How, for the past 40 years, we have been trying to remove the barriers hindering medical research into Minamata disease in Japan

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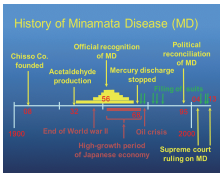
About Minamata disease

Over 500,000 people, in the Minamata area, were estimated to have been exposed to methylmercury poisoning caused by the contaminated wastewater released by the Chisso Corporation, between 1932 and 1968. Brought to public notice in 1956, the disease was soon named Minamata disease, and eventually, in 1968, was formally recognized by the Japanese government. Kumamoto University researchers, searching for the cause, studied severely affected inhabitants. The intensity of research gradually diminished but gained momentum again when Kumamoto University performed a large epidemiological study (1971-1972). However, the results were ignored and further research on Minamata disease was reduced. There has been no constructive research into the pollution by the government, at any level.

From the outbreak of the disease (1956) to the end of acetaldehyde production (1968)

In 1956 (April), two sisters, 2 & 5 years old, were admitted to a Chisso Hospital. From 1956 to 1960 H. Tokuomi et.al in 1st Internal Medicine Department, Kumamoto University reported 34 cases of Minamata disease. In July, 1959, Kumamoto University's Study Group determined the cause to be a type of organic mercury. The following day the Government dissolved the group.

Prof. Tokuomi, H. (1917 – 2014) From Okami Association of Kumamoto University , 2015



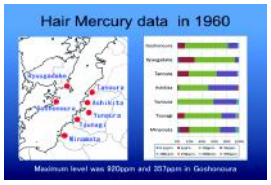
After that, the Chisso continued production. Mercury contaminated waste water continued to be released until 1968. Dr. Tokuomi et al. studied 34 cases with severe Hunter-Russell syndrome. From this and following studies, he concluded that Minamata disease had finished by 1960 and that a total of only 87 patients had been affected. No further clinical studies took place for more than 10 years.

In 1961, Dr. Tatetsu became a professor at the Neuropsychiatry Department, Kumamoto University. Prof. Tatetsu started research, and at the same time, Dr. Harada found fetal Minamata disease in 1962. They thought milder cases were overlooked in Minamata disease diagnosis.

Children of Congenital Minamata disease, 1962

From 1960 to 1962, hair mercury level was studied in some areas along the Shiranui Seacoast. In 1960, the hair mercury level was 50μg/g or more in 23.5% (227/967) of the subjects and 10μg/g or more in 85.5% (827/967) of them. At that time most of these subjects had not been examined. After 1963, administrative organizations stopped measuring human mercury levels.

In May 1968, Chisso finally stopped producing acetaldehyde. In September the Japanese Government officially recognized that the cause of Minamata disease was the methylmercury contained in the wastewater from the Chisso factory. In March, Dr. Fujino (one of the authors) graduated from Kumamoto University and took up a position in the neuropsychiatry department the following year.



Prof. Tatetsu, S. (1915-1999)

Prof. Harada, M. (1934-2012)

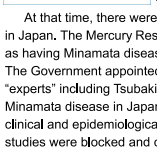
From the outbreak of the disease in Niigata (1965) to "Mercury Panic" (1973)

In 1965, a second Minamata disease broke out in Niigata, where the Syoden Kanose factory produced acetaldehyde and had released mercury contaminated waste water released into the Agano River. Prof. Tsubaki of Niigata University, one of the founders of the Japanese Society of Neurology (1960), discovered Niigata Minamata disease. He started medical examination and measured hair mercury concentration for all residents of the polluted area. He found milder cases in the exposed residents and diagnosed Minamata disease with sensory disturbance only (without ataxia, visual constriction, and so on).

Prof. Tsubaki, T. (1921-1987) From Consulted Works from Niigata University & Tokyo Metropolitan Neurology Hospital, 1990

In 1969, the patients demanded compensation for damages from Chisso and filed a lawsuit. The Minamata disease patients were not able to get any proper compensation until the case was settled in 1973. In 1970, Fujino studied junior high school students and found milder neurological and psychiatric abnormalities in those who were born in the1950s, the same period that fetal Minamata disease patients had been found.

After 1970, a group of volunteer doctors began going door to door and examining residents in the Minamata area. Under these circumstances, Fujino began to examine residents and patients in and around Minamata city. When Fujino visited patients' homes, he found patients suffering from severe symptoms of classic Minamata disease who had been left at home without any medical diagnosis or therapy. In 1972, Fujino stayed in a hospital in Minamata and began the medical examinations of patients who had been left without being diagnosed or treated. At that time he began a deeper research into the disease.

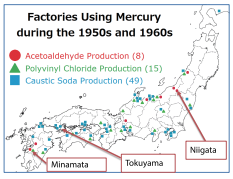


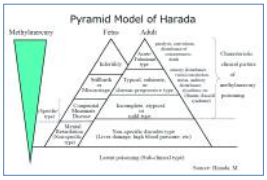
Epidemiological Study by Tatetsu et al.

From 1971 to 1972, Prof. Tatetsu performed an epidemiological study in Minamata, Goshonoura, and Ariake (Control). He found 28.5% of the residents in a district of Minamata were suffering from Minamata disease. In Goshonoura, cats had become "crazy" and died. In 1960 one of them was found with a record high level of hair mercury (920μg/g). In March 1973, Tatetsu reported finding more victims than expected. He pointed out the existence of chronic milder type of Minamata disease caused by a lower level of methylmercury and that some of the victims had begun showing symptoms of the illness after 1968.

He also found residents with Minamata disease symptoms in Ariake, the control area. Prof. Tatetsu noted that there were two other factories using mercury in the control area. After this report was announced by the media, "Mercury Panic" broke out in Japan.

At that time, there were more than 70 factories that were using, or had used mercury in Japan. The Mercury Research Group of Yamaguchi University suspected three patients as having Minamata disease in Tokuyama, where two big factories were using mercury. The Government appointed Prof. Tsubaki as a chairman of "Panel of Experts," and "experts" including Tsubaki and Tokuomi refused to recognize the existence of any Minamata disease in Japan other than that discovered in Minamata, without further clinical and epidemiological research. After this groundless conclusion, epidemiological studies were blocked and certification criteria became stricter than before. In 1977, the Government decreed that sensory disturbance and other symptoms, such as ataxia, visual constriction must be present to diagnose as Minamata disease. These criteria were called "1977 Criteria." Meanwhile the Government was strongly advising Japanese caustic soda manufacturers to find and implement alternative processes that did not use mercury.





After observing many residents, Dr. Harada proposed a pyramid model of methylmercury poisoning. But after "Mercury Panic", the continued study of mercury poisoning by the Kumamoto University Group became so difficult that it was almost impossible.

Foundation of Minamata Clinic (1974) to Political Resolution (1996)

In 1974, Fujino founded a clinic across from the Chisso Company, and later established the Minamata Kyoritsu Hospital in 1978. They began to work for residents and patients with Minamata disease. At that time, thousands of patients had been left untreated in the polluted area. Their main symptoms were somatosensory disturbance, upper/lower limb and truncal ataxia, visual constriction, auditory disturbance, and so on.

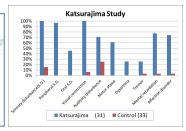
The clinic began house-call for the care and nursing for Minamata disease patients.

Minamata Clinic

A woman, who felt no pain after she cut her hand with a sickle.

They also visited polluted areas around the Shiranui Sea and examined residents and patients. From 1974, Fujino et al. performed an epidemiological study in Katsurajima Island, and found that there were many cases of mild to severe Minamata disease. They found cases of methylmercury poisoning in patients who had only sensory disturbances.

In 1971, Kagoshima University and Kagoshima Prefectural Government studied Katsurajima Island and found very few Minamata disease patients there. But, after the study, many of the inhabitants of Katsurajima were officially certified as Minamata disease patients.



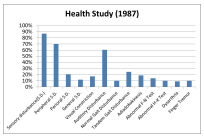
Year of Birth (n)	~1945 (45)	~53 (12)	~62 (7)	~66 (8)	~72 (19)
A. [S]+[A]+[V]+[M]+[D]	12				
B. [S] + 1 of [A], [V], [M], [D])	17	1			
C. [S] + 2 of ([A], [V], [M], [D])	10	2			
D. [S] + 1 of ([A], [V], [M], [D])	3	4			
E. [S]	1	5	6		1
F. 1-4 of ([A], [V], [M], [D])	2				
G. None of ([S], [A], [V], [M], [D])			1	8	12

[S] Sensory disturbance, [A] Auditory disturbance, [V] Visual constriction, [M] Motor ataxia, [D] Dysarthria

This study supported the introduction of criteria that a patient who had been exposed to methylmercury and had four limb sensory disturbance should be diagnosed as having Minamata disease. Our criteria were supported in the "Second Minamata Disease Lawsuit" which was filed at the Fukuoka High Court in 1985. But the Government did not accept this decision. The Environmental Agency again appointed Prof. Tsubaki as a chairman of another "Panel of Experts" and the panel accepted the "1977 Criteria." However, when the Japanese Society of Psychiatry and Neurology* asked for details from the panel, they received no clear information on any scientific data.

*The "Japanese Society of Psychiatry and Neurology" is a society mainly for psychiatry and different from the "Japanese Society of Neurology," that Prof. Tsubaki et al. founded and belonged to.

Fujino and his colleagues continued the examination in the polluted area, which now stretched all the way to Yatsushiro city (northern), Akune city (southern), and Azuma town (western). By the 1990s a total of ten thousand residents had been examined. In 1987, a health survey was performed around the Shiranui Sea. 1,088 residents were examined and four limb sensory disturbance was found in more than eighty percent of the subjects along with other neurological abnormalities.

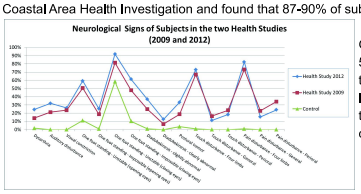


In 1995, in the process of settling "the Third Minamata Disease Lawsuit," the Government agreed to compensate Minamata disease patients based on the criteria of four limb sensory disturbance of hands and feet. More than eleven thousand victims were compensated by this settlement, and the criteria became the norm for the future compensation of a large number of victims.

From Supreme Court Judgment (2004) to Time-Limited Relief (2009-2012)

Even after the 1996 settlement, the Minamata Disease Kansai Lawsuit continued. On October 15, 2004, the Supreme Court judged, that the Government was responsible for the spread of Minamata disease and certified milder cases of the disease. After this judgment, the governor of Kumamoto Prefecture, Yoshiko Shiotani, proposed a health and environmental research plan in the polluted area. But the Environmental Agency refused and did not change their criteria and policy.

However, the number of patients who applied to be examined for Minamata disease began to increase. We have examined several thousand residents. Up until 2004 residents had been reluctant to complain about pollution and health impairment due to the pressure from discrimination. This court judgement released the pressure. In 2009 and 2012, we performed the Shiranui Sea Coastal Area Health Investigation and found that 87-90% of subjects had Minamata disease signs and symptoms.



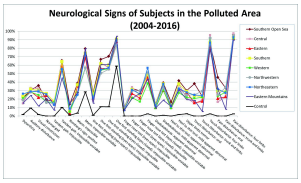
*The Law Concerning Special Measures for the Relief of Minamata Disease Victims and the Settlement of Minamata Disease Issues (2009-12)

After filing the No-More-Minamata Disease Lawsuit (2005), the Government passed a time-limited special law for relief* and 55,658 victims were compensated. But the Government revoked the law policy in July 2012 and a lot of patients, in the area, were left without the compensation they were entitled to. This also meant that the criteria, once again, was limited to a special area and a certain age-group.

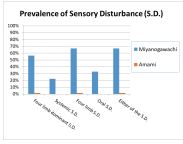
Number of publicly recognized Minamata disease patients	Kumamoto	Kagoshima	Total
Patients Certified with Minamata disease (until and including May,2017)	1,789	493	2,282
Patients with Definite Sensory Disturbance, who received Partial Compensation (until and including 1996)	8,831	2,706	11,537
Patients Compensated with Medical Expenses (about 10,000 uncompensated patients were excluded) (from 2004 until and including July,2012)	39,114	16,544	55,658
Patients Appling for Minamata Disease Certification (until and including May,2017)	1,101	962	2,063
Total	50,835	20,705	71,540

The discovery of Minamata disease in the outlying areas and lower age groups

Since 2009, when the special measure began, many residents with Minamata disease have been found in the outlying areas along the Shiranui coast. We found that their symptoms and signs in the those areas were the same as those in the central areas near Minamata city. In, 2016, we calculated over 10,000 subjects had been examined. On the whole, the health impairment of the subjects who had lived in the polluted areas around the Shiranui Sea are the same, and the spread of methylmercury poisoning is more than we had previously thought. Even younger people exhibit symptoms caused by methylmercury exposure.



The results of long-term population studies show health problems have continued to appear in a large number of residents. But except for Katsurajima Island study, much of our research was restricted to subjects who had hoped to be examined for Minamata disease. Recently, we have been accumulating population based epidemiological data.



In 2015, we compared the prevalence of sensory disturbance between Miyanogawachi (non-designated exposed area) and Amami (control). Four limb dominant sensory disturbance (both of touch and pain) in the subjects was 56.4% (53/94) in Miyanogawachi and 1.4% (1/70) in Amami. The prevalence of sensory disturbance was expected to be 27.6% (53/192) in Miyanogawachi and 1.4% (1/70) in Amami. The attributable risk on sensory disturbance for Miyanogawachi residents was (27.6-1.4)/27.6=94.8%. The attributable risk was calculated by Prof. Tsuda of Okayama University, and was already over 95% in the designated area.

Original Designated Area by Pollution-Related Health Damage Compensation (PRHDC) Law (1971)

Practical Designated Area by PRHDC Law

Designated Area by the special time-limited special Law* (2010 -2012)

Area where patients with Minamata disease symptoms have been observed by now

In Japan, a physician cannot diagnose Minamata disease freely. If a resident wants to be diagnosed and treated for Minamata disease, they have to be certified by the Government, even if they had the same history and same symptoms of methylmercury poisoning. It is not only the history and physical examination that has to be taken into account, but also the residential area must be within the Government designated areas. The left figure was designated area decided by the Pollution-Related Health Damage Compensation (PRHDC) Law (1971). But soon Minamata disease spread outside of that area (second left figure). After 2009, during the period of the time-limited special law*, the areas spread a little further (second right figure). However, many patients have been found in more outlying area (yellow areas in the right figure)

*The Law Concerning Special Measures for the Relief of Minamata Disease Victims and the Settlement of Minamata Disease Issues

Discussion and Conclusion

Methylmercury pollution and its effect on residents along the Shiranui Sea were enormous, but the whole picture has not been elucidated until now. The most important reason for this is that administrative organizations, universities and research institutions have not done enough clinical and epidemiological research in these areas. Disease must be elucidated by symptoms, signs, or other data of residents and patients who had been exposed to methylmercury. Unfortunately there was no data available on the effects of methylmercury poisoning on humans when the criteria were first determined.

"1977 Criteria" were determined by administrative organizations in Japan, and were accepted by some specialists of the Japanese Society of Neurology without any supporting evidence. The importance of epidemiology in the clinical research on methylmercury poisoning in Japan was greatly underestimated or completely ignored. Since the 1980s, most of the specialist neurologists in Japan had neither examined methylmercury-exposed residents and patients nor studied them closely.

The research of the exposed subjects, which is essential in determining reliable scientific facts, was hindered by the "1977 Criteria" as well as the social discrimination against Minamata disease. Despite these obstacles, our research was made possible by continuous contact with residents and patients while providing medical assistance.

The full extent of the Minamata problem is yet to be revealed. We must continue our efforts to carry out further research into Minamata disease and methylmercury poisoning and put pressure on the administrative organizations and research institutions to support us in achieving our very important goal.