Minamata Disease and Kumamoto University Researchers who Dedicated Themselves to the Elucidation of Its Cause

Haruhiko Nakata

1. Introduction

It was around 1962 that environmental contamination by artificial chemical substances came to be widely known to the general public, following the publication of *Silent Spring* by Rachel Carson, a biologist from the United States (Fig. 1). Her finding that DDT had serious effects on the ecosystem as a result of bioaccumulation through the food chain gravely shocked people all over the world because insecticide was widely used in agriculture.

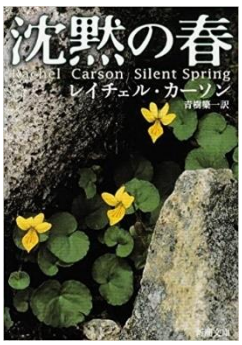


Fig. 1 Silent Spring **by Rachel Carson**

As for Minamata disease, it was as early as 1956, six years before the publication of *Silent Spring*, that its existence came to light for the first time, and it is often called "the origin of pollution issues." To understand why Minamata disease is considered to be the origin of the pollution issue, let us begin by deepening our understanding of what pollution is and what Minamata disease is.

2. Four Big Pollution Diseases of Japan and toxic substances

The Japanese novelist Ryôtarô Shiba wrote in the opening of his novel *Saka no ue no kumo* (*Clouds Above the Hill*), "[Japan as] a small island nation was about to enter a

period of great cultural change." We can feel from this phrase the elated atmosphere in Japan just starting on its path to modernization following the Meiji Restoration. If that was Japan's first flowering period, the second was most likely the period of rapid economic growth after the end of the Pacific War. During the 1950s and the 1960s, Japanese citizens' revenues doubled, the transportation networks of the Shinkansen Bullet Trains and motorways were laid out across the country, and the country's post-war reconstruction advanced on a full scale. Many Japanese were finally able to experience material abundance for themselves. At the same time, serious problems, mostly consequences of these developments, emerged all over Japan. One of them was harm to human health caused by toxic substances released into the environment from factories. During this period, the word "*kôgai* (pollution)" became widely known to the public.

The Four Big Pollution Diseases of Japan refer to Minamata disease, Niigata Minamata disease, Itai-Itai disease, and Yokkaichi asthma, which occurred, respectively, in Kumamoto, Niigata, Toyama and Mie Prefectures. All of them, caused by the release of toxic substances from chemical factories and mining sites during the period of Japan's rapid economic growth, brought about enormous health damage to large numbers of people. In Japanese, *Yondai kôgai-byô* (*Four Big Pollution Diseases of Japan*), a book written by Dr. Atsuko Masano and published by Chukô Shinsho (Fig. 2), provides an accessible overview of

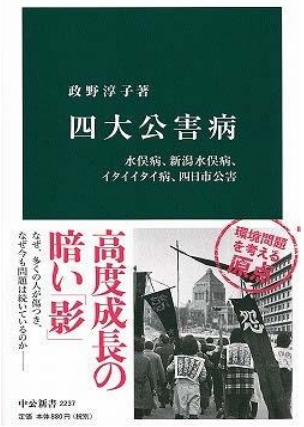


***Fig. 2 Yondai kogai-byo (Four Big Pollution Diseases of Japan)* by Atsuko Masano**

these diseases. While we will only focus on Minamata disease in this lecture, you are encouraged to read about the other pollution diseases, which are discussed in numerous published books, documents, and academic papers, some of which are available in Kumamoto University's libraries.

3. What is Minamata disease?

On May 1, 1956, Dr. Hajime Hosokawa, director of the hospital affiliated with Chisso Corporation in Minamata City, Kumamoto Prefecture, reported to the Minamata Public Health Center the hospitalization of four patients presenting neurological conditions of unknown causes. It thus became the official day of discovery of Minamata disease. Patients with Minamata disease complained of numbness in their hands and feet, difficulty in moving their arms and legs as they wished, narrowed vision, hearing impairment, and other symptoms. Shortly thereafter, the number of people who visited the hospital with similar symptoms increased rapidly.

Minamata disease is caused by the consumption of large quantities of fish and shellfish containing organic mercury in high concentration. Organic mercury was discharged into Minamata Bay by Chisso Corporation from its Minamata factory. At that time, however, the factory was using an inorganic mercury of low toxicity, rather than organic mercury which is mercury combined with carbon. This was one factor that made it extremely difficult later to pinpoint the cause of Minamata disease.

Minamata disease is not contagious like a common cold, nor is it a hereditary disease

transmissible from parent to child. However, when it was first discovered, practically nothing was known about it, and for this reason and due to the preconceived idea that it could be contagious, Minamata disease patients were subjected to severe discrimination. People are generally afraid of the unknown. When a problem occurs, it is necessary to search for its causes at once, partly to eliminate such fear and anxiety that people often feel.

It was learned later, when babies were born with the same symptoms as those of Minamata disease, that organic mercury contained in the food that the mother ate during pregnancy was transferred to the fetus in the womb. This is called “congenital Minamata disease.” Present-day medicine has no complete cure for Minamata disease, congenital or otherwise, and this irreversibility is one frightening aspect of health damage caused by chemicals.

4. Outbreak of Minamata disease and search for its cause

In August 1956, about three months after the discovery of Minamata disease, the Strange Disease Countermeasures Committee, mainly composed of representatives of Minamata City and the Minamata Public Health Center, requested Kumamoto University School of Medicine to conduct a study to elucidate the cause of the mysterious disease. Immediately, Kumamoto University put together a Minamata Disease Medical Research Team. The researchers visited and interviewed patients countless times. Kumamoto University Hospital also conducted a variety of clinical tests and pathological analyses,

including autopsies of deceased patients. In July 1959, the Research Team made a formal announcement: “Minamata disease is a neurological disease caused by the consumption of local fish and shellfish (caught in Minamata Bay) contaminated with a toxic substance, which is strongly suspected to be mercury.”

This was three years after the outbreak of the strange disease and the request for the study. Let us trace back how the Kumamoto University researchers conducted their study and reached this conclusion.

5. The earliest academic paper reporting Minamata disease

I have a copy of the academic paper titled “Results of an Epidemiological Study on a Central Nervous System Disease of Unknown Cause Occurred in the Minamata Region,” which was published in the *Journal of the Kumamoto Medical Society* in June 1957 (Fig. 3). This earliest academic paper reporting the existence of Minamata disease was written by 10 researchers, including Prof. Shôji Kitamura of the School of Medicine, Kumamoto University.


熊本醫學會雜誌

原著

水俣地方に發生した原因不明の中樞神經系疾患に關する疫學調査成績

喜田村正次
Shoji KITAMURA
富田仲蔵 Chuzo MITATA
富田實 Minoru TOMITA
伊達昌喜 Shoki DATE
上田京二 Kyoji UEDA
三隅達二 Kiyoji MISUMI
小島照和 Terukazu KOJIMA
宮本宏 Hiroshi MIYAMOTO
黒木晉 Susumu KUROMOTO
野口芳之 Yoshiyuki NOGUCHI
中川良二 Ryoji NAKAGAWA

Fig. 3 **The earliest paper reporting investigation results on Minamata disease**

The paper mainly presents the results of the detailed epidemiological investigation that commenced in September 1956 mainly through repeated visits to 40 households with Minamata disease patients, as well as 68 households

without patients as a control group. Carefully read, the paper reveals that there were already Minamata disease patients in 1953, three years prior to the official discovery of the disease. The paper provides in tables and hand-drawn diagrams the names of districts with large numbers of patients, the numbers of patients classified by gender and age group, their main occupations, and other details concerning the households studied. It also details the numbers of cats found dead in the streets in the last four years in the areas studied. It is noteworthy that the paper also contains the meteorological conditions (temperature, humidity, precipitation, number of fine days, wind direction, etc.) in Minamata City in 1956.

I am sure that the detailed information that was collected in this investigation, but not included in the paper due to limited space, surpassed manyfold the information contained therein. Fifty years ago, without the Internet, the researchers must have encountered enormous difficulty in amassing as much information as possible on all sorts of subjects, including those whose causal relationship to Minamata disease was uncertain. Nevertheless, this seems to indicate to us the importance of accurate and voluminous information in tackling the challenge of solving an unprecedented problem: importance that is the same now as it was then. Based on findings from the investigation, the authors state in the paper that the disease in question is not a conventional infectious central nervous system disease such as Japanese encephalitis, epidemic meningitis, or acute graying pancreatitis. The clear evaluation that Minamata disease differed from conventional contagious diseases must have somewhat relieved local residents and others

concerned about its potentially uncontrollable spread.

6. Kumamoto University researchers who dedicated themselves to the elucidation of the cause of Minamata disease

I believe that a large number of Kumamoto University researchers were involved in the study on Minamata disease. Among them, Prof. Masazumi Harada of the School of Medicine, who was a physician and a researcher, stands out as the leading scientist who dedicated his life to this research project and published various findings, always conscious of the patients' situations. The University libraries have a total of some 60 books either written by or about Dr. Harada. I encourage you to check out one of them and read it sometime.

Besides Dr. Harada, there were other Kumamoto University researchers who worked on Minamata disease. In this lecture, I would like to introduce to you the following two in particular:

- Katsurô Irukayama (Professor, Department of Public Health, School of Medicine)
- Fumiaki Kai (Research Associate, Department of Public Health, School of Medicine; later Dean of the Faculty of Science, Kumamoto University)

7. Prof. Irukayama's research

At the time of the discovery of Minamata disease, Prof. Katsurô Irukayama belonged to the Department of Public Health of the School of Medicine. One of the early papers

that he wrote on Minamata disease, “Contamination of Minamata Bay and Its Relationship with Minamata Disease,” was published in the *Kumamoto Medical Journal* in 1957. In the study presented in this paper, samples of water and mud had been collected from several locations of the canal laid out like a moat around the Chisso Minamata factory and along the coast of Minamata Bay, and heavy metals contained in these samples were measured (Fig. 4). The study also included an experiment in which fish mixed with mud from Minamata Bay was fed to cats to see if they would present symptoms similar to Minamata disease. The experiment identified three metals, namely, manganese, selenium and thallium, as substances that might be causing Minamata disease. Yet, due to insufficient evidence, the author concludes, “We have not yet reached the stage where these substances could be linked with the disease in our study.”

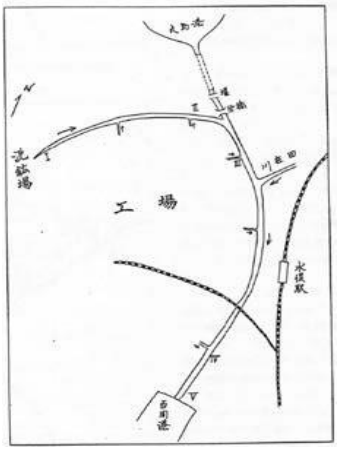


Fig. 4 **A drawing indicating spots of sample collection near the factory**

Two years later, in 1959, Prof. Irukayama published a new paper, “Contamination of Minamata Bay and its Relationship to Minamata Disease—Report II” in the *Kumamoto Medical Journal*. In the study presented in the paper, a toxicity test was carried out in which arsenic and several other metals were injected into mice. However, the conclusion reads, “We conducted the experiment, but the results did not conform to our hypothesis.” The two papers, in which it was impossible to name the chemical causing the disease, relate well how Dr. Irukayama was groping for clues while conducting his research.

Personally, I am impressed by the passage where Dr. Irukayama clearly states that he failed to identify the cause while conducting the study, assuming the heavy responsibility of not having elucidated the cause of Minamata disease. I am moved by both his frankness and the big-hearted atmosphere in which the research must have been carried out in those days, which is quite different from today.

The paper also mentions an experiment in which oysters caught in Minamata Bay were crushed into powder, and some were burned to ashes. These were then fed to rats to observe their reactions. As a result, the rats given the ashes did not show any effects of toxicity, whereas the rats given powdered oysters not treated by heating presented symptoms similar to Minamata disease, such as disturbance of gait and general paralysis, and died within 30 days. This experiment indicated that the substance causing Minamata disease was decomposed by heating, which reinforced the hypothesis that an organic substance or an organic metal was responsible. At that time, the word "mercury" had not yet been mentioned in the paper, and the culprit remained unidentified.

A major changed occurred in 1960, one year later. In the paper submitted in that year ("Contamination of Minamata Bay and its Relationship to Minamata Disease—Report III"), Dr. Irukayama writes at the outset, "Our attention is focused on mercury as the substance possibly responsible for the contamination of fish and shellfish in Minamata Bay," thus developing the discussion on the hypothesis that mercury was the cause of Minamata disease. I believe that this was a follow-up on the announcement that Kumamoto University's research team made to media on July 23, 1959 to the effect that

it was highly likely that Minamata disease was caused by mercury (Fig. 5).


有機水銀の中毒
水俣病の原因
尿や魚介から検出
全員一致して発表
魚が死ぬ水俣川口
「九分通り間違いなし」
目立ってタ

Fig. 5 **The Kumamoto Nichi-nichi Shimbun article on the first report by the Kumamoto University Research Team identifying mercury as the causal substance of Minamata disease (dated July 23, 1959)**

In many of the papers that followed, written by Dr. Irukayama and other scientists, discussions and experiments were based on the assumption that Minamata disease was caused by mercury. Concretely, the focus of discussions shifted to questions about how, at what stage, the inorganic mercury of low toxicity used at the factory was transformed into highly toxic organic mercury, as well as the exact chemical structure of organic mercury as the substance causing Minamata disease.

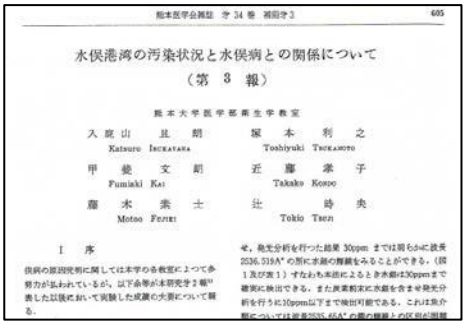
8. Prof. Kai's research

During the seven-year period from 1961 to 1967, Dr. Irukayama published nine papers titled "Studies on the organic mercury compound in the fish and shellfish from Minamata Bay as the causative agent of Minamata disease and he formation of the poison" as serialized reports. Prof. Fumiaki Kai was one of the co-authors of five of these papers.

Prof. K ai originally belonged to the Department of Chemistry of the Faculty of Science and later served as the Dean of the same Faculty. At the time Minamata disease surfaced as a serious problem, Prof. Kai was a research associate in Prof. Irukayama's laboratory. Prof. Kai analyzed fish and shellfish caught in Minamata Bay and wastewater

from Chisso's Minamata factory. This analysis eventually led to the specification of the chemical structure of organic mercury responsible for the onset of Minamata disease. In this process, Prof. Kai's knowledge and experimental expertise as a chemist proved extremely useful.

Specifically, Prof. Kai's experiment proceeded in the following manner. Shellfish collected from Minamata Bay were crushed and soaked in salt water. In this process, mercury was partially transferred to the salt water. The crushed shellfish was put through a sieve with openings of a certain size for analysis. It was revealed that mercury remaining in the shellfish had almost entirely bound to proteins. The proteins were then decomposed with alkaline or acid agents and mixed into a reagent that facilitated the transfer of organic substances. Mercury then shifted to the reagent layer. This solution was evaporated, and the remaining oily substance was injected into mice. In the mice, an almost abnormal amount of mercury was concentrated in the brain, as in the case of severe Minamata disease patients. The results thus obtained pointed to the conclusion that organic mercury was obtained from the shellfish. The logical and practical way this experiment proceeded is similar to the way a veteran detective piles up circumstantial evidence to drive the criminal into a corner (Fig. 6).



水俣港湾の汚染状況と水俣病との関係について
（第 3 報）

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甲斐 文朗 Fumiaki Kai
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藤木 素士 Motoo Fujiki
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I 序

Fig. 6 **Paper co-authored by Prof. Fumiaki Kai reporting that methyl-mercury is the substance causing Minamata disease**

In another experiment in which mercury slag in the reaction tubes at Chisso's Minamata factory was processed in various manners, a methyl group-chlorine compound was detected. Exactly the same substance was also detected in shellfish caught in Minamata Bay. Furthermore, when this substance was fed to rats, rabbits and dogs, the animals presented exactly the same symptoms as Minamata disease. These findings finally demonstrated that Minamata disease was caused by methylmercury discharged from the Chisso factory. This paper was published in 1964, eight years after the formal discovery of Minamata disease.

From September 30 through October 4, 2006, the Asahi Shimbun ran in its morning edition a series of articles titled "Minamata Disease—A Sealed Darkness (1-5)." In the articles, Prof. Kai recalls how he continued burning sludge from the Chisso factory with a burner day and night, obtaining a deposit of white scale-like crystals in a glass container and confirming that it was methylmercury. Referring to the process leading up to the elucidation of the cause of Minamata disease, he says, "There were also chemists working at the factory. I had to stick to my guns to prove that I too was a chemist." As I contemplate these words, I think that they came from Prof. Kai's suspicion and anger toward Chisso and its chemists, who must have known that their wastewater contained organic mercury because in those days they had the most advanced equipment installed at the factory before the official discovery of Minamata disease, and still did nothing about it.

9. Conclusion

As mentioned above, it took many years and the overcoming of a considerable amount of complex situations for the Kumamoto University Research Team to arrive at the conclusion that Minamata disease was caused by methylmercury discharged from Chisso's Minamata factory. After the public announcement of this conclusion in 1959, Kumamoto University was bombarded with criticism, objections and refutations from various quarters, including Chisso Corporation, the Japan Chemical Industry Association and prominent academics of other universities. I imagine that the Kumamoto University researchers were under tremendous pressure in those days. Nevertheless, in 1968, the Japanese government announced its official view, which was identical to Kumamoto University's conclusion. The hypothesis that organic mercury is the cause of Minamata disease has thus become established without any doubt. In the elucidation of the cause of Minamata disease, science played an extremely powerful role. However, science itself has no view or intention. It was Kumamoto University researchers who believed in the power of science as they patiently worked in search of the truth, never shying away from society's scrutiny.