CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/13286202

https://www.iajps.com/volumes/volume11-august-2024/12-issue-08-august-24/

Available online at: http://www.iajps.com *Review Article*

MINAMATA DISEASE: A REVIEW

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Abstract:

Humans that consume fish or shellfish polluted with Methylmercury (MeHg) from chemical plant discharges are susceptible to the poisoning known as Minamata disease (Chisso Co. Ltd.). It was found in May 1956 in Minamata City, on Kyushu Island in southwest Japan. Minamata Bay's marine products showed elevated mercury pollution levels (5.61 to 35.7 ppm). High concentrations of mercury (maximum 705 ppm) were found in the hair of patients, their relatives, and locals living around the Shiranui Sea coast. The following are typical signs of Minamata disease: ataxia, dysarthria, narrowing of the visual field, auditory problems, tremor, and sensory disturbances (glove and stocking type).

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Please cite this article in press Pavankumar Wankhade et al., **Minamata Disease: A Review.,** *Indo Am. J. P. Sci, 2024; 11 (08).*

INTRODUCTION:

Methylmercury poisoning that results in neurological symptoms is known as minamata illness. The illness may manifest after regularly consuming highly contaminated seafood. In the 1950s, a chemical factory released enormous amounts of mercury compounds into Minamata Bay, which poisoned fish consumed by humans. This was the first documented case of Minamata sickness in Japan. [1] On the Shiranui Sea shore, there were a number of tiny fishing settlements near Minamata, Japan. The inhabitants of these settlements consumed a lot of seafood, of course.
The villagers noticed their cats were acting strangely and plunging into the sea in the middle of the 1950s. There were those who believed the cats were killing themselves.Not too long after, there seemed to be a peculiar sickness circulating. The locals claimed to be numb in.[2] Not too long after, there seemed to be a peculiar sickness circulating. The peasants complained of lip and limb numbness. Some people had trouble seeing or hearing. Others experienced walking difficulties, tremors in their arms and legs,

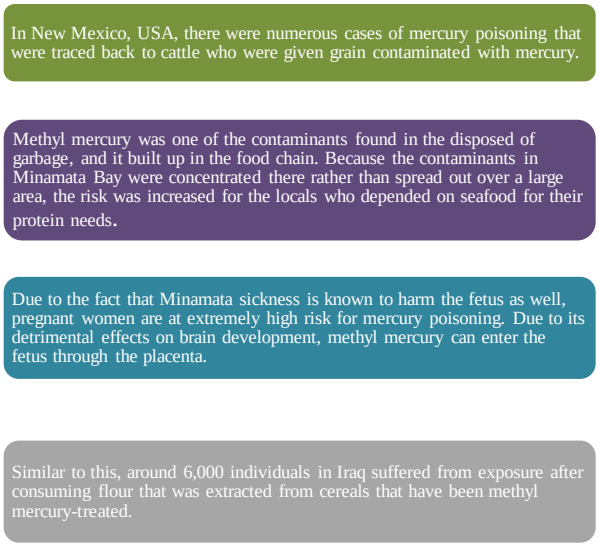
Scientists suspected that the fish in Minamata Bay were being poisoned since the villagers and cats that displayed symptoms appeared to have a common diet of fish.[3] Eventually, in July 1959, Kumamoto University researchers identified high amounts of mercury poisoning as the illness's cause, which they dubbed Minamata disease. The mercury was thought to have come from a sizable Chisso Corporation petrochemical facility in Minamata.[4] Chisso refuted the accusations and carried on with manufacturing without altering its technique. Chisso persisted in denying any participation and any illness caused by its mercury pollution. Chisso Corporation was later estimated to have disposed approximately 82 tons of mercury compounds in Minamata Bay.[5] Poisoned mothers gave birth to poisoned children as long as the mercury was dumped. These infants had serious birth defects, such as mental retardation, blindness, deafness, and twisted limbs.
In 1959, Minamata fisherman started demonstrating against Chisso Corporation. They insisted that Chisso stop disposing of harmful garbage and pay them damages for the illnesses they had. In response, Chisso attempted to negotiate with victims of mercury poisoning by presenting court documents that said it would pay damages to victims but would not take on any current or future obligations. Many signed the documents because they believed this was their only opportunity to get paid at all.[6] A number of significant facts were left out by the company, including the following: 1) it was hypothesized that methylmercury could have formed during the and even brain damage. Additionally, some individuals were acting abnormally and yelling incoherently, just like the cats. There was a problem with their nervous system.

chemical reaction in the synthesizing chamber containing inorganic mercury; 2) the production of acetaldehyde had increased significantly in the Minamata factory during the 1950s; 3) manganese dioxide, an oxidizer of the synthesizing process, was replaced by ferric sulfide in 1951; and 4) After ingesting a food laced with the waste liquid from the factory's acetaldehyde process, in addition to fish and shellfish taken in Minamata Bay, the cats at the Chisso laboratory developed neurological symptoms mimicking Minamata sickness. The yield of methylmercury in the reaction chamber is currently thought to be impacted by the oxidizer modification. Regarding the contradictory results regarding the methylmercury extraction from biological samples, it has subsequently been discovered that methylmercury covalently binds to the cysteine residue of polypeptides in organisms (discussed below), and that organic solvents are unable to extract methylmercury without first hydrolyzing protein.[7]

Causes :

The fundamental cause of the symptoms in each of the multiple Minamata disease epidemics has been pollution. Methyl mercury is absorbed into the body from a variety of environmental sources, but seafood is the main source of minamata sickness. Hair samples are used to measure the amount of mercury in the body, and it is generally accepted that nerve damage is likely to occur when the level is greater

than 50 ppm (parts per million). Residents of Minamata reported average levels as high as 700 ppm, compared to 4 ppm for those living outside the area.



"Fig.1", There are several causes in addition to mercury poisoning from environmental pollution and contamination, which the main causes are given in the fig.1

Methyl-mercury deposits have been shown to be concentrated in neural tissues of Minamata Bay region people. This pattern also explains the effect of neurotoxicity, particularly in newborns since the toxin cannot be prevented during fetal transfer.[8]

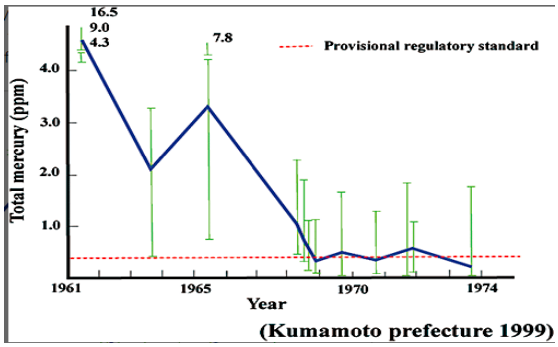
Symptoms and Signs of Minamata Disease :

"Fig. 2", Some common signs and symptoms

Research from Minamata revealed that symptoms frequently appeared suddenly. Individuals who experienced problems with hearing, vision, and swallowing declined especially rapidly, going through convulsions, comas, and eventually passing away. The degree of symptoms varied according to the amount of mercury exposure. Less methylmercury led to milder symptoms, but in more severe cases, the symptoms were irreversible. The death rate from Minamata sickness is hard to determine. There were 2,282 cases with official acknowledgment as of 2019. It is conceivable that a great number of cases have remained unrecognized.

Pathology

This review concentrates on human cases of Minamata sickness in Kumamoto Prefecture, where the neuropathology of the disease has been extensively researched. Lesions in the nervous system linked to Minamata illness have a distinct distribution. All instances of Minamata disease were discovered to involve the calcarine cortex in the cerebral cortex, specifically along the calcarine fissure. In the anterior regions of the calcarine cortex, there was a noticeable loss of nerve tissue. Sometimes, in extended cases following acute onset, the centrifugal pathway from the visual and visual association areas (internal sagittal stratum) displayed secondary degeneration. The alterations in the postcentral, precentral, and temporal transverse cortices were comparable but not as dramatic. Secondary bilateral degeneration of the pyramidal tracts developed as a result of intense lesions in the precentral cortex. The injuries were located further into the hemisphere in the cerebellum. The population of granule cells was most impacted. Sensory nerves were more impacted than motor nerves in the peripheral nerve system. In rare instances of protracted or chronic illness, secondary degeneration of Goll's tracts was observed.[10] At first, it was thought that low-level, continuous exposure to mercury caused brain damage in the pathogenesis of chronic types of MD.[12] However, it was later discovered that the mercury levels in fish abruptly dropped in 1968, indicating that residents of the Minamata Bay area had ingested high levels of mercury between 1951 and 1968.

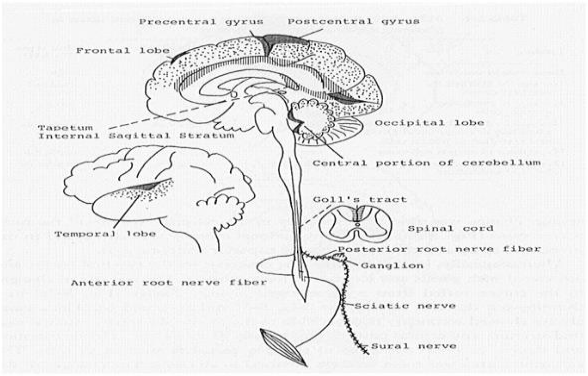


"Fig. 3", Fish mercury levels dropped sharply in 1868 after Chisso Co. ceased discharging wastewater into Minamata Bay.

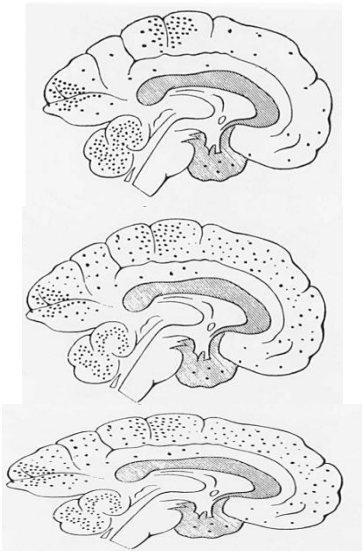
Furthermore, it took a while to determine the pathophysiology of selective susceptibility in the cerebral cortex. Using common marmosets, Eto al et al.[13,14] experimentally showed that edema in the white matter close to the deep sulci may be a factor in the cerebral cortex's selective injury. Over the past ten years, new reports have shown that medical studies have solved the MD problem.

Research

Seven distinct clinical forms of Minamata illness have been identified through research.[12] The acute variety is distinguished by an onset-death interval of less than two months, abrupt onset, and severe neurological symptoms. The onset-death interval for the subacute kind is between two and twelve months, however it still has acute onset and severe neurological symptoms. The onset-death pattern of the prolonged-severe type is characterized by severe neurological signs and symptoms with an abrupt or subacute onset. A period longer than a year. A longer than 12-month onset-death interval and moderate neurological symptoms are characteristics of the prolonged-mild form. The neurological symptoms of the chronic form are hazy and have a sneaky beginning. Due to intrauterine and postnatal exposures to Me-Hg, respectively, the fetal and postnatal kinds of MD occur in both infants and children. There were two standout characteristics in acute MD. One was a disruption in circulation brought on by the Me-Hg compound's deterioration of the blood-brain barrier. Brain edema was noted in the perivascular area, and it was more prominent in the areas that bordered the perivascular area. Eto et al.'s 2001 study on Me-Hg poisoning in common marmosets shed light on the cerebral cortex's specific sensitivity.[13] Along the deep cerebral fissures or sulci, there was selective cortical degeneration [11, 12].



"Fig. 4", Preferential locations for pathological alterations in moderate, chronic forms of MD in the neurological system. In decreasing order of severity, the meshed region has the greatest degree of brain injury, followed by the stippled and hatched regions. Crosses indicate the sensory nerves that are susceptible to pathogenic alterations. Reproduced from Eto [16]



"Fig. 5", Distinctive arrangement of lesions in the central nervous system among various forms of MD with extended duration. MD type: top is adult; middle is infantile; bottom is fetal. Inspired by Takeuchi.[17]

The following three case reports are from autopsy cases in Kumamoto Prefecture; they include an adult case, a mild type of MD, a postnatal MD, and a prenatal MD. Five cases of MD that occurred after birth all had significant neuronal loss and spongy changes in the cerebral cortex. The neurological system was hypoplastic in five embryonic cases of MD, but the cerebral cortex did not exhibit a spongy alteration.

OVERVIEW OF THE PATHOLOGICAL CHANGES OF MD

The primary characteristic of strong organ selectivity in MD, or Me-Hg poisoning in general, is noteworthy. Therefore, major pathogenic alterations are primarily restricted to the neurological system. Based on research conducted by the Kumamoto University study group, [17] minor alterations occurred in other organs and tissues, such as the duodenum's erosive inflammation, the bone marrow's hypoplasia, the lymph node's atrophy, the liver and kidney's fatty degeneration, and the pancreatic islet cells' modification. Pathological alterations in both mild and severe forms of MD were very minor in the liver and kidney, where mercury levels were always higher at the time of death than in the brain. Although there were no obvious clinical alterations, the kidney's proximal convoluted tubule epithelial cells showed extensive mercury deposits. Mercury deposits were seen in Kupffer cells and hepatocytes in the liver, but there was little tissue damage.On the other hand, harm to the nervous system brought on by mercury ions can be fatal. It never, however, impacts the system equally; typically, the cerebral and cerebellar cortices suffered the most damage, with certain regions being more severely impacted than others. The spinal cord was least impacted and the brain stem was less affected. Peripheral nerve pathology, on the other hand, is distinct in that it seems to be linked to a protracted course of the illness: the nerves are only impacted in situations other than acute and subacute ones. In chronic situations, there is selective injury to the sensory nerves followed by regeneration.

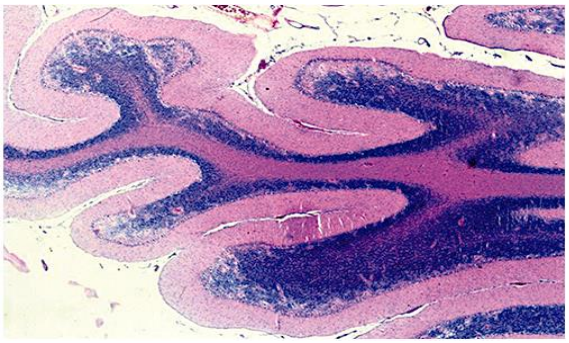
Case 1 (adult case)

- **Clinical history**

The patient, a 64-year-old fisherman, resided in Minamata City, which is located in the southern portion of Minamata Bay. It was discovered that the mercury in the bay was contaminated by the neighboring Chisso Co. Speech disturbance and foot numbness were symptoms of the disease's onset in the spring of 1959. From May 1965 until July 1968, the patient received pulmonary tuberculosis treatment at Minamata City Hospital. Neurological test conducted in October 1968 and December 1969 revealed adiadochokinesis, muscle rigidity, increased tendon reflexes, tremor in the fingers, dysgraphia, and a minor constriction of the temporal side of the visual fields. Additional clinical observations included a mask-like face, dyskinesia, raised blood pressure of 170–192 mmHg, dysesthesia in the hands and areas below the knees, and labyrinthine deafness, hyperesthesia, and hypalgesia. In January 1970, the patient passed away from a large hemorrhage caused by a gastroduodenal ulcer.

- **Autopsy pathology**

Autopsy samples were fixed in paraffin and stained using HE, KB, and Bodian staining techniques on the cerebrum, cerebellum, brain stem, spinal cord, and peripheral nerves. Peripheral nerves such as the sciatic nerve, radial nerve, sural nerve, and ventral and dorsal root nerve fibers were cut into frozen sections and dyed using Suzuki's axon staining technique and Sugamo myelin. Kultschiky's procedure was modified to apply Sugamo myelin stain on frozen slices. Photo-emulsion was used to detect inorganic mercury.Both hemispheres' gyri were atrophic, and their sulci were enlarged. This was especially noteworthy in the pre- and postcentral gyri and calcarine cortex. The calcarine fissure on the coronal section widened, and the surface of the calcarine cortex exhibited significant atrophy. Using the KB staining technique, Gennari's band on the calcarine cortex was palely stained. As is frequently seen in cases of chronic MD, light microscopic inspection revealed extensive degeneration in the deep white matter and depopulation of neurons in the calcarine, temporal, pre-, and postcentral cortices. There was a significant loss of entire layers of neurons in the calcarine cortex. In the cerebellar hemispheres, there was a moderate loss of granule cells beneath the Purkinje cell layer (Fig. 6). The granule cell layer and Bergman's glial cells were found to contain mercury granules through the use of a photo-emulsion histochemical technique for inorganic mercury. Although there was evidence of degeneration of the fasciculus gracilis, or Goll's tract, in the spinal cord, the ganglion cells in the spinal ganglion were largely intact.Dorsal roots and sural nerves, two examples of sensory nerves, were broken apart, displaying Büngner's bands and a loss of nerve fibers accompanied by a rise in collagen fibers. Myelin staining revealed that the myelinated nerve fibers in the ventral root were well maintained, but the dorsal root showed evidence of myelin sheath breakdown. The dorsal nerve fibers displayed a band-like increase in the tiny nerve fibers together with the concomitant proliferation of fibroblasts and Schwann's cells, despite the ventral root nerve fibers' axons being well preserved, according to axon labeling.



"Fig. 6", Scars in Case 1's cerebellum are linked to a mild to moderate loss of granule cells beneath the Purkinje cell layer (HE stain).

- **Biopsy findings**

On December 9, 1969, approximately one month prior to his passing, a sural nerve biopsy was carried out because the patient's condition was first identified as MD. The sural nerve biopsy revealed a reduction in myelinated nerve fibers and an increase in short axons, along with the concomitant growth of Schwann's cells and fibroblasts. The sural nerve revealed abnormal Schwann's cells and the presence of fibroblasts with an increase in collagen fibers under an electron microscope. Regressive alterations included inadequate regeneration with unusually short axons, wavy myelin degeneration with extremely thin and electron-dense axons, inflated myelin, partial myelination, and loss of myelin.[18]

Case 2 (infantile case) [19]

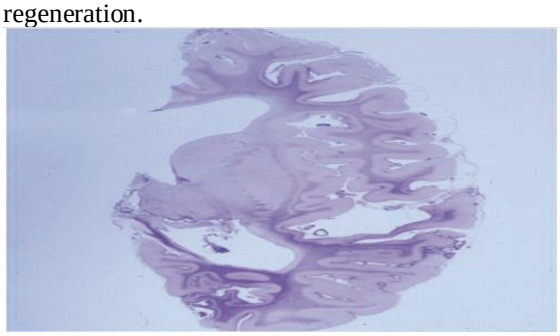
- **Clinical history**

A 23-year-old woman who was born on November 8, 1950, was the patient. At the age of five years and seven months, on June 8, 1956, Minamata began to suffer from the sickness, which ultimately claimed her life after eighteen years. She was raised in a family of medical professionals. The noticeable part of salivation started on June 8, 1956. The upper limbs' movements, particularly the fingers', were jerky on June 15. Finger tremors and a change in stride started to manifest on June 18. After her speech became unintelligible on June 20, she was admitted to the hospital in Chisso County. She developed severe walking impairments and neck tremors on July 3. Appearing on July 30 was Aphasia. Her condition worsened over time, and as somnipathy and dysphagia set in, she went insane. She was moved to the pediatric department at Kumamoto University Hospital in Kumamoto on August 30. Physical testing revealed the existence of tonic paralysis, which made walking and standing daily activities impossible. There were visual acuity disorders, hearing disturbances, aphasia, and consciousness disturbances. Pathological reflexes, tremors in all four limbs, and ankle clonus were seen along with a noticeable increase in tendon reflexes. Additionally, there was Kernig's sign and neck rigidity. The eye grounds did not exhibit any notable anomalies. Her first convulsion occurred on June 5, 1957, and she experienced similar episodes almost ten times a day after that. Occasionally, she would flex her hips and knees into right angles or assume a position in which all four limbs were extended. Her dementia worsened. Her four extremities' tonicity and spasticity worsened, and she completely lost her ability to move and think. She was moved to the Minamata City Hospital on July 29, 1959. She could swallow when food and liquids were put straight into her mouth. She closed her mouth to refuse food that was served in excess. There were sometimes general convulsions in her. A tracheotomy was done against aspiration on May 22, 1974. She was put on a naso-gastric tube for the alimentation of synthetic formula after oral alimentation became unfeasible. Her apallic syndrome was evident. She suffered recurrent urethral infections and respiratory problems before passing away on August 25, 1974.

- **Autopsy pathology**

The atrophy degree was 37% and the brain weighed 775g, whereas the control brain weighed 1234 ± 17.9g. A large portion of the cerebral hemisphere was affected by the lesions, and the pre- and postcentral gyri, as well as the calcarine cortex, suffered significant damage (Fig. 5). In line with the severe injury to the cerebral cortex, the white matter of the cerebrum showed secondary degeneration. The corticofugal fibers that run from the occipital lobe to the superior colliculi and the lateral geniculate bodies comprised the pyramidal tracts from the precentral gyri and internal sagittal strata. Their myelin staining was either minimal or absent. Less visibly implicated were the fibers of the corpus callosum that were identified as the tapetum. The cerebellar lesion was quite serious. Compared to the neurons in the cerebellar cortex, the neurons in the dentate nucleus were comparatively well maintained. In this instance, there were noticeable alterations to the Purkinje cell and torpedo dendrites. In the molecular layer, stellate cells were discovered as part of a Hunter-Russell case report. While there was no discernible loss of neurons in the brain stem or basal ganglia nuclei, the cell bodies of the neurons commonly atrophied. The lateral column was the primary site of secondary systemic injury to the Goll's and pyramidal tracts. Apart from sporadic atrophy, there were no notable alterations in the neurons of the anterior and posterior horns. In contrast to the circumstances in the brain

cortex, there was comparatively little satellitosis in the spinal ganglia after ganglion cells were lost. Most of the damage to the dorsal roots was caused by regeneration.



"Fig. 7", A horizontal section of the right hemisphere showing gliosis in the white matter corresponding to the affected areas of Case 2 (Holzer stain). From Eto and Takeuchi.[19]

Case 3 (fetal case)(20)

- **Clinical history**

  The patient was a 29-year-old Minamata resident who was born in 1957 and passed away in 1987. Her parents, as well as four out of her eight siblings—four boys and four girls—were all diagnosed with MD. In 1959, there was 101ppm of total mercury in her mother's hair. The mother, who was 55 years old, passed away from rectal cancer in 1972.The patient weighed 3000g at birth. She was primarily given her mother's milk and formula when she was a newborn. At six months old, she sucked badly, developed slowly, and had an unfixed neck. When she was three years old, she experienced her first convulsive seizure and was brought to a private hospital. She was given the diagnosis of "Kibyo"—a peculiar disease—there; this word was used early in the MD pandemic. She experienced seizures repeatedly. When the patient was eight years old, an EEG during sleep revealed high-voltage, diffuse, sluggish waves. Both mental and physical development was delayed. ThisShe was bedridden, never learned to talk, and drooled a lot. Ankle clonus, deep-tendon reflexes that were enhanced, primitive and pathological reflexes, and spastic quadriparesis were all found during the neurological evaluation. Athetotic and choreographic motions were seen in short bursts. There was aberrant dentition and external strabismus. Finally, at the age of 29, she passed away from bronchopneumonia. Her hair had a total mercury concentration of 61.9 ppm in 1959 when she was two years old, and 5.4 ppm in 1959 when she was 17 years old.

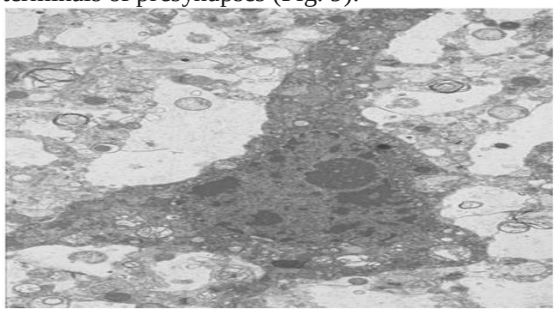
- **Autopsy pathology**

The body was 23 kg in weight and 143 cm tall. There were 920g in the brain. The brain showed grossly marked widespread atrophy of the cerebral cortex and white matter, thalamic status marmoratus, and thinning of the corpus callosum.In the calcarine, postcentral, and precentral cortices of the cerebrum, there was atrophy and a minor decrease in the number of neurons exhibiting gliosis under a microscope. There was calcification in the globus pallidus and a reduction in the number of neurons in the basal ganglia. According to HE stain, granule cells in the cerebellum were comparatively well-preserved. However, gliosis in the granule cell layer underlying the Purkinje cell layer was seen, along with subtle but noticeable pathological changes in the apex of the folia, known as apical scar formation. Mercury deposits were discovered in the liver, kidney, and brain by histochemical examination. Neurons and other brain cells in the cerebral cortices, basal ganglia, ependymal cells, choroid plexus epithelial cells, cerebellum nuclei, and brain stem were discovered to have deposits. They were discovered sporadically in the cerebellar cortex's granule cells. The spinal cord's ventral nerve roots were undamaged, but the endoneurium of a few tiny bundles of dorsal nerve roots had more connective tissue. A teasing technique exposed segmental demyelination in the dorsal nerve fibers.

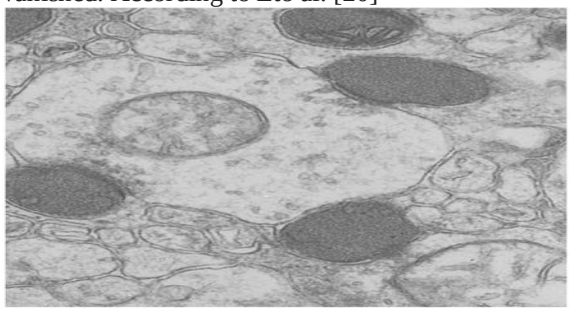
- **Electron microscopic findings**

Nerve cells in the cerebrum were smaller, darker-stained, and had more nuclear chromatin. The cytoplasm of neurons contained diffusely distributed free ribosomes that were focally aggregating. The number of rough endoscopic reticula (ER) was significantly reduced. Neurons' cytoplasm did not include aggregates of rough ER (Nissl bodies), but some enlarged cisternae were visible. The cisternae of the Golgi apparatus were often enlarged, and it was occasionally discovered. Additionally, lipofuscin was seen in the cytoplasm. The mitochondria were in good condition (Fig. 8). Furthermore, the quantity of autophagosomes increased. They swallowed some fragments of cytoplasm or membrane structures in big or small vacuoles, and they occasionally grouped together to locate broadly in perikaryon. The cerebrum included membrane-bound globular dense masses with a diameter of 0.3–1.8 μm. Both the neuron's perikarya and dendrites displayed one or more of these features. Purkinje cells in the cerebellum had a high electron density and were atrophic. Chromatin aggregation shrank the nuclei of Purkinje cells, and the nuclear membrane occasionally became hazy. There were numerous autophagosomes in the Purkinje cell perikarya, just as there were in the cerebral neurons. The cisternae of

the Golgi apparatus were enlarged. Purkinje cell cytoplasm was shown to include membrane-bound dense bodies. Cerebellar granule cells exhibited a high electron density and localized atrophic behavior. Others had an edematous perikaryon and were clear. Every atrophic granule cell had a few free ribosomes, but inflated granule cells had fewer of them.The molecular layer consisted of a mixture of parallel fibers. The parallel fibers had not all been kept to the same size. Purkinje cell spines have a high electron density. The large parallel fibers were synaptically connected to these spines. Large mitochondria or synaptic vesicles were present in the expanded terminals of presynapses (Fig. 9).



“Fig. 8”, An electron micrograph of a neuron located in Case 3's calcarine cortex. Nerve cells exhibit a reduction in size, a black stain, and a rise in nuclear chromatin. The cytoplasm is filled with free ribosomes, some of which are aggregating in certain areas. It is seen that well-preserved mitochondria and rough endoplasmic reticula (Nissl bodies) have vanished. According to Eto al. [20]



“Fig. 9”, An electron micrograph of the cerebellum's molecular layer displaying Case 3's enlarged presynaptic terminals, long parallel fibers that are well-developed and irregularly thick, and Purkinje cell spines generating synapses (center). According to Eto al. [20]

Epidemiology

In March 2001, Chisso had formally certified 2,265 victims [21], and over 10,000 persons had received financial compensation [22], even if they were not legally recognized as victims. Because a comprehensive epidemiological research has never been carried out and patients were only recognized upon voluntary application to a certifying body in order to pursue monetary compensation, the problem of estimating the impact of Minamata disease is challenging.[23, 24] If those with Minamata disease disclosed their symptoms in public, many of them would have faced prejudice and exclusion from the neighborhood. Many locals were intensely loyal to Chisso, relying on the corporation for their livelihoods, and some individuals believed the disease to be contagious. Those who were impacted were reluctant to come out and apply for certification in this environment. In spite of this, more than 17,000 individuals have submitted certification applications to the council. Additionally, by identifying a candidate as having Minamata illness, the Certification Council made the patient eligible for Chisso to pay for their care. Because of this, the council has consistently faced tremendous pressure to deny claims and lessen the financial strain on Chisso. The council's choices were always influenced by the political and economic circumstances around Minamata and the Chisso corporation, rather than the council of medical recognition. In addition, the payment of compensation to the victims sparked ongoing conflict in the community, resulting in false allegations that some of the individuals requesting compensation were not afflicted with the illness.[25] Rather than a medical "disease," the impact is more appropriately described as a criminal "poisoning." 'Environmental victims' frequently face these types of obfuscation in various nations.[26] Minamata is home to the National Institute for Minamata Disease, which was founded in 1978. The Department of Clinical Medicine, the Department of Epidemiology, the Department of Basic Medical Science, and the Department of International Affairs and Environmental Sciences make up its four departments.[27] The Institute joined the WHO as a Collaborating Center for Studies on the Impact of Mercury Compounds on Health in 1986.[28] The Institute studies mercury compounds, their effects on organisms, and possible detoxification mechanisms in an effort to enhance the medical care provided to patients with Minamata sickness. In addition, the payment of compensation to the victims sparked ongoing conflict in the community, resulting in false allegations that some of the individuals requesting compensation were not afflicted with the illness.[25] Rather than a medical "disease," the impact is more appropriately described as a criminal "poisoning." 'Environmental victims' frequently face these types of obfuscation in various nations.[26] Minamata is home to the National Institute for Minamata Disease, which was founded in 1978. The Department of Clinical Medicine, the Department of Epidemiology, the Department of Basic Medical Science, and the

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Environmental protection :

Environmental protection in Japan rose largely as a result of the Minamata victims' and activists' fight for redress and the public outcry it generated. The 1970 Japanese Diet session is known as the "Pollution Diet" because the Japanese government intervened in response to mounting pressure from the Minamata sickness campaign and other significant environmental tragedies including Yokkaichi asthma and itai-itai disease. In a single session, fourteen new environmental laws were established, giving Japan the strictest environmental protection regulations in the world at the time.[30] Among these new legislation were national controls of harmful discharges and the Water Pollution Act. The idea of "polluter pays" was first presented. In 1971, a national environmental agency was established, which subsequently transformed into the Ministry of Environment.[31] Between 1970 and 1975, national government spending on environmental issues nearly doubled, while local government spending tripled.

Diagnosis

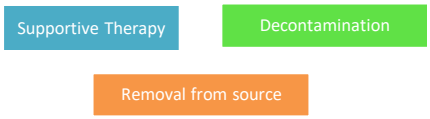
The most common method of diagnosing mercury poisoning is having a hair sample tested at a lab to determine the mercury levels. This is a pretty simple method that is clearly non-invasive. Health care professionals would probably ask for testing if you reside in an area where mercury poisoning cases have occurred or if there has been a significant increase in cases with symptoms similar to those of mercury poisoning. Because of legal requirements for compensation and health incidents related to pollution, the national government and local governors in Japan also determine whether a person has Minamata sickness. In circumstances when symptoms are difficult to diagnose, particularly in recent cases with moderate symptoms, medical professionals may seek optokinetic nystagmus pattern (OKP) and electro-ophthalmography (EOG) in order to acquire referential data if they suspect Minamata Disease.[32]

Medical expenses and compensation

Medical costs and a lump sum payment are made to patients who meet the requirements set forth by the Japanese law "Concerning Compensation for Pollution-related Health Damage" and are deemed to have Minamata sickness. But in Kumamoto and Kagoshima prefectures, hardly any patients have recently received certification from the Pollution-related Health Damage Certification Councils.You are entitled to help with the cost of medical care if you have a medical treatment notebook or a Minamata illness Patient's Record Book. On the other hand, you will not be eligible for reimbursement if you have not been making the regular health insurance premiums. Regarding nursing care insurance, you will receive help with the one-time costs for public nursing care insurance, which offers care, home care, and rehabilitation at home or in a facility. All medical treatments, with the exception of dental care, will be covered by compensation.[33]

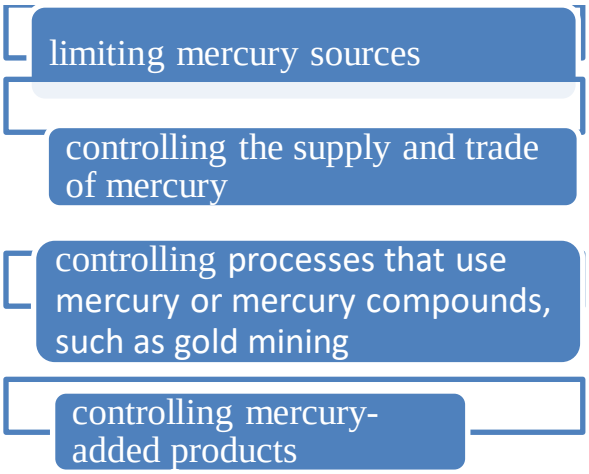
Treatment

Research has demonstrated the importance of early detection, suggesting that if preventive measures had been implemented to minimize contamination earlier on, the initial Minamata disease outbreak would have been considerably less. There are few treatment guidelines available for methylmercury poisoning. The principal measures comprise:



“Fig. 10”, Principle Measures

However, because the neurological symptoms of Minamata illness are often irreversible, there is no known cure for the condition. In line with the Sustainable Development Goals and to tackle the widespread issue of Minamata illness, the United Nations formulated the Minamata Convention on Mercury in 2013.To protect people from exposure to mercury and its derivatives, an international accord known as the Minamata Convention on Mercury was developed.



"Fig. 11", The agreement listed several steps to accomplish this goal.

Depending on the severity of the ailment and the symptoms, different treatments may be required. Nonetheless, several conventional methods are employed as follows:

- Locating and severing the exposure source to stop more exposure. This is the initial stage, without a doubt, and it serves as a requirement for treatment in many ways.
- Using chelating agents to remove mercury from the body is the most crucial part of treatment. Chelating chemicals interact with bodily tissue and bind with it in order to stop heavy metals like mercury from doing so. Naturally, this has a unique set of side effects, which is why specialists suggest using drugs with the least amount of toxicity.
- Patients frequently have paralysis and loss of muscle function. While the severity of these conditions varies, physical therapy is nearly always required or beneficial since it gives patients some degree of control over their mobility.
- Mercury is very bad for the body since it also raises levels of reactive oxygen, which can be lowered by taking antioxidants.
- In certain circumstances, patients may experience convulsions, in which case doctors would prescribe anticonvulsant medicines.[35]

It is essential to locate and eliminate the mercury's source. It is necessary to take off clothing, wash skin with soap and water, and flush the eyes with saline solution as needed in order to decontaminate. Iodide salts were administered orally prior to the development of organic chelating agents; Louis Melsens and several physicians from the late nineteenth and early twentieth centuries greatly popularized this practice.[36, 37]

Chelation therapy

Chelation therapy, a once widely used treatment for acute inorganic mercury poisoning, involved the use of dimercaprol (BAL), D-penicillamine (DPCN), 2,3-dimercapto-1-propanesulfonic acid (DMPS), or DMSA.[38] The only medication for treating mercury poisoning in children that has FDA approval is DMSA. However, DMSA treatment for mercury vapor poisoning did not appear to provide any discernible clinical effect in many studies.[39] The FDA has not approved any chelators for methylmercury or ethylmercury; the most common treatment for severe methylmercury poisoning is DMSA, which is taken orally, has less side effects, and has been found to be more effective than BAL, DPCN, and DMPS.[38] When administered promptly after exposure, α-lipoic acid (ALA) has been demonstrated to protect against acute mercury poisoning in a number of mammalian species; nevertheless, the right dosage is necessary because the wrong dosage increases toxicity. Rat experiments have produced conflicting results, despite the theory that regular modest dosages of ALA may have potential as a mercury chelator. While some doctors advise taking glutathione and N-acetylcysteine (NAC), studies have shown that these supplements raise mercury levels in the kidneys and brain.[40] If chelation therapy is given improperly, it can be dangerous. A five-year-old autistic kid died in August 2005 after receiving the wrong kind of EDTA (edetate disodium), which was used for chelation therapy and caused hypocalcemia and cardiac arrest.[41]

Other

The results of epidemiological studies and experimental animal research have validated the relationship between methylmercury and selenium. Epidemiological studies have shown that improved nutritional (i.e., omega-3 fatty acids, selenium, iodine, vitamin D) intakes as a result of ocean fish eating during pregnancy improve maternal and fetal outcomes, rather than leading to a deterioration in neurodevelopmental outcomes.[42] For instance, consuming more ocean fish when pregnant was linked to IQ increases in children of 4-6 points.

CONCLUSION:

A common illustration of the harm that pollution causes to health in Japan is Minamata Disease, Following years of research into the origins of the illness, the government ultimately declared in 1968 that it believed fish and shellfish tainted with

methylmercury compound released from a chemical facility were the cause of Minamata Disease. It is recognized that Minamata Disease is a central nervous system. The removal of polluted sediments from the bay and riverbed, the monitoring of methylmercury levels in fish and wastewater, and other actions have all been taken as countermeasures against environmental contamination.To determine the amount of health damage and provide relief for the victims, a comprehensive survey of health harm was conducted. The way the system is set up, people who are certified by the government as having Minamata Disease based on the Pollution-related Health Damage Compensation Law are eligible to receive compensation from the company that caused the pollution if their condition is confirmed by medical science.Furthermore, beginning in the 1992 fiscal year, the government conducted health examinations on local residents and provided financial assistance for medical treatment of those exhibiting symptoms similar to those of Minamata Disease in an effort to allay concerns about the health of those who may have been exposed to methylmercury. Furthermore, the government has provided funding to the accountable corporation to aid in the payment of substantial compensation and has encouraged research and investigation regarding Minamata Disease, including the creation of the National Institute for Minamata Disease. In this way, the Minamata Disease case in Japan highlights how actions that prioritize economic objectives over environmental concerns result in irreversible harm and unfavorable outcomes even from an economic perspective, given the extensive measures, high costs, and extended duration needed to mitigate these effects. We hope that other countries will take note of Japan's experience and realize once more how vital it is to protect the environment, and that steps will be taken to prevent environmental contamination there.

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