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Article

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Our Preferred Poison: a little mercury is all that humans need to do away with themselves quietly, slowly, and surely

Let's start with a straightforward fact:
Mercury is unimaginably toxic and dangerous.
A single drop on a human hand can be irreversibly fatal.
A single drop in a large lake can make all
the fish in it unsafe to eat.

Often referred to as quicksilver, mercury is the only common metal that is liquid at room temperature. Alchemists, including the young Sir Isaac Newton, believed it was the source of gold. In the modern era, it became a common ingredient of paints, diuretics, pesticides, batteries, fluorescent lightbulbs, skin creams, antifungal agents, vaccines for children, and of course, thermometers. There is probably some in your mouth right now: So-called silver dental fillings are half mercury.

Mercury is also a by-product of many industrial processes. In the United States coal-fired power plants alone pump about 50 tons of it into the air each year. That mercury rains out of the sky into oceans, lakes, rivers, and streams, where it becomes concentrated in the flesh of fish, shellfish, seals, and whales. Last year the Food and Drug Administration determined there is so much mercury in the sea that women of childbearing age should severely limit their consumption of larger ocean fish. The warning comes too late for many mothers. A nationwide survey by the Centers for Disease Control shows that one in 12 women of childbearing age *already* have unsafe blood levels of mercury and that as many as 600,000 babies in the United States could be at risk. But that begs a critical question: At risk for what?

Infants born to mothers contaminated by mercury in Japan's Minamata Bay in 1956 had profound neurological disabilities including deafness, blindness, mental

retardation, and cerebral palsy. In adults, mercury poisoning can cause numbness, stumbling, dementia, and death. "It's no secret that mercury exposure is highly toxic," says toxicologist Alan Stern, a contributor to a 2000 National Research Council report on mercury toxicity. But high-level exposures like those at Minamata cannot help scientists determine whether six silver fillings and a weekly tuna-salad sandwich will poison you or an unborn child. "The question is, what are the effects at low levels of exposure?" he says.

Data now suggest effects might occur at levels lower than anyone suspected. Some studies show that children who were exposed to tiny amounts of mercury in utero have slower reflexes, language deficits, and shortened attention spans. In adults, recent studies show a possible link between heart disease and mercury ingested from eating fish. Other groups claim mercury exposure is responsible for Parkinson's disease, multiple sclerosis, Alzheimer's, and the escalating rate of autism.

How—and in what form—mercury inflicts damage is still unclear. Yet scientists and policymakers agree that more regulation is imperative. The Environmental Protection Agency plans to finalize its controversial first rule on reducing mercury emissions from power plants this month, and delegates from the United Nations Environment Programme met in late February to discuss an international convention limiting mercury use and emissions.

A decade ago researchers and lawmakers agreed that lead, another heavy metal, was harmful to children at levels one-sixth as high as previously recognized. But it took scientists decades to establish the scope and subtlety of lead poisoning. Mercury is now a ubiquitous contaminant. The average American may have several micrograms of it in each liter of blood, and the atmospheric burden of mercury has perhaps tripled since the industrial age. Whatever needs to be done to protect humanity from its love affair with quicksilver, it had better happen soon.

In August 1996 Karen Wetterhahn, a chemistry professor at Dartmouth College in Hanover, New Hampshire, spilled a few drops of a laboratory compound called dimethyl mercury onto one of her hands. She was wearing latex lab gloves, so she didn't think much of it. A colleague saw her at a conference the following November. "She said she thought she was coming down with the flu," says toxicologist Vas Aposhian of the University of Arizona. By the time Wetterhahn was diagnosed with mercury poisoning, in January, it was too late. Despite subsequent treatment that helped clear the metal from her body, she lapsed into a vegetative state in February and died the following June.

Scientists are at a loss to explain why mercury often takes months to exert its effects. "If we knew that, we'd know a lot more about how mercury poisons the

brain," says Tom Clarkson, a toxicologist at the University of Rochester Medical Center.

The degree of mercury's toxicity depends on the form and route of exposure. You can swallow the liquid form of elemental mercury without much fear because it doesn't easily penetrate the lining of the stomach and intestines. On the other hand, liquid mercury vaporizes at room temperature, and when you inhale the vapor it moves right from the lungs to the bloodstream to the brain. A broken thermometer can release enough mercury vapor to poison the air in a room—one reason why some cities and several states discourage the sale of mercury fever thermometers.

Mercury also binds with other elements in salts and organic compounds of varying toxicity. Dimethyl mercury, the substance that poisoned the Dartmouth chemist, is a synthetic form of organic mercury rarely found outside a lab. A simpler organic compound called methylmercury is of greater concern because methyl- mercury is the form found in the flesh of fish.

Seafood is one of the two most common sources of mercury exposure in adults. Although concentrations of mercury in air and water are increasing, they are still too small for alarm. But bacteria process the mercury in lakes and oceans into a form that accumulates in living tissue. Plankton take in the bacteria and are in turn eaten by small fish. With each meal, the mercury concentration rises. Then larger fish eat the small fish, increasing tissue concentrations still more. Fish at the top of the food chain accumulate the most mercury. The species singled out by the recent FDA advisory—big predators such as albacore tuna, shark, and swordfish—can have 100 times more mercury in their tissues than smaller fish do.

The methylmercury in fish passes readily from the human gut to the bloodstream and on into all organs and tissues. It seems to act most powerfully on the brain because the compound is strongly attracted to fatty molecules called lipids, and the brain has the highest lipid content of any organ. Methylmercury crosses the protective blood-brain barrier by binding with an essential amino acid that has dedicated carrier proteins for shunting it into brain cells. Once inside brain cells, some of it gets converted to an inorganic form that sticks to and disables many structural proteins and enzymes essential to cell function. "It can destroy the biological function of any protein it binds to," says Boyd Haley, a biochemist at the University of Kentucky.

Researchers learned how much mercury the body can tolerate from studies of victims of catastrophic poisoning, such as the Japanese sickened by eating fish from Minamata Bay and the Iraqis who ate grain treated with a methylmercury-based

preservative in the early 1970s. But those studies do not reveal how *little* mercury it takes to cause harm. At the time of her diagnosis, the Dartmouth chemist had 4,000 micrograms of mercury per liter in her blood. A diet consistently high in fish can create a blood-mercury level of about 25 micrograms per liter. That's far below a lethal dose, but it still may not be safe.

Concerns about low-level toxicity haunt discussions of another ubiquitous source of mercury exposure: silver dental fillings. Elemental mercury, which makes up half of silver fillings, releases mercury vapor, just as liquid mercury does. The vapor from dental amalgams is the primary source of the one to eight micrograms of mercury per liter of blood, that is, according to some sources, in the average American adult. That amount uncomfortably overlaps the Environmental Protection Agency's current safe level of 5.8 micrograms per liter. But the EPA's safety level is based on methylmercury exposure, about which more is known. No human studies have assessed prolonged exposure to low levels of mercury vapor. One study hints at subtle neural and behavioral anomalies in dentists, who collectively use 300 metric tons of mercury in amalgams each year and who often have two to five times the typical concentration of mercury in their urine. "I think the methylmercury in fish is probably our least toxic exposure," says Haley, who broadcasts the hazards of dental fillings.

Silver-mercury fillings have never been tested for safety. "The amalgam question will never be solved until we do a clinical trial like those we do with other medical devices," says Aposhian.

"It's really unclear what's going on with dental amalgams," says Stern, who notes that the issue is complicated by the potential for panic and lawsuits. "It's a snake pit."

One of the lessons of Minamata is that mercury, like lead, is harder on fetuses than on the women carrying them, or adults in general. In the Japanese event, women with no overt symptoms of poisoning gave birth to severely disabled children. "It was evident there was a major difference in susceptibility between the developing brain and the mature brain," says Philippe Grandjean, an epidemiologist at the Harvard University School of Public Health. "When we saw serious poisonings in Minamata, that made us wonder whether mercury could be like lead."

Studies of lead have shown that IQ decreases approximately two or three points for every doubling of prenatal and early postnatal exposure. To see if mercury has comparable effects, Grandjean, along with Pál Weihe at the University of Southern Denmark, is conducting the largest study to date of children's cognition and behavior in a population routinely exposed to low levels of mercury. His work in the Faeroe Islands of Denmark includes 1,000 mother-child pairs and spans almost 20 years. In a typical year, Faeroe islanders consume 1,000 pilot whales, or one

whale for every 50 islanders. "They belong to one of the most fish-eating populations in the world," says Grandjean.

Whale meat is one of the most highly contaminated seafoods because whales are at the top of the food chain. Even so, the mercury content of whale meat is considerably lower than that of the hypertoxic Minamata fish. An earlier study of shark eaters in New Zealand suggested that relatively high levels of mercury in a mother's hair during pregnancy correlated with a loss of three IQ points in her child. High levels, in that study, were identified as six parts per million and above in the hair shaft.

Grandjean gave a battery of sophisticated cognitive and developmental tests to the Faeroese children when they were 7 and 14. His results indicate that IQ drops 1.5 points for every doubling in prenatal exposure to mercury. The 2000 National Research Council report concluded that the risk documented by Grandjean "is likely to be sufficient to result in an increase in the number of children who have to struggle to keep up in school."

"We learned there is a response at low levels," says Grandjean. "It's not a huge loss, but it's certainly not negligible."

Yet in another large, long-term epidemiological study conducted on the Seychelles Islands in the Indian Ocean, Clarkson has so far found *no* effect on neurological development from prenatal exposure to low levels of mercury in seafood. "We can't exclude effects from 20 parts per million or even 12 parts per million," he notes. But he concludes there is no graded risk that extends to the lowest exposure levels.

The 2000 research council report evaluated the Faeroe, Seychelles, and New Zealand studies and recommended that the EPA set safety standards based on Grandjean's more sobering findings. The agency did. Then, for good measure, it added a 10-fold uncertainty factor—a safety margin to protect against scientific unknowns and individual differences in response to a toxin. The uncertainty factor lowers the threshold to a figure of 5.8 micrograms per liter of blood and 1.2 parts per million in hair.

The problem with safety factors is that they create a toxicological limbo between demonstrably harmful doses and levels that have been declared safe. Thus, when Centers for Disease Control surveys find that one in 12 American women of childbearing age—8 percent—have blood mercury levels above the safety threshold, the implications aren't clear, either for them or for the children they bear. Epidemiologist Tom Sinks says, "It doesn't tell us there's a hazard."

"The whole idea of a safety factor is to protect people," Clarkson says. "You can't turn it around to use as an indication of who's at risk. If you're just above it, you aren't necessarily in trouble."

That kind of hedging, along with disagreement among population studies, leaves regulators with plenty of wiggle room. The FDA, for example, uses a more relaxed safety standard for mercury based on studies from the 1970s and 1980s. Where the EPA safety level for daily exposure is 0.1 microgram per kilogram (about 2.2 pounds) of body weight, the FDA's standard is about 0.4 microgram per kilogram per day. The difference is four times as much mercury.

Concern about early exposure to mercury doesn't end at birth. Until recently, many infants received regular injections of mercury on a state-mandated, medically sanctioned schedule. The mercury came from a compound called thimerosal that has been used as a preservative in vaccines and other medicines since the 1930s. In 1999 the FDA recommended that thimerosal no longer be used in pediatric vaccines, and manufacturers have removed it from all but the influenza vaccine. But some scientists and many more aggrieved parents are convinced that thimerosal in childhood vaccines has already caused, or at least catalyzed, the U.S. epidemic of autism.

An estimated 400,000 Americans today have autism, a once rare neurological disorder characterized by social withdrawal, difficulty communicating, and involuntary, repetitive movements. Although the exact numbers are in dispute, the rate of diagnosis seems to have climbed sharply in the last decade. In California the incidence of autism was six times higher in 2002 than in 1987.

During that period, federal health officials added four new kinds of vaccines to the childhood immunization schedule, and the amount of mercury routinely administered to infants in the first six months of life more than doubled. Throughout the 1990s, a 3-month-old baby might receive as much as 63 micrograms of mercury in a single visit to a doctor—roughly 100 times the daily EPA safety level. By the age of 6 months, properly immunized children were exposed to at least 188 micrograms of mercury in a series of at least nine injections. Although the 1999 FDA action minimized such exposure, some infant flu vaccines still contain 12.5 micrograms of mercury per dose—more than 10 times the daily EPA safety level for a 20-pound baby.

Circumstantial evidence also implicates mercury in autism. Some of the symptoms of autism and mercury poisoning are similar, and Haley has garnered evidence from hair samples that autistic children do not clear mercury from their bodies as efficiently as most kids do. They may have a genetic susceptibility that allows more mercury to accumulate in their tissues, he says. That could make them more

vulnerable to mercury-laced vaccines and the continuous low-level exposure from their mothers' dental fillings. "It is amazing to me that no one has taken the tissue of autistic children to see if there is excess mercury there," Aposhian told a committee at the Institute of Medicine in Washington, D.C., last year. "That's one thing that really has to be done."

There are other sources of uncertainty. The form of mercury in thimerosal—an organic compound called ethyl mercury—is the least studied of all mercury's incarnations. When scientists argue about its toxicity, they typically rely on data from methylmercury, which may not be an equivalent form of exposure. Experts even disagree about whether ethyl mercury can cross the blood-brain barrier. (It probably does.) "There are no good ways to measure ethyl mercury in tissue," toxicologist Polly Sager of the National Institute of Allergy and Infectious Diseases told the Institute of Medicine committee.

The Institute of Medicine concluded last May that no claim could be made for a causal link between mercury-laced vaccines and autism, but several independent researchers had complained that their access to federal vaccine databases, which could provide evidence of a link, had been repeatedly blocked. A few scientists, including Haley and neuropharmacologist Richard Deth of Northeastern University in Boston, continue to study possible mechanisms for the connection. Deth reported last year, for example, that in human nerve cells thimerosal blocks a chemical reaction called methylation that is critical to gene activity and that is also disabled by exposure to lead.

The report that first triggered worries about a connection between vaccines and autism was published in the British medical journal *The Lancet* in 1998. It described eight children whose behavioral problems surfaced within two weeks of receiving the measles-mumps-rubella vaccine. *The Lancet* and most of the article's coauthors ultimately disowned the study because its lead author had not divulged that he was also being paid to conduct research for parents seeking to sue vaccine manufacturers. Nonetheless, the number of parents in the United Kingdom willing to immunize their babies with the vaccine dropped from 90 percent in 1998 to less than 80 percent in 2004.

Health officials in the United States addressed suspicions about immunization by recommending that thimerosal be removed from pediatric vaccines. Thimerosal might yet prove harmless, they reasoned, but the threat to public health posed by a drop in immunization rates was not worth risking. The same balance of risks exists regarding the issue of mercury in fish. The current Federal Dietary Guidelines Advisory Committee Report recommends at least two fish meals a week. Fish are high in omega-3 fatty acids, which have proven benefits in preventing heart disease, the number one killer in the United States. "We know mercury is a hazardous

substance," says the CDC's Sinks. "We know that less is better than more. We know that fish and shellfish are the principal source of methylmercury. But we also know that fish and shellfish are pretty nutritious food: high in protein, high in vitamins. They contain healthy fats."

But troubling evidence suggests that methylmercury in fish might *cause* heart disease. A seven-year study of more than 1,800 men in Finland showed that those who ate the most fish doubled their risk of heart attack compared with those whose diets had less fish. The same men showed the same increase in risk for death from coronary and cardiovascular disease. And Grandjean's Faeroe Islands study found that prenatal exposure to mercury caused significant increases in blood pressure among 7-year-olds.

The most troubling aspect of this controversial heart-disease data is that deleterious effects occur at mercury-exposure levels equal to or lower than for any other toxicological outcome, including the subtle neurological symptoms in the Faeroe Islands study. In Grandjean's most recent examination of 14-year-olds, he has found a doubling of certain neurotoxic effects at five parts per million in hair samples. In the Finnish study, the men with the doubled risk of heart attack had hair samples with only two parts per million of mercury. They were eating little more than an ounce of fish a day. Stern speculates that 10 percent of American men may already eat enough fish to raise their risk of heart attack. "There's this interaction between mercury and fish oils that makes it very complicated because they both come from the same place," he says.

The National Research Council report noted that low levels of mercury contamination might also harm the immune and reproductive systems. And mercury is being investigated in relation to Alzheimer's, Parkinson's, attention deficit disorder, and multiple sclerosis. But many low-level developmental effects will be difficult to identify, Stern says, because the compromised organ or function still falls within the range of normal. The intelligence scores of the Faeroese children, for example, were not pathologically low; it took rigorous statistical analyses to prove they were simply lower than they would have been otherwise. Likewise heart disease, as the nation's leading killer, has plenty of confounding variables. "You're looking to pull a signal out of a lot of noise," Stern says.

That signal might soon get a lot stronger. While mercury contamination is no longer a threat in most childhood vaccines, it is likely to get worse in fish. "Because of the beneficial effects of fish consumption, the long-term goal needs to be a reduction in the concentrations of [methylmercury] in fish rather than a replacement of fish in the diet by other foods," said the council's report.

That goal is nothing less than unrealistic.

Mercury was a naturally occurring element in Earth's atmosphere long before coal-fired generators, medical-waste incinerators, and chlor-alkali plants put more there. Some mercury escapes into the air when volcanoes erupt and mountains erode. It stands to reason that mercury has been accumulating in the flesh of fish, shellfish, and marine mammals since humankind began eating them—which is most likely why humans have a protein called metallothione to help detoxify mercury and other heavy metals.

But human activities have caused the mercury content of the atmosphere to rise by 1.5 percent a year, according to the U.S. Geological Survey, and the problem is global. Roughly half of the mercury deposited on U.S. soils and streams comes across the Pacific from Asia. Last year a United Nations report found that the toxin can travel thousands of miles in the atmosphere to contaminate pristine and uninhabited areas, such as the Arctic. Still, the United States has so far balked at attempts by the United Nations Environment Programme to draw up a binding protocol to reduce mercury pollution worldwide.

In the 1990s the United States made considerable progress in curbing emissions from incinerators for medical and municipal waste. Yet the number of states issuing local fishing advisories went from 27 to 48 in the last decade. Due to heightened concern, advisories for mercury are increasing faster than for any other pollutant.

The EPA is in the final stages of formalizing a rule that would limit emissions from coal-fired utilities, which produce 42 percent of the nation's domestic mercury pollution. The agency's standing proposal has been for a 70 percent reduction in mercury emissions by 2018. But environmentalists argue that the Clean Air Act calls for a 90 percent reduction by 2008. In 1992 the Natural Resources Defense Council sued the EPA for not maintaining the act's standards, and in 1994 the parties reached a settlement. Under the terms of the agreement, the agency is required to issue a cleanup rule this month.