The Delayed Appearance of a Mercurial Warning

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Abstract: The publication of a 1971 study from Japan on chronic methylmercury poisoning in adults provides an occasion to reexamine the history of Minamata disease and its social and political repercussions. Research findings were suppressed or held back due to controversies that were tearing the Japanese scientific community apart. Similar controversies occurred outside of Japan as well. Only now are the long-term adverse effects of environmental methylmercury exposure becoming clear. The delayed release of the 1971 results therefore reminds us as epidemiologists of our obligation, even in the presence of scientific uncertainty, to call attention to preventable risks.

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The tragic tale of Minamata disease is well known,[1,2] but its epidemiologic aspects keep unfolding. As early as 1953, the local inhabitants in this Japanese fishing village knew that their cats were dying from cramps, which they dubbed the "dancing disease." Fish were found belly-up in Minamata Bay and in nearby waters. The company doctor at a local chemical factory was able to reproduce the dancing disease by feeding cats effluent water from the factory. However, this research was suppressed by the company, and the results became public only 40 years later.[3]

The first cases of Minamata disease were reported in 1956. The cause of this chronic neurologic syndrome (with tunnel vision, dysarthria, ataxia, and paresthesias) was unknown at first. The link to seafood consumption was quickly revealed, and the prefectural authorities issued a warning against eating seafood from Minamata Bay (Fig. 1). However, the national government soon thereafter declared that the warning was illegal because the contaminant had not been identified. Expert committees investigated the possible causation, at first without reaching a conclusion. These discussions were derailed by requests to consider even far-fetched possibilities, such as leakage of dumped explosives from the Second World War that was proposed by the Japan Chemical Industry Association.[4]

As sensitive chemical analyses were developed and experimental studies were completed, the evidence became overwhelming by 1960 that methylmercury was indeed the cause of Minamata disease. Several years later, the causal connection was finally recognized by the governmental authorities. Meanwhile, pollution of the bay continued, and the number of patients with obvious Minamata disease increased. Eventually, some forms of compensation were arranged, and the medical profession was then challenged to develop criteria for the Minamata disease diagnosis and eligibility of compensation. These criteria and the means of compensation were the object of much discussion and legal proceedings. Still, as late as 1971, a representative from the polluting factory revived a previously refuted hypothesis that the disease was due to rotten fish (scombrotoxin) and not mercury contamination from the factory.[4] Only after a legal defeat did the company agree to pay compensation to the victims. In 1977, the Japan Environment Agency issued formal rules on certification for recognition of Minamata disease patients. Although some legal issues are still lingering in court, the major case on compensation to Minamata disease patients was finally resolved in 2004—almost 50 years after the disease had first appeared. During all of this time, the scientific community was divided by protracted controversies.

The delayed appearance of the 1971 study of widespread methylmercury toxicity in this issue of EPIDEMIOLOGY[5] should be seen in the light of the drawn-out debates on Minamata disease and the legal and political repercussions. Had they been reported earlier, the conclusions of this study would have spurred further and perhaps irreconcilable controversy. The social and political situation in Japan at the time was characterized by rapid industrial growth as a national priority to recover from the Second World War. Minamata disease patients were therefore an unwelcome reminder of the costs of unrestrained environmental pollution, and stigmatization of the afflicted was widely reported. But to explain away the delays in recognition of Minamata disease as only a local political phenomenon would overlook the common tendencies of epidemiologists and scientists in general to highlight uncertainties in empirical studies.

Minamata disease began to raise attention worldwide, and expert meetings were convened by UN agencies. It was concluded that pregnant women "may be" at greater risk, but a proposed exposure limit for methylmercury at first aimed

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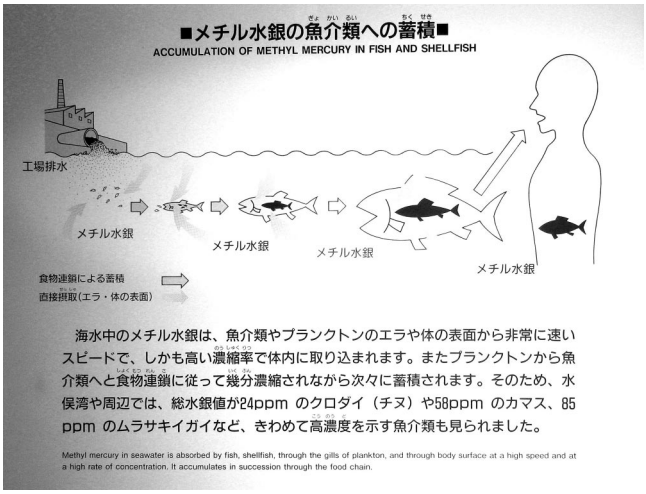

FIGURE 1. An illustration of mercury poisoning from an exhibit at the Minamata Disease Municipal Museum.

only at protecting adults. Meanwhile, evidence accumulated from epidemiologic studies in the Faroe Islands and elsewhere on neurobehavioral deficits in children prenatally exposed to methylmercury through maternal seafood diets. In 1998, US authorities called a meeting of international experts.[6] Their conclusions spelled out uncertainties of the scientific evidence and some apparent disagreements among studies. However, a US National Research Council committee[7] soon thereafter concluded that neurodevelopmental deficits are the most sensitive and well-documented effects of methylmercury exposure, and that these effects warranted a low exposure limit. This conclusion was internationally accepted.[8] Chronic methylmercury toxicity in adults is now becoming more widely documented due to unfortunate experiences elsewhere.[9]

Seen in present-day perspective, the 1971 study has limitations due to its cross-sectional design, the crude classification of exposure and neurologic manifestations, and the possible misclassification due to the large number of examiners. However, it was the first and largest population-based study conducted in Minamata, and it benefited from a high participation rate in all of the 3 study areas. The study was clearly visionary and courageous for its time. Its message on nonspecific, subclinical dysfunction as an outcome of low level exposures to environmental toxicants remains important. From the above consideration of the political and scientific controversies on Minamata disease, it seems clear why the 1971 study was not released in Japan at the time. Could it have been published, elsewhere, perhaps in the United States? We think not. The scientific community was not ready. Even the first papers from the Faroes studies on developmental toxicity were repeatedly rejected by major journals before eventually being published, and that was only in the 1990s.

As epidemiologists, we must recognize an important warning reflected by this delayed paper on Minamata disease. For decades, scientific uncertainties on mercury led to exaggerated controversies that delayed preventive action.[10] However, when uncertainties are interpreted as support of the null hypothesis, the costs to human health and society can be enormous.[11] We have a responsibility to combine our epidemiology talents and insights with the courage to elicit preventive action against the harm caused by environmental chemicals. Emphasis on uncertainties amid skepticism from colleagues, regulatory agencies, or stakeholders should not allow us to forget to call attention to preventable risks. Although seemingly fleeting (or mercurial), this is the true warning from the 1971 paper.

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REFERENCES

1. Harada M. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Crit Rev Toxicol.* 1995;25:1–24.
2. Ui J. Minamata disease. In: Ui J, ed. *Industrial Pollution in Japan*. Tokyo: United Nations University Press; 1992:103–132.
3. Eto K, Yasutake A, Nakano A, et al. Reappraisal of the historic 1959 cat experiment in Minamata by the Chisso Factory. *Tohoku J Exp Med*. 2001;194:197–203.
4. Mishima A. *Bitter Sea, the Human Cost of Minamata Disease* (translated by Gage RL, Murata SB). Tokyo: Kosei; 1992.
5. Yorifuji T, Tsuda T, Takao S, et al. Long-term exposure to methylmercury and neurologic signs in Minamata and its neighboring communities. *Epidemiology*. 2008;19:
6. NIEHS. Workshop organized by Committee on Environmental and Natural Resources (CENR), Office of Science and Technology Policy (OSTP), The White House: Scientific Issues Relevant to Assessment of Health Effects from Exposure to Methylmercury, November 18–20, 1998. Available at: http://ntp.niehs.nih.gov/index.cfm?objectid=03614B65-BC68-D231-4E915F93AF9A6872.
7. National Research Council. *Toxicological Effects of Methylmercury.* Washington, DC: National Academy Press; 2000.
8. Joint FAO/WHO Expert Committee on Food Additives.Methylmercury (evaluation of certain food additives and contaminants). *World Health Organ Tech Rep Ser*. 2004;922:132–140.
9. Yokoo EM, Valente JG, Grattan L, et al. Low level methylmercury exposure affects neuropsychological function in adults. *Environ Health*. 2003;2:8.
10. Grandjean P. Mercury risks: controversy or just uncertainty? *Publ Health Rep*. 1999;114:512–515.
11. Needleman H. The removal of lead from gasoline: historical and personal reflections. *Environ Res*. 2000;84:20–35.