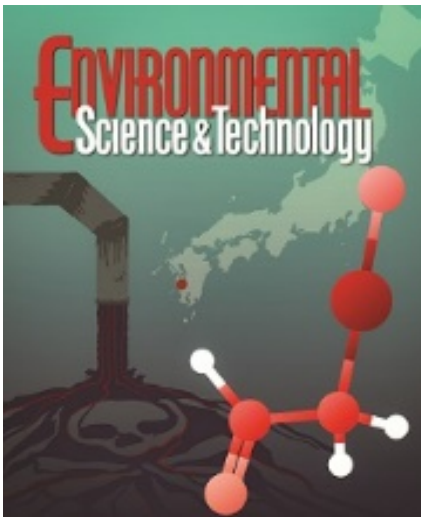
Rethinking the Minamata Tragedy: What Mercury Species was Really Responsible?



In the 1950's and 60's in the coastal fishing community of Minamata, Japan, industrial mercury dumping caused one of the most notorious mass-poisonings seen in human history. At the start, the cause of what later became known as Minamata disease was not clear. It was the local cat population that first showed "dancing cat disease" with neurological signs and death. Shortly thereafter, residents of Minamata village began to show similar symptoms. A local chemical plant used a mercury catalyst in the manufacture of acetaldehyde, and industrial waste from the plant was dumped into the Minamata River, which flows into Minamata Bay.

In late 1960 the plant physician tested his suspicions that industrial dumping of mercury might be the cause of Minamata disease by feeding ten cats food laced with the industrial waste from the plant. All the cats rapidly developed Minamata disease, and while the doctor was not allowed to pursue his experiments, one specimen was preserved; the brain of Cat 717.[1] In subsequent years it became widely accepted that industrial dumping of mercury was to blame for Minamata disease. For decades the poisoning was thought to derive from waste contaminated with inorganic mercury compounds (used in the chemical plant) flowing into Minamata Bay. Here, microbes in anaerobic muds and sediments were thought to methylate inorganic mercury to form methylmercury, which can accumulate up the food chain, eventually ending up in fish and other seafood that might be consumed by humans. It was thought that through these microbial transformations, and subsequent consumption of fish is what caused the harmful effects to the local human populations. The tragic mass poisoning at Minamata is used as a classic example of the biomethylation process and is taught to undergraduates.[2] Moreover, much of what we thought we know about how methylmercury affects humans is derived from the Minamata tragedy. More recently a re-evaluation of the histology of Cat 717 showed effects that were consistent with organic mercury exposure[1] and direct release of methylmercury by the factory the factory was suggested to have been responsible, although conventional analysis showed only a minor fraction of methylmercury in the brain of Cat 717.

A collaborative research team (*University of Saskatchewan*, *University of Rochester*, *National Institute for Minamata Disease, Stanford Synchrotron Radiation Lightsource*) has used high-energy resolution fluorescence detection x-ray absorption spectroscopy (HERFD-XAS, *beam line 6-2*, *SSRL*) to re-examine cerebellar brain tissue from the historic samples from Cat 717 to reveal two forms of mercury, a majority component of sulfur-bound organometallic mercury with smaller amounts of β-HgS (metacinnabar). These observations were complemented with analysis of the extended X-ray absorption fine structure (EXAFS, beam line 7-3 SSRL) indicating quantitatively similar mercury environments of sulfur-bound organometallic mercury and a small contribution of β-HgS, which might be a by-product of organometallic mercury degradation over time. These results showed for the first time that a large quantity of organic mercury was present within the brain tissue of Cat 717. Given that the cats were fed plant effluent directly, with no environmental transformation, this means that the plant was dumping organic mercury. Moreover, exposure to organic mercury is consistent with the pathology observed following dosing of the cats, but not with inorganic mercury which would

cause different signs. Finally the subsequent histology of Cat 717 is also consistent with organic mercury exposure.

However, until now the only form of organic mercury that has been considered is methyl mercury. New Density functional theory (DFT) calculations of the reaction mechanism of acetaldehyde production showed that there was no energetically tractable mechanism by which methymercury could form. These calculations instead suggested that the form being dumped was in fact α-mercuri-acetaldehyde, or a chemically related species. While such compounds are well-known chemically as high-melting stable solids, α-mercuri-acetaldehyde and related compounds are as yet un-researched organic mercury compound.

The narrative of Minamata disease is fraught with controversy. Since the 1950s, both inorganic mercury and then methylmercury have been considered to be the cause of the disease. This work, using HERFD-XAS, EXAFS and DFT found that a previously unexplored form of organic mercury, α-mercuri-acetaldehyde is likely the organic form of mercury that was released from the Chisso factory and ultimately responsible for the devastation of Minamata disease observed decades ago. Furthermore, these findings highlight the possibility that instances of organic mercury poisonings in the past where methylmercury, the most commonly studied form of organic mercury, was assumed to be the cause may in fact be incorrect. In these cases, it is apparent that more toxicological research is necessary on alternative organic mercury species. More broadly, attention to unambiguously pinpoint chemical species in toxicological studies is significant as this may better improve our understanding of chemical mechanisms consequential to the health of biological and environmental bodies.

References

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2. C. D. Klaassen, "Toxic Responses of the Ocular and Visual System", in *Casarett & Doull's Toxicology: The Basic Science of Poisons;* Fox, D.A., Boyes, W.K., Eds.; McGraw-Hill: New York (2013), Ed. 8.

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Contact

Graham George, University of Saskatchewan

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