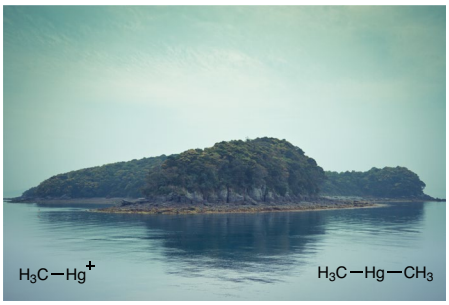
Methylmercury as a molecular imposter

Amina Schartup relates how our understanding of methylmercury has changed in the 170 years since it was discovered — as well as some of the disasters that occurred along the way.

Organometallic chemists first synthesized methylated mercury compounds almost two centuries ago. In 1849, Edward Frankland discovered that he could produce organometallic compounds by reacting zinc with methyl iodide, and his group's attempts to replicate the reaction with mercury resulted in the preparation of a range of organomercury compounds including 'iodide of hydrargyromethylium' (methylmercuric iodide)[1]. But in 1865 two colleagues inhaled toxic volatile dimethylmercury while cleaning a spill. Both died, one within two weeks and the other about a year later, becoming the first documented cases of methylmercury poisoning[2]. Yet interest in methylmercury did not diminish, and the following century is filled with mono- and dimethylmercury disasters.

Methylmercury's ability to kill also fed its usage. It is a powerful antiseptic, disinfectant, fungicide and weed killer — so much so that by 1914 it became a commercial treatment for seeds: methylmercury would protect the seeds until germination but would not transfer to the plant. Treated seeds were stored in grain sacks carrying various warning signs against direct consumption — but warnings are only useful if they can be understood. The warning labels in foreign languages meant nothing to farmers in rural Iraq supplied with treated seeds in the winter of 1971/72 — too late in the agricultural cycle to be planted that year — who used some of the seeds for bread. This failure of communication resulted in one of the largest recorded mass poisonings with hundreds of human (and farm animal) deaths and over 6,000 people hospitalized.

This disaster occurred just after another infamous case of methylmercury poisoning, which unfolded on the shores of Minamata Bay, Japan. Aside from the magnitude of the human and environmental damage inflicted by the Minamata disaster, it is also the case that established methylmercury as an environmental pollutant — and gave its name to both the disease caused by methylmercury exposure and the international agreement that calls for curbing human mercury releases.



Minamata Bay, Japan, overlaid with the structures of monomethylmercury (left) and dimethylmercury (right). Credit: Gregory Ferguson / Moment Open / Getty

In 1932, a chemical factory in Minamata began producing acetaldehyde using a mercury catalyst. Methylmercury — a by-product of this process — was unknowingly dumped with the industrial wastewater into Minamata Bay. There it accumulated in fish, and by 1952 reports of dead fish and 'drunk' cats and birds were widespread. A 'mysterious disease' also began spreading among humans, but it was not until 1958 that methylmercury poisoning was identified as the culprit, almost a century after the symptoms were first described[2]. It took another half a century for victims of this disaster to receive compensation.

In 1967, two Swedish researchers, Sören Jensen and Arne Jernelöv, made a stunning discovery that changed the course of mercury research[3]. They found that inorganic mercury released into the environment can be naturally transformed into mono- and dimethylmercury by microbes living in the sediment of aquatic systems. Therefore, methylmercury would remain present in the environment and accumulate in aquatic life, even if all industrial sources of methylmercury are halted.

By the 1970s, researchers were finding elevated methylmercury levels in fish, fish-eating birds and marine mammals. The highest concentrations were reported in top predators, indicating that methylmercury biomagnifies — that is, it increases exponentially with each level in the food chain. This did not bode well for humans, who are the ultimate predator, and environmental agencies worldwide began monitoring methylmercury levels and issuing advisory notices on safe fish consumption.

Today, we know that methylmercury is ubiquitous — it is found in snow and ice of the North Pole[4], in the open ocean[5] and in deep-sea fish[6]. Methylmercury's global footprint is due primarily to hundreds of years of inorganic mercury usage and releases into the environment[7], where both biotic and abiotic processes convert the inorganic mercury into mono- and dimethylmercury[8,9]. Once formed, these compounds enter organisms and accumulate, so that relatively low-level but long-term exposure has been associated with a wide range of health impacts[10].

Methylmercury toxicity is thought to be due to its ability to bind with cysteine and mimic the amino acid methionine. This imposter can enter the brain via the blood–brain barrier where it breaks down into inorganic mercury. But inorganic mercury cannot traverse this barrier — instead, it binds to and deforms important proteins and damages the brain. The insidious nature of methylmercury has made it one of the most studied but still intriguing environmental neurotoxicants. ❐

Amina T. Schartup ✉
Scripps Institution of Oceanography, University of California, San Diego, La Jolla, CA, USA.
Twitter: @Tamina38
✉*e-mail: aschartup@ucsd.edu*

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