risks.

We also discuss what to do if you suspect you have been exposed to dangerous levels of metals.

DESCRIBING METALS THAT AFFECT HUMAN HEALTH

Many articles and news stories about the health risks of metals equate "heavy" with toxicity, which isn't accurate. Technically, a heavy metal has a high atomic mass on the periodic table of

elements. But without a chemistry degree, it's tricky for the average individual to use the correct terminology.

"Grouping metals as essential versus non-essential is a more meaningful way to categorize metals affecting human health," said environmental health scientist Dr. Kelly Bakulski, associate professor of epidemiology at the University of Michigan School of Public Health.

"Non-essential metals, like lead and cadmium, are not required for bodily functions and are toxic at higher doses. By contrast, essential metals such as manganese and iron are needed by the body. Health problems result when essential metal levels are too high or too low."

NON-ESSENTIAL METALS

LEAD

Toxicity from lead exposure is a historic and modern health issue. Public health measures to remove lead from paint and gasoline were successful, but it remains in contaminated soil and dust.

If your home was built before 1970 and has paint containing lead, you may be inhaling lead in dust. Older plumbing may also contain lead, as seen in Flint, Michigan, in 2014 when corroded pipes leached dangerous amounts of lead into the drinking water. Lead is also still used in many industrial processes, such as the manufacturing of automobile batteries and electronic waste recycling.

Lead can be ingested, inhaled, or absorbed through the skin and then can enter the bloodstream.

"Lead has a similar size and charge as calcium, a key element for building bone. When lead circulates in our body, it can take calcium's place," explained Dr. Bakulski, lead author of a comprehensive review of exposure to lead, cadmium, and manganese and their relationships to AD and related dementias published in 2020 in *Journal of Alzheimer's Disease*.

"A large portion, 70 to 95%, of lead absorbed in early and middle years gets stored in bones. It can re-enter the bloodstream decades later during accelerated bone turnover that occurs with aging or osteoporosis and then travel to the brain."

Lead that crosses the blood-brain barrier can cause oxidative stress, altered signalling of essential metals, neuroinflammation, overstimulation of neurotransmitters, and the death of neurons.

Animal models of lead exposure in mice and monkeys have demonstrated elevated levels of hallmark signs of AD-related

neurodegeneration, including precursors of amyloid-beta, and tau, as well as memory deficits.

Human population studies have found an association between lead exposure and neurodegeneration. While lead has been associated with cognitive impairment and cognitive decline over time, there is currently no prospective evidence linking lead exposure directly with AD risk, Dr. Bakulski said.

CADMIUM

Cadmium is a known cause of cancer, according to the World Health Organization's International Agency for Research on Cancer. The U.S. Centers for Disease Control and Prevention's Agency for Toxic Substances and Disease Registry (ATSDR) notes that breathing high levels can cause severe lung damage, consuming high amounts in food or drinking water can severely irritate the stomach, and long-term exposure increases the risk of kidney damage, osteoporosis, hypertension, decreased lung function, and diabetes.

Some cadmium is found in all soil and rocks.

DIET IS THE PRIMARY CADMIUM EXPOSURE SOURCE: ALL FOODS CONTAIN LOW LEVELS OF CADMIUM, WITH THE HIGHEST FOUND IN SHELLFISH, KIDNEY MEATS, AND LIVER.

Drinking water can be contaminated, and inhalation exposure can occur by breathing air in or near workplaces where cadmium is processed, such as mining and refining, waste disposal and incineration, and phosphate fertilizer manufacturing.

Cigarette smoke is another source of inhalation exposure of cadmium for smokers and non-smokers alike.

"Normally, only small amounts of cadmium can cross the blood-brain barrier in adults," explained Dr. Bakulski. "But when inhaled, it interacts directly with the olfactory bulb, bypassing the blood-brain barrier. Tobacco is one of the best plants at accumulating cadmium from soil and concentrating it in its leaves."

"Animal models have shown cadmium directly causes oxidative stress, neuroinflammation, and the death of brain cells. It may also induce toxicity by changing the permeability of the blood-brain barrier, leading to the production of amyloid beta and tau tangles," said Dr. Bakulski.

"There are emerging studies linking cadmium exposure in humans with AD. Aging studies have found it is associated with cognitive impairment and AD features, but more research is needed to understand how cadmium moves into and affects the human brain." →

ALUMINUM

In the 1960s and 1970s, many people worried about exposure to aluminum from pots and pans, beverage cans, and antacids after aluminum emerged as a potential risk factor for AD. Since then, studies have failed to confirm that aluminum causes AD, and few experts believe everyday sources of aluminum pose health risks, according to the Alzheimer's Association.

They state that age is by far the greatest risk factor for AD, and other factors, such as a family history of disease and head injury, can increase the odds.

Exposure to aluminum mainly occurs through processed food, water, and products containing aluminum, such as antacids, analgesics, and medications for treating diarrhea or ulcers, according to the ASTDR. People working in aircraft, car, and metal products manufacturing facilities may have a higher risk of exposure.

"Rats given aluminum chloride are used to model Alzheimer's disease in scientific studies and to evaluate potential treatments," said Dr. Allison Reiss, an associate professor at the NYU Grossman Long Island School of Medicine and a member of the Alzheimer's Foundation of America's Medical, Scientific & Memory Screening Advisory Board. "The aluminum chloride administration mimics impaired learning and memory and brings on the accumulation of amyloid plaques."

IN HUMANS, ALUMINUM IS POORLY ABSORBED THROUGH ORAL OR INHALATION EXPOSURE. IT BINDS TO VARIOUS RECEPTORS IN THE BLOOD AND CIRCULATES TO ALL AREAS OF THE BODY, WITH THE HIGHEST LEVELS FOUND IN THE LUNGS AND BONES.

Major deodorant brands offer aluminum-free formulations, although this may be a marketing gimmick as they do not make overt health claims about the lack of aluminum: Their websites say only that these products help you "start your day with confidence" or "freshen up" with a "gentle deodorant that delivers 48-hour protection and the care you deserve."

Still, the worry about potential links between aluminum and human neurodegenerative diseases persists. Researchers at the University of Toronto and Louisiana State University conducted the largest study of aluminum concentration in post-mortem brain tissue of individuals who had neurological and neurodegenerative diseases. Their paper was published in *Journal of Alzheimer's Disease & Parkinsonism* in 2019.

The investigators examined 511 brain samples from individuals affected by one of 18 different neurodegenerative diseases

and two matched control groups. They found a statistically significant trend for increased aluminum in the brain tissue of people diagnosed with AD, Down syndrome, and dialysis dementia syndrome compared to age- and gender-matched control samples from the same brain areas.

They did not find an increase in the other disorders investigated, which included Parkinson's disease, amyotrophic lateral sclerosis, and multiple sclerosis.

"Many studies show an association between higher aluminum exposure and neurodegeneration, and chronic high levels of aluminum do result in neurotoxicity in the human brain," noted Dr. Reiss. "However, we don't have causal evidence showing it's a major player."

ESSENTIAL METALS MANGANESE

Manganese is essential for several body functions, including bone growth, blood clotting, carbohydrate metabolism, immune response, and brain function. Most manganese in our bodies comes from eating whole grains, rice, nuts, and leafy vegetables.

Elevated levels of manganese in drinking water or air are neurotoxic, impairing cognitive function that may contribute to AD development.

Excessive workplace exposure to manganese can occur in mining, welding, and battery manufacturing. A large exposure to manganese can accumulate in the brain, causing an irreversible Parkinsonian syndrome called manganism.

Dietary manganese moves across the blood-brain barrier in a regulated fashion. However, when inhaled, it is absorbed through the olfactory bulb in the brain, bypassing the blood-brain barrier, said Dr. Bakulski.

"Animal models have demonstrated that excessive manganese levels cause oxidative stress and an accumulation of amyloid beta and tau tangles. In human epidemiologic studies, researchers have found manganese bound to amyloid beta and identified that elevated manganese levels found in occupational settings were associated with cognitive decline," noted Dr. Bakulski.

"However, a direct causal relationship between excessive manganese and AD has not yet been found and will require further studies."

IRON

Iron is one of the most critical essential metals in the body. We obtain it primarily from dietary sources, including meats, poultry, seafood, and fortified bread and cereal.

Almost half of the iron in our bodies is bound to hemoglobin, enabling blood to transport oxygen to our cells. In the brain, iron is involved in myelin sheath formation, neurotransmitter production, and antioxidant enzyme function. The blood-brain barrier regulates its entry and exit from the brain.

Dr. Julie Schneider is the Deborah R. and Edgar D. Jannotta Presidential Professor of Pathology (Neuropathology) and Neurological Sciences and the Associate Director and Neuropathology Core Leader of the Rush Alzheimer's Disease Center at the Rush University Medical Center in Chicago.

Together with colleagues from the University of Melbourne in Parkville, Australia, she studied the relationships between brain iron levels and AD's biological signs and clinical outcomes. They published their findings in *Molecular Psychiatry* in 2020.

They examined brain tissue generously donated by participants in the Rush Memory and Aging Project, an ongoing long-term study collecting nutrition habits and cognitive assessment and neurological exam results of individuals without dementia when they entered the study.

"We found iron accumulation was only weakly associated with amyloid and tau. However, it was strongly associated with the rate of cognitive decline, even when iron levels were normal," said Dr. Schneider.



Our findings suggested iron plays a role in AD cognitive decline that is independent of amyloid or tau accumulation.

Dr. Schneider and her collaborators suspect iron leads to neurodegeneration when iron is stored by the protein ferritin, which provokes a cell death process called ferroptosis. According to their preliminary data, Dr. Schneider and colleagues further hypothesize that dietary fats elevate brain iron, and iron interacts with brain lipids to instigate this cell death process.

They are now conducting more studies to explore these hypotheses, including how these mechanisms may differ in the presence of misfolded proteins associated with AD, and by sex and APO4E status, the genetic marker associated with

an increased risk of developing AD. A grant from the National Institutes of Health funds their work.

PROTECT YOUR BRAIN HEALTH

Limiting exposure to non-essential metals at home or in the workplace will help protect your brain health. For example, quitting smoking or reducing your exposure to second-hand smoke, testing your soil and paint for lead if you're living in a home that was built before 1970, and testing your drinking water and using a filter or drinking bottled water if lead levels are high, are great ways to lower your risks.

Symptoms of severe metal poisoning include abdominal pain, dehydration, diarrhea, nausea or vomiting, and a scratchy throat.

Severe symptoms include an abnormal heartbeat, anemia, brain damage, memory loss, kidney damage, liver damage, and miscarriage. Keep in mind that many other conditions can cause these symptoms, making metal poisoning challenging to diagnose.

If you have been exposed to elevated levels of non-essential metals, speak to your doctor about testing, which may include blood work, urine testing, X-ray imaging, and kidney and liver function tests. Treatment may involve taking medications or stomach pumping to remove the excess metal or hemodialysis to treat kidney failure.

So, is it safe to eat dark chocolate? Without access to an accredited food testing lab, it's hard to know whether your favourite bar has unsafe levels of lead or cadmium.

"The lead and cadmium levels found in the Consumer Reports study were concerning, especially since the serving size was quite modest," Dr. Bakulski said. "However, individuals should not bear the burden of deciding whether foods are safe. Public health authorities should better regulate industries, ensuring the right tests and steps are in place to reduce non-essential metals in food products, and then educate consumers about less dangerous choices. We already have national food safety standards for cadmium in rice, so we should be able to establish standards in other industries." 🌱

MORE INFORMATION ON TOXIC METALS

The U.S. Centers for Disease Control and Prevention's Agency for Toxic Substances and Disease Registry produces summaries of hazardous substances in a series called ASTDR ToxFaq's™. Learn more at <https://www.cdc.gov/TSP/ToxFaq's/ToxFaq'sLanding.aspx>