

NIMD Annual report 2024

(April 2024 to March 2025)



National Institute for Minamata Disease
Ministry of the Environment
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Report on Research and Other Activities
in the Fiscal Year 2024

1. Pathomechanism Group

The aim of the study group is to understand the molecular mechanisms underlying methylmercury (MeHg) toxicity in humans. The goals are as follows: 1. To understand the initial signs of MeHg poisoning, 2. to evaluate MeHg toxicity, 3. to develop methods to protect against MeHg-induced disorders, and 4. to develop new treatment options for MeHg poisoning. Techniques in the fields of biochemistry, molecular biology, and pathology are used in cell cultures and animal models in to achieves the objectives.

The group conducted the following research during the fiscal year 2024.

[Research theme and summary]

[1] Fundamental research on neurotoxic mechanism of methylmercury and its prevention and treatment

(Project research)

Masatake Fujimura

(Department of Basic Medical Sciences)

1) Research on selective cytotoxicity of MeHg

We found that levels of brain-derived neurotrophic factor (BDNF) increase in an exercise-loaded model and suppresses MeHg toxicity. Additionally, we presented two papers as first authors at conferences.

2) Research on individual susceptibility to MeHg neurotoxicity and related biomarkers

We established a measurement method using liquid chromatography-mass spectroscopy (LC-MS) to identify polythiolation of blood proteins. We also measured micro RNAs (miRNAs) in extracellular vesicles, analyzed their functions, and discovered miRNAs that are promising biomarkers. In addition, as the first authors, we presented two papers at conferences.

3) Research on the onset of neuropathic pain caused by MeHg and its drug effect.

We investigated the therapeutic effects of gabapentin on neuropathic pain in a rat model of MeHg intoxication. Furthermore, one paper has been accepted and published in an international journal as the first author.

4) Joint research with external research institutes

We conducted joint research with external institutions on MeHg toxicity not conducted at our research center, focusing on endoplasmic reticulum (ER) stress and the epigenome. We presented two papers as co-authors at an international conference, one on the effects of endoplasmic reticulum stress inhibitors on MeHg exposure and the other on epigenomic genes affected by MeHg. Two papers have been accepted for publication in international journals. Additionally, we established the “Department of Biometalscience” as an extramural course of the Okayama University Graduate School of Medical, Dental and Pharmaceutical Sciences, and accepted one student into the program.

[2] Study on reducing the health risk of methylmercury by food ingredients

(Fundamental research)

Masaaki Nagano

(Department of Basic Medical Science)

This study aims to reduce the health risks of MeHg by utilizing the function of food ingredients. So far, we have demonstrated that daily intake of raw wheat bran (raw bran) significantly reduces tissue mercury concentration in mice exposed to MeHg. Wheat bran is commonly used to add texture and richness to bread, cereal, and other baked goods.

In FY 2024, we examined the effect of roasted bran on mercury excretion in mice after single administration of MeHg. Tissue mercury concentrations were significantly lower in both the raw and roasted bran

groups compared to the control group; however, no significant difference was observed between the two bran groups. Urinary mercury excretion was also significantly higher in the bran-fed groups than in controls, and the results were consistent with the tissue mercury concentrations. These results indicate that the effect of roasted bran on the accumulation and excretion of MeHg is comparable to that of raw bran, suggesting that the consumption of foods containing bran may enhance mercury excretion.

[3] Research on the methylmercury-induced alteration of protein function and its protective factors

(Fundamental research)

Takamitsu Unoki

(Department of Basic Medical Sciences)

- 1) We focused on Caspase-3, which was found to undergo MeHg-dependent desulfurization in neurons based on a previous year's analysis. Protease activity was measured in solid-phase Caspase-3, and was found to decrease due to transsulfuration, followed by an increase upon MeHg exposure. One part of MeHg-induced neuronal cell death is mediated by apoptosis, and Caspase-3 acts as the executor. This suggests that the MeHg-induced desupersulfuration of Caspase-3 enhances apoptosis.
- 2) We constructed an analytical system to measure the amount of trans-sulfur by LC-MS by preparing a cysteine-containing model protein and solid-phasing it onto beads. The amount of trans-sulfur in the model protein decreases upon exposure to MeHg. Therefore, it is suggested that MeHg deprives cysteine residues in the trans-sulfur polymers, which is consistent with the findings of 1).
- 3) A review article on supersulfur metabolism and MeHg toxicity defense has been co-authored and accepted for publication.

[4] Development of sensor for methylmercury toxicity and research on the mechanism of methylmercury neurotoxicity

(Fundamental research)

Akio Sumioka

(Department of Basic Science)

MeHg induces electrophilic stress in the brain, leading to neurodegeneration. However, the mechanisms underlying the cell-specificity and age-dependency of MeHg toxicity remain unclear. Therefore, we developed a new sensor vector, Krab-Sec/Luc, to detect MeHg toxicity and studied its underlying molecular mechanisms.

In addition to the traditional balance model, we propose a novel target-specific model, which involves specific interactions among electrophiles, nucleophiles, and proteins. Based on this hypothesis, expression profiles of target proteins in each cell may contribute to the cell-specific toxicity of MeHg, and we investigated to verify this model.

1) Development of sensor vectors to detect methylmercury toxicity

To develop MeHg toxicity sensors, we performed additional validation studies, such as the measurement of selenoprotein TrxR1 activity. These findings were published in Scientific Reports.

The sensor vector system comprised pCT-Luc and Krab-Sec. In FY 2024, we successfully generate F1 mice with pCT-Luc and confirmed luciferase signals in the cerebellum. Moreover, we generated F0 mice carrying the Krab-Sec component.

2) Research on the mechanisms of neurotoxicity induced by methylmercury

In FY 2024, we utilized primary cultures of mouse cerebellar granule cells to assess the changes in MeHg toxicity sensitivity under the influence of various inhibitors. As a result, we successfully classified MeHg toxicity specific to the cerebellum.

3) Analysis of sensitivity to MeHg exposure

Using the toxicity sensor developed in previous years,

we examined the factors contributing to MeHg sensitivity in FY2024. Upon evaluating various conditions, we observed changes in sensitivity caused by the cell density, culture medium, and several reagents.

Among these, cell density exerted a remarkable ~10-fold effect on sensitivity to MeHg, strongly suggesting the presence of endogenous factors that confer resistance to MeHg toxicity. This finding has significantly enhanced the reproducibility of MeHg toxicity assays and enabled reliable observations under lower MeHg concentrations.

The type of culture medium affected both MeHg sensitivity and the intensity of sensor signaling, implying that it contains active components that influence MeHg toxicity. It will be necessary to identify these factors in future studies.

The results of these investigations were presented at research symposium.

2. Medical practice • Welfare • Society Group

Group Research

As the population of patients with Minamata disease (MD) ages, their neurological symptoms are becoming more complex due to complications such as cervical spondylosis and metabolic syndrome. This makes it increasingly difficult to diagnose MD based solely on the clinical and neurological findings. Consequently, there is an urgent need to establish objective diagnostic methods to distinguish methylmercury poisoning from other diseases, including MD.

In addition, involuntary movements such as spasticity, dystonia, neuropathic pain, and ataxia significantly affect the quality of life (QOL) of MD patients, highlighting the need for effective treatment methods.

Detailed planning is required for regional revitalization in areas affected by MD.

Therefore, our research group is conducting studies to establish objective evaluation methods for neurological function using magnetoencephalography (MEG) and magnetic resonance imaging (MRI), to investigate the efficacy and safety of magnetic stimulation therapy for the aforementioned symptoms and to analyze the challenges of regional revitalization in areas affected by MD from multiple perspectives.

The research conducted by our group during FY 2024 is outlined below.

[Research theme and summary]

- [1] Research on health effects of methylmercury exposure in humans and therapeutic development
(project research)
Masaaki Nakamura
(Department of Clinical Medicine)

This year, in the analysis of magnetoencephalography (MEG) data, we extracted estimated neural activity time series data for the primary somatosensory cortex (SI) and motor cortex (MI) from somatosensory evoked

fields data and performed calculations of cross-correlation values and frequency spectrum analysis. In patients with MD who were determined to be within the normal range based on a previous MEG analysis, a decrease in cross-correlation values and rebound were observed in M1, suggesting that adding MI analysis data may improve the sensitivity of MEG examination. Additionally, we examined the extent of atrophy in the thalamus and cerebellum in detail using MRI. In patients with MD, atrophy of all thalamic subregions was observed, and cerebellar hemispheres VIIB, VIII, and VIII of the vermis were identified as diagnostically useful.

Recently, it has been reported that normalizing the PAF through non-invasive brain stimulation methods is beneficial for symptom relief in neuropathic pain. In this study, we successfully enhanced the alpha frequency band in the sensory cortex by combining otDCS and tACS to stimulate the motor cortex in healthy individuals.

Furthermore, given that GABA in the thalamus and SI is involved in the pathophysiology of neuropathic pain, we measured GABA and glutamate levels in the thalamus and SI of 15 healthy individuals. In the future, we plan to verify the efficacy of this method in treating neuropathic pain.

- [2] Area studies about the regional revitalization in Minamata City and neighboring cities

(Fundamental research)

Rie Harada

(Department of International Affairs and Research).

This research project has been conducted with four pillars: (i) understanding the actual situation of Minamata disease damage, (ii) uncovering regional issues, (iii) developing methods for regional revitalization, and (iv) researching specific case studies.

This year, one paper on issue (i) is being revised, and

another was published in a specialized sociological book. The contents of these two papers have been presented at conferences. Regarding the identification of regional issues in (ii), the analysis up to the previous year was completed. This will continue as a supplementary issue in the midterm plan. Regarding (iii) the development of methods for regional revitalization, this study reflected some of the findings from field research conducted with the help of local studies. In case study (iv), artists and creators were invited from Japan and abroad, and a project was organized at the Minamata Memorial, which was changed to the Minamata Disease Archives on November 2. This study addresses the possibility of regional regeneration through art and the importance of preserving historical remains.

Activities

Considering the aging population of patients with Minamata disease (MD), we are actively working with relevant organizations to improve welfare in the region and implement measures to address MD. To explore effective home support options for MD victims and their families, we implemented the “Home support model study, including care prevention” (FY 2006–2008), the “Community development project for home care support, including healthcare practice” (FY 2009–2011), and the “Community welfare promotion business for supporting MD victims” (FY 2012). Based on the results obtained thus far, we will continue to support welfare activities in Minamata City, Izumi City, and Tsunagi Town to further establish care prevention projects in areas affected by MD.

In fiscal year 2016, we began improving handicraft programs based on questionnaire surveys. In fiscal year 2017, we began promoting community living rooms through the website and Facebook of the National Institute of Minamata Disease to increase the number of participants.

We organized conventional rehabilitation activities,

including daycare facilities for fetal- or infantile-type patients with MD, along with annual workshops on rehabilitation and assistance techniques. We also examined the usefulness of lumbar nerve root magnetic stimulation for spasticity, belt electrode skeletal muscle electrical stimulation for maintaining and increasing lower limb muscle strength, neuromuscular electrical stimulation (NMES) for dysphagia and dysarthria in patients with MD, and walking training using walking learning support robots and non-powered walking assist devices.

Additionally, we shared knowledge and disseminated information to the community through rehabilitation awareness activities (rehabilitation and assistance technique seminars).

Since pathological tissue specimens from MD autopsy cases are extremely valuable, we digitized the pathology slides for permanent preservation and published them on a website to train students and doctors in pathology.

Based on the comprehensive cooperation agreement with Minamata City, we also supported the survey related to regional revitalization, including “Moyainaoshi” in collaboration with Minamata City.

To obtain basic data that contribute to the improvement of activities of daily living (ADL) in patients with chronic MD, we conducted a survey to clarify ADL changes in patients with chronic MD and differences in sequential ADL decline depending on the clinical entity of chronic MD.

The following section outlines the clinical and social practices conducted by this group in FY 2024.

[Activity theme and summary]

[3] Community development project for home care support, including health care practice

Masaaki Nakamura
(Department of Clinical Medicine)

To examine methods to support aging patients with

MD and their families, including rehabilitation to improve ADL, the following projects were implemented: “Home support model study, including care prevention” from FY 2006 to FY 2009, “Community development project for home care support, including healthcare practice” from FY 2009 to FY 2012, and “Project for Promotion of Community Welfare for Support of Minamata Disease Victims” from FY 2012 to FY 2013. In addition, for one year since FY 2012, we implemented the “Community Welfare Promotion Business to support MD victims.” Based on these achievements, further activities have been undertaken to help care prevention projects take root in areas where MD occurs.

In Minamata City, we supported the community center activities of the Minamata City Council of Social Welfare by providing “brain training through handicrafts.” In Izumi City, we supported the “Fureai Iki-iki Salon” activities of the Izumi City Council of Social Welfare, Takaono and Noda Branch Offices. In Tsunaki Town, we held handicraft classes at the “Itte-miyu-kai” project for preventing bone fractures from falls and at the “Tatshaka Juku” program conducted by the Tsunagi Town Office.

To provide better handicrafts, we surveyed participants in each district and developed a handicraft program that resulted in higher participant satisfaction. Notably, because one-quarter of the participants in the handicraft classes recognized hearing loss, a dialogue support speaker (Comuoon) was utilized to make it easier for people with hearing loss to participate, and improvements in audibility were observed among participants with hearing loss.

Measures to prevent frailty are recommended to extend the healthy life expectancy. In recent years, we have collaborated with the Minamata City Council of Social Welfare to launch a project aimed at preventing frailty in Minamata City and have begun collecting basic data and implementing exercise classes. This year, we examined the effects of exercise interventions on

frailty improvement.

To encourage local residents to participate in the care prevention program, we actively conducted publicity activities for local residents on the National Institute for Minamata Disease website and Facebook page (activity reports of handicraft classes held each time and a notice for the next class).

[4] Rehabilitation programs for patients with Minamata disease and dissemination of information on care and rehabilitation

Atsushi Nakamura

(Department of Clinical Medicine)

We continued to provide rehabilitation to the patients with Minamata disease (MD) improves the quality of life (QOL). We introduced a new gait-learning support robot (Orthobot) and combined it with peripheral magnetic stimulation, belt electrode-type skeletal muscle electrical stimulation, and non-powered walking aids (alQ) to provide ongoing rehabilitation, focusing mainly on walking disorders.

We have been working on a neuromuscular electrical stimulation (NMES) intervention as rehabilitation for swallowing dysfunction in patients with MD, which has recently become a contributing factor to a decline in ADL. Although the effects of rehabilitation on dysphagia vary depending on the degree of dysfunction, early intervention is expected to maintain and improve the swallowing function. We plan to propose early intervention for fetal MD as one of the measures to prevent dysphagia.

Face-to-face workshops were held to promote rehabilitation and welfare techniques in the MD outbreak areas. Continuing from the previous year, the workshop was recorded and made available on the center's website for those who were unable to attend the workshop and for those who attended the workshop to learn afterwards.

As efforts related to information dissemination to local residents and care prevention, we visited the Orange hall,

which was established as part of the “Moyai-naoshi project,” twice a month. At the Orange hall, we conducted physical and cognitive function evaluations, ADL evaluations, and health exercise classes for local older people, including patients with MD.

[5] Appropriate management and information provision of pathological specimens related to Minamata disease

Masumi Marumoto
(Department of Basic Medical Sciences)

Unlike other diseases, autopsy histopathological specimens related to Minamata disease are extremely valuable, because humans will never be able to obtain them again. However, they are difficult to store permanently because they fade over time. We are continuously digitizing the histopathological specimens of Minamata disease cases with the aim of permanently preserving them.

We will also create a website that utilizes digitized histopathology specimens as educational materials for students and researchers studying pathology. Simultaneously, a pamphlet explaining the pathology for the general public and children will be prepared.

In addition to histopathological specimens, the center contains a large number of valuable pathology-related samples, and we will continue to organize and preserve these samples.

This year, the Japanese and English versions of the website were updated. In addition, Japanese and English versions of the Brain Cutting Manual, which can be used when encountering suspected cases of Minamata disease, were completed.

[6] Needs survey on the agreement for comprehensive cooperation with Minamata City

Rie Harada
(Department of International Affairs and Research).
The Study Group on the Use of Vacant Houses and Support Measures for Migrants, Minamata City

organized a study tour of Ei Town in Kagoshima Prefecture, an area at the forefront of vacant house use, from July 7 to 8. The group also organized a study meeting on February 2 to summarize past activities.

The number of users gradually increasing through the website and social media. Some vacant houses had tenants because of the study group's activities. In some cases, vacant houses have succeeded in attracting migrants.

The activities and ideas that emerged from the study group will be compiled into a report and distributed to the relevant authorities to ensure that the report's contents are utilized.

[7] Temporal trend analysis of activities of daily living (ADL) in patients with Minamata Disease

Sawako Horai
(Department of Environment and Health)

This study aimed to clarify the changes in ADL in chronic-type of Minamata disease patients and the differences in ADL decline over time depending on the disease type.

Evaluation methods for ADL (Ability to Activities of Daily Living), IADL (Instrumental Ability to Perform Activities of Daily Living), N-ADL (N-type ADL rating scale for the elderly), and the NM Scale (N-type Mental Status Scale for the elderly) were used. A questionnaire survey regarding the symptoms was conducted. To characterize the actual ADLs of patients with Minamata disease (n = 16), 44 residents of Kagoshima City and Makurazaki City, Kagoshima Prefecture, were used as controls and compared with patients with Minamata disease.

The results showed that the N-ADL score (on a 50-point scale) was not significantly different between the adult-type Minamata disease group and the control group, whereas the fetal/childhood-type Minamata disease group was significantly lower ($p=0.001$). Patients with MD showed a significant decrease in walking and sitting up. From these results, it was

inferred that patients with Minamata disease are prone to walking difficulties. In addition, there was a significant difference between the Minamata disease patients and control groups in the assessment of living areas ($p=0.001$). This finding suggests that walking difficulties result in smaller residential areas.

In the I-ADL assessment, there were no significant differences among the control and Minamata disease patient groups in men; however, a significant difference was found in women with Minamata disease ($p < 0.0001$). This could be attributed to the fact that only women included the items “meal preparation,” “laundry,” and “housework” and both items were significantly lower in the patient group than in the control group ($p = 0.0003$, $p = 0.0031$, and $p = 0.0031$, respectively). Among these three items, the percentage of those who were unable to do so was higher in the fetal/childhood-type Minamata disease group. The percentage of respondents with Minamata disease was significantly lower in the “shopping” category ($p=0.0012$), including both males and females.

A frailty/sarcopenia assessment was conducted and the percentage of those determined to have possible sarcopenia was 2.3% in the control group and 50% in the Minamata disease patient group. Approximately 30% of male patients showed the possibility of sarcopenia, whereas more than 80% of female patients did. In the frailty assessment, the percentage of those with frailty symptoms corresponding to 3 or more of the 5 items were 4.5% in the control group, 18.2% in the fetal/childhood-type Minamata disease patient group, and 0% in the adult-type Minamata disease patient group. The percentages of pre-failure (1-2 out of 5 items) were 47.7%, 63.6%, and 75% in the control group, fetal/childhood-type Minamata disease group, and adult-type Minamata disease groups, respectively. These results suggest that patients with Minamata disease, especially fetal/childhood-type female patients, have difficulties in performing daily activities due to muscle weakness. In future, from the viewpoint of QOL

maintenance and prevention, it will be necessary to conduct ongoing surveys to clarify when and how this decline occurs.

3. Risk Assessment Group

High-risk groups for MeHg exposure included populations exposed to high concentrations of Hg and those with high sensitivity to Hg. The risk assessment group comprehensively assessed human exposure to Hg and its effects on health caused by environmental pollution. We will conduct both epidemiological and experimental studies to assess various confounding factors, such as selenium (Se), to elucidate the exposure, risk assessment, and health effects of MeHg, especially in populations exposed to high concentrations of MeHg and vulnerable populations such as fetuses, children, and those with diseases.

[Research themes and summary]

- [1] Studies on coexisting of mercury and selenium in Minamata disease and effects of methylmercury to fetus and breast-feeding infants

(Fundamental research)

Mineshi Sakamoto

(Special advisor to the Director-General)

Minamata disease, widely regarded as the origin of Japan's environmental pollution issues, was officially recognized in 1956 following reports of patients exhibiting unexplained neurological symptoms along the coast of Minamata Bay. Early investigations found high levels of selenium in the livers and kidneys of affected cats and humans, leading to the initial hypothesis that selenium may be the causative agent. However, subsequent research identified methylmercury, discharged in wastewater from the Chisso Minamata Factory, as the actual cause. Despite its accumulation in humans and animals, the biological role of Se has not been adequately studied. The objective of this study was to assess the role of selenium in the onset and progression of Minamata disease through a reanalysis of historical environmental and biological samples, including bay sediments, seafood, and patient organ tissues. We re-analyzed archived

environmental and pathological specimens related to Minamata disease, measuring the concentrations of mercury and selenium, and calculated their molar ratios of Hg to Se. Our analysis revealed for the first time that both methylmercury and selenium were discharged into Minamata Bay and subsequently accumulated at high levels in human organs via the food chain. The Hg/Se molar ratios in the contaminated seafood exceeded 3, which was substantially higher than that in typical marine products, indicating severe methylmercury pollution. In the liver and kidneys of patients, mercury levels were extraordinarily high, and selenium levels were markedly elevated, suggesting a possible protective effect of selenium in these organs. In contrast, selenium concentrations in the cerebrum and cerebellum were only moderately elevated, and Hg/Se molar ratios in these tissues were 4 times higher than those in other organs, indicating that the protective role of selenium against methylmercury neurotoxicity may have been limited to the central nervous system. This study highlights the importance of considering the biological interactions of selenium when assessing the toxicity of methylmercury exposure. The reanalysis of historical samples offers novel perspectives and may contribute to a deeper understanding of the pathogenesis of Minamata disease.

- [2] Enhancement of the exposure assessment system for groups at high risk of methylmercury exposure

(Fundamental Research)

Megumi Yamamoto

(Department of Environment and Public Health)

- (1) Tissue distribution of methylmercury in the mother and fetus was analyzed using K_p values (total mercury in each tissue of the mother or fetus/total mercury in the maternal plasma). In the obese condition with mildly abnormal glucose metabolism, K_p values in the maternal brain and liver of HFD mice tended to be

lower than those of Ctrl mice, while no significant differences were found between groups in the kidneys or blood cells. The K_p values for fetal tissues (brain, liver, kidney, and placenta) tended to be lower in HFD mice than in control mice. Pregnant mice showed a trend toward higher brain K_p values and lower kidney K_p values than non-pregnant mice, regardless of the diet. These results have been submitted for publication and are accepted (J. Appl. Toxicol.).

(2) An evaluation system for the inhibition of methylmercury transfer from mother to fetus using mice is currently under investigation.

(3) We analyzed the mercury levels in biological samples (hair, blood, placental tissue, and umbilical cord tissue) collected from mothers and infants. We plan to proceed with a related analysis of each sample.

(4) Pathological analysis of the placentas of pregnant women with abnormal glucose metabolism showed increased expression of LAT1, an amino acid transporter involved in the fetal transfer of methylmercury. A collaborator has submitted a paper for publication, which was accepted (J. Obstet. Gynaecol. Res.).

(5) To establish a methylmercury analysis method for biological samples based on the NIMD-B method, the toluene layer (organic mercury fraction) of the NIMD-B method using fish and shellfish samples spiked with ethylmercury and thimerosal was analyzed by GC-ECD, and preliminary data on the separation conditions for each organic mercury were obtained.

[3] Exposure assessment of mercury in developing countries and technology transfer

(Fundamental research)

Megumi Yamamoto

(Department of Environment and Public Health)

(1) With regard to understanding the actual situation of methylmercury exposure among pregnant women in Hanoi, Vietnam, we are proceeding with a correlation analysis of analytical data for each sample (hair

mercury, fecal mercury, nail Se), FFQ, etc., and plan to submit a paper as soon as possible.

(2) As it has become difficult to continue the survey in the ASGM region of Indonesia, which was our original objective, we are negotiating with counterparts in other surveyed areas.

(3) Preliminary studies on the training and technology transfer of mercury analysis to developing countries and the actual situation and research on mercury pollution were conducted (*Diponegoro University, Indonesia; * University of Jember, Indonesia; * University of Ibadan, Nigeria).

[4] Relationship between the exposure level and dose-response of methylmercury and essential trace elements in mammals with high mercury levels

(Fundamental research)

Sawako Horai

(Department of Environment and Public Health)

To elucidate the biological defense mechanism against methylmercury toxicity, we investigated (1) the transfer of mercury and essential trace elements between dams and fetuses and (2) the concentration dependence of mercury and essential trace elements using the small Indian mongoose, which is a mercury-accumulating species. (3) The relationship between selenium compounds (selenoproteins and selenium-containing enzymes) and mercury concentrations in the blood of mongooses, cetaceans, and Taiji residents to characterize the dose-response relationships of mercury, selenium, and other essential trace elements in methylmercury-tolerant species.

Regarding (1), we reanalyzed data on maternal whole blood, fetal liver, cerebrum, and whole blood of 29 small Indian mongoose mother-fetus pairs collected and measured for trace elements, including Hg. In the fetal liver, cerebral, and whole blood mercury concentrations did not change significantly with increasing fetal body weight. In contrast, in the liver, O/THg (%) decreased significantly with increasing

fetal body weight ($p < 0.05$), indicating that mineralization of organic mercury in the liver occurs during the fetal period. Next, we analyzed the relationship between the fetal blood/maternal blood (FB/MB) ratio of Hg, which is considered an indicator of maternal-to-fetal mercury exposure, and fetal organ concentrations, and found significant negative correlations in the liver ($p < 0.05$) and cerebrum ($p < 0.01$). These results indicate that a higher FB/MB ratio decreases the Hg concentration in fetal organs. Next, to elucidate the cause of the variation in the FB/MB ratio, we analyzed the relationship between the FB/MB ratio and Hg concentrations in maternal and fetal whole blood, and found a significant negative correlation ($p < 0.0001$) between Hg concentrations in maternal whole blood and the FB/MB ratio. The slope between fetal whole-blood Hg concentration and the FB/MB ratio differed depending on the degree of maternal Hg exposure. These results suggested that the lower the maternal Hg exposure, the greater the variation in the FB/MB ratio.

Regarding (2), Hg co-localized with Se mainly in the choroid plexus and lateral ventricular wall astrocytes, but may not be HgSe. The results of this study are summarized in Devabathini, P., Fischer, D. L., Chen, S., Pattammattel, A., Bury, G., Antipova, O., Huang, X., Yong S., Chu, Y., Horai, S., Pushkar, Y. (2023): Wild high-resolution imaging of Hg/Se aggregates in the brain of a terrestrial species (small Indian mongoose)—Insights into intracellular Hg detoxification—and published in *Environ. Chem. Lett.* In addition to that, A partial results of this study were summarized in Horai, S., Kawano, N., Nakata, K., Sekizawa, O., Kunisue, T. (2024): Analysis of mercury and other trace element localization in the brain of the small Indian mongoose, and published in *SPRING-8/SACLA Research Reports* (in Japanese).

With respect to (3), the urinary selenium metabolites in small Indian mongooses and mice were compared. The urinary selenium metabolite of mice was SeSugarB,

and TMSe was detected, whereas the selenium metabolites of mongooses included a low proportion of SeSugarB, and TMSe was hardly detected. In contrast, the ratio of SeSugarA to unknown substances was higher in mongooses than in mice. It was inferred that the physiological requirement for selenium in the human body was higher than that in mice, which was influenced by exposure to Hg. The next year's goal will be to analyze the relationship between body Hg levels and urinary selenium metabolites.

[5] Evaluation of methylmercury-induced neurological symptoms and the association of selenium compounds with toxicity in common marmosets

(Fundamental research)

Megumi Yamamoto

(Department of Environment and Public Health)

(1) To establish a quantitative evaluation system for neurobehavioral disorders associated with methylmercury exposure in common marmosets, based on experimental conditions in previous studies, marmosets were administered methylmercury (1.5 mg Hg/kg BW of methylmercury for 2 weeks followed by 2 weeks without administration; Yamamoto et. al, *J Toxicol. Sci.* 2012), and locomotion (spontaneous locomotion and walking) were captured using video cameras. The video analysis captured a decrease in spontaneous locomotion and movement speed of the marmosets. Further analysis of motor dysfunction associated with methylmercury exposure (knee angle, hip position, etc.) is underway.

(2) We obtained data on Proteomic analysis of the cerebrospinal cord. We are currently conducting analysis together with collaborators.

[Activity theme and summary]

[6] Information service using hair mercury analysis

Masaaki Nagano

(Department of Basic Medical Science)

In 2024, 302 hair samples were collected from visitors

to the National Institute for Minamata Disease, and Minamata Disease Archives. The total mercury concentration in the samples was measured. The analytical results were sent to each individual.

Hair mercury concentrations were analyzed in 901 individuals between 2020 and 2025.

4. Nature Environment Group

This group consists of eight research projects and two work projects and conducts comprehensive research, including field studies, laboratory experiments, and various types of analyses, with the aim of elucidating the environmental Hg cycle from the global to the regional level and around Minamata Bay and the Yatsushiro Sea. The research of this group targets a wide range of media, including air, water, soil, sediment, and living organisms, and, in particular, a wide range of research topics covering primary producers, such as phytoplankton, to top predators, such as swordfish. In field studies, Hg in air and precipitation has been monitored in various parts of the Japanese islands, and marine Hg observations have been conducted in a wide range of areas, from coastal areas, such as Minamata Bay and the Seto Inland Sea, to the open North Pacific Ocean. We also attempt to elucidate Hg emission sources and chemical reaction processes using stable Hg isotope ratios and to observe Hg fluxes from forests. Furthermore, in cooperation with domestic and international research institutions, we have been working to obtain comparable data that will contribute to the validity assessment of the Minamata Convention since it has been entered into force in 2017. Simultaneously, we are actively engaged in outreach activities targeting elementary, junior high, and high school students for the purpose of education and dissemination of Hg research and the entire field of science.

The outlines of each research and working activity for FY 2024 are as follows:

[Research theme and summary]

- [1] Study of factors influencing the vertical distribution in speciated mercury in the ocean

(Project research)

Kohji Marumoto

(Department of Environment and Public Health)

This study aims to understand the factors controlling the vertical distribution of Hg in the ocean, mainly in the western North Pacific, and to understand of the atmospheric-oceanic Hg fluxes and Hg uptake by phytoplankton, which may influence the variability of Hg concentrations in the surface and sub-surface layers. This study also examined the factors responsible for the relatively high concentrations of MeHg observed in the mesopelagic layer and the leaching of Hg from suspended solids in the deep layer.

The results of observations of atmospheric Hg concentration and dissolved gaseous mercury (DGHg) in seawater using an equilibrator during research cruises KH-22-7 (conducted in August 2022) and KH-23-2 (conducted in June 2023) showed that despite being in almost the same area, there were differences in atmospheric Hg concentration, and the values observed in August 2022 were higher than those observed in June 2023. Although there may have been seasonal differences, no differences were observed between the two periods in Oga City, Akita Prefecture, which is the closest ground-based observation site to the same sea area. Compared at the same latitude, the surface seawater temperature was 5-10°C higher in August 2022, which may have been influenced by the La Niña event that occurred from November 2021. The DGHg concentrations in seawater tended to be higher in the south than in the north, which may be due to stronger solar radiation and greater biological activity in the south, facilitating the formation of DGHg from divalent Hg compounds in seawater. During both cruises, DGHg in the seawater was supersaturated, and Hg was released from the ocean to the atmosphere. The release flux was several $\text{ng m}^{-2} \text{h}^{-1}$, which is greater than the global mean oceanic emission of $1.1 \text{ ng m}^{-2} \text{h}^{-1}$. This suggests that the study area is one of the areas with high Hg emission fluxes.

On the other hand, plankton larger than 100 μm in size

were collected using Norpac plankton nets during these research cruises and further fractionated by size for analysis of total Hg and MeHg. The results showed that MeHg concentrations and partition coefficients increased with increasing size north of the equator. However, the concentrations decreased north of 40° N latitude. The chlorophyll-a concentration, an indicator of phytoplankton abundance, was extremely high at this site, suggesting a decrease in the concentration due to bio-dilution. Meanwhile, no consistent trend was observed for the total Hg concentration.

For various reasons, it is impossible to conduct planned laboratory experiments on Hg elution from suspended solids in the deep sea. Therefore, we plan to conduct laboratory experiments in the mid-term to deepen our understanding of the concentration distribution of Hg in the ocean by form and MeHg formation in the deep sea.

[2] Researches on the behaviors of mercury in soil, water and sediment

(Fundamental research)

Akito Matsuyama

(Department of International Affairs and Research).

Each outline of outcomes in this theme is described as follows:

① Study of Hg methylation characteristics in seawater

In addition to the results of the previous year, we conducted a follow-up test to confirm the change in dissolved MeHg concentration when the incubation temperature in Minamata Bay seawater was changed.

② Analysis of MeHg concentrations in soil and sediments using the Akagi method

We prepared technical points to note for the analysis of MeHg concentration in soil/sediment using the Akagi method as supplementary technical data for the Akagi method and prepared it in both Japanese and English. After the contents of the document were confirmed by Professor Takashi Tomiyasu of the

Graduate School of Science and Engineering, Kagoshima University, firstly the Japanese manuscript was revised based on his opinions, and finally the revised English manuscript was prepared.

③ Understanding changes in the characteristics of Minamata Bay sediments due to changes in the water quality of Minamata Bay

To date, this project has conducted combination incubation experiments using a batch model that uses Fukuro Bay sediments. This year, surface sediment was collected from the center of Minamata Bay, and a combination incubation experiment was conducted under the same experimental conditions as those used for the Fukuro Bay sediment. The same experimental results as those for Fukuro Bay were obtained, and the properties of bottom sediments deposited in Minamata Bay and Fukuro Bay were found to be identical. An article is currently being prepared based on the results of the research obtained during this midterm plan.

④ Understanding the chronologically changes in Hg characteristics in artificially Hg-contaminated soil
Artificially contaminated soil was created using four representative soils in Japan (brown forest soil, red-yellow soil, Kuroboku soil, and sandy soil), and the dynamics of Hg in the soil were examined from the perspective of the total Hg and MeHg concentrations in each soil.

[3] Bioprotection of methylmercury toxicity by complex formation with selenium in large marine mammals

(Fundamental research)

Masumi Marumoto

(Department of Basic Medical Sciences).

MeHg taken into the body through food is gradually converted into inorganic Hg. Mineralization ability varies among animal species. Selenium (Se), an essential metal, plays a major role in mineralization; however, its full extent is unknown. The distribution of

Hg and Se in organs has been studied pathologically using an X-ray probe microanalyzer (EPMA), which can reveal the cells in various organs that aggregate with Hg and Se. We will use EPMA to determine which cells in various organs aggregate Hg and Se to clarify the tissue distribution of Hg and Se in large marine organisms, especially in toothed whales, sharks, and sailfish. This year, electron microscopic searches of the skeletal muscles and livers of lesion-free hand dolphins revealed the subcellular localization of Hg and Se.

[4] Research on primary producer dynamics and mercury bioaccumulation to fish through food chains

(Fundamental research)

Kenji Yoshino

(Department of Environment and Public Health)

This study investigates in Minamata Bay the seasonal dynamics in biomass, carbon and nitrogen stable isotope ratios ($\delta^{13}\text{C}$ and $\delta^{15}\text{N}$), and total Hg content of phytoplankton and microphytobenthos, which are main components of primary producers in aquatic ecosystems. In addition, $\delta^{13}\text{C}$ and $\delta^{15}\text{N}$, and total Hg of fish and macrobenthos samples are also analyzed for clarifying the main pathway of Hg bioaccumulation in the food web. Similar to the results of the last year, $\delta^{13}\text{C}$ of primary producers greatly changed depending on the seasons. $\delta^{13}\text{C}$ of POM (particulate organic matter; a proxy of phytoplankton) was often close to that of fish and macrobenthos, except for spring seasons, when $\delta^{13}\text{C}$ of microphytobenthos was. Phytoplankton biomass in the water column is usually higher than that of the microphytobenthos in the surface sediment. Moreover, the total Hg content of the POM was higher than that of the microphytobenthos. These results suggest that the primary producer fueling the food web in Minamata Bay is phytoplankton, which forms the basis of the Hg bioaccumulation pathway for organisms of higher trophic levels. Because the total Hg of POM decreased with chlorophyll-*a* content, the Hg burden of the food web would be expected to decrease through the

bio-dilution effect if the nutritional state in this bay was improved.

[5] Characterization of stable isotopic composition of mercury at the emission sources

(Fundamental research)

Satoshi Irei

(Department of Environment and Public Health)

This research project aimed to provide novel information on the stable isotopic compositions of Hg in emissions and their variations to promote Hg cycle research in the natural environment. The goal we set for the fiscal year 2024 was to conduct chemical analysis of gas and plant samples collected in field studies, and then to write and publish scientific articles about those results.

The analysis of atmospheric samples collected during prescribed grassland burning has already been completed and the development of plant sample analyses is ongoing. A comparison of the gaseous Hg concentrations and carbon monoxide mixing ratios showed a good correlation, and the slope was found to be $0.7 \text{ ng m}^{-3} \text{ Hg} / \text{ppmv CO}$. Besides, the field surveys for biomass loading of the grasslands resulted in the range from 0.6 kg m^{-2} to 2.0 kg m^{-2} . The analysis of carbon content of the biomass exhibited $43.3 \pm 0.9 \%$. Given a biomass loading of 1.5 kg m^{-2} and the 43% of carbon content of the biomass, as well as the area of prescribed burning that the municipalities report, we estimated that each of the prescribed burnings of the grasslands we have ever studied (the frequency of once in every year) has emitted from 280 g to 147 kg of Hg to the atmosphere. Compared to the annual total man-made Hg emissions of 20 t, this quantity accounted for only 0.8%.

[6] Study of microbes involved in mercury speciation in the ocean

(Fundamental research)

Yuya Tada

(Department of Environment and Public Health)

This study aimed to evaluate microbial Hg speciation (methylation, demethylation, and reduction) in the ocean using metagenomic, metatranscriptomic, and molecular biology approaches. This year, I continued to analyze the total Hg and MeHg in dissolved and suspended particulate fractions, along with Hg-related genes, in seawater samples from Minamata Bay. Hg-methylation genes were exclusively detected in the particle-attached fraction throughout the year, indicating that microbial Hg methylation likely occurred within the suspended particles. Additionally, metatranscriptomic analysis of the November 2023 samples identified transcripts of both Hg methylation and demethylation genes in the particle-attached fraction, suggesting the potential transformation of MeHg within these particles. Furthermore, metagenomic analysis of bottom sediment samples collected from Minamata Bay in February and April 2024 revealed that methylation and demethylation genes were more abundant in sediment than in the seawater column, suggesting that active Hg cycling was mediated by microorganisms in the bay sediments. Quantitative PCR analysis of samples from the western North Pacific (five remaining stations) showed an increase in *Nitrospina*-*hgcA* copy number within the mesopelagic zone, with a high MeHg-to-total Hg ratio. This finding suggests that the *Nitrospina* lineage plays a crucial role in the distribution of MeHg in the oceans.

[7] Study on factors influencing long-term trend of atmospheric mercury concentrations in Asia-Pacific regions

(Fundamental research)

Kohji Marumoto

(Department of Environment and Public Health)

The aim of this study was to obtain continuous data on atmospheric and precipitation Hg concentrations to contribute to the assessment of the effectiveness of the Minamata Convention and to clarify their seasonal and

interannual variations and the factors behind them.

Monitoring of Hg in the air was continued in Minamata and Fukuoka this year, and monitoring of Hg in precipitation was continued at six sites in Minamata, Hirado, Fukuoka, Matsue, Omaezaki, and Tsukuba. Regarding Hg in precipitation monitoring, in order to ensure the reliability of data as a response to the Minamata Convention, we have participated in an international accuracy control programme led by the U.S. Geological Survey this year as well. In addition, joint research with the National Central University of Taiwan and comparative experiments with precipitation samplers used in Japan and Taiwan were conducted, and analysis values that were almost in agreement were obtained. Regarding the observation of atmospheric Hg, we verified the feasibility of one-week sampling using the method of the Manual on Hazardous Air Pollutants, which stipulates 24-hour sampling, and generally obtained good results.

On the other hand, in order to investigate the effects of Hg emissions from the volcano, continuous monitoring of Hg by atmospheric form was carried out at Sensuikyo, located to the north of the first crater of Mt Aso Nakadake, as in the previous year, but no data were obtained from June to December this year due to malfunctioning of observation equipment, and after December, only gaseous elemental mercury (GEM) was investigated. The relationship between the concentration of GEM and the other gaseous and particulate components until June was investigated, and it was found that the concentration maxima of SO₂, which is one of the main components of volcanic gases, were coincident with those of GEM. However, the concentration ratios are not constant.

[Activity theme and summary]

[8] Implementing of Seawater quality monitoring in Minamata Bay and supporting of various regional activities around Minamata area

Akito Matsuyama

(Department of International Affairs and Research)

Each outline of outcomes in this theme is described as follows:

① Hg monitoring in Minamata Bay

Hg monitoring in Minamata Bay was conducted three times a year (June, August, and November 2024). Water samples were collected from three locations in the Minamata Bay (Hadakase, Wanoh, and Kojishima). Hg monitoring in the hydrophilic revetment in Minamata Bay was conducted four times a year (June, September (twice), and December) at five locations around the reclaimed land of Minamata Bay, as in the past. The whole average dissolved total Hg concentration in Minamata Bay in 2024 was 0.30 ± 0.13 ng/L, and dissolved MeHg was 0.04 ± 0.02 ng/L. The average total dissolved Hg concentration in the hydrophilic bank water quality monitoring was 3.35 ± 2.36 ng/L.

② Development of efficient oyster farming techniques in Minamata Bay

Based on the results of the research in 2023, we propose that as a measure to reduce the number of oyster deaths in the summer, cheesecloth should be set on oyster farming rafts to avoid the rise in sea surface temperature due to direct sunlight in the summer. This proposal was put into practice, and the cheesecloth was established in early August 2024. In 2024, the outside temperature was higher than usual, the seawater temperature exceeded 30°C as early as July, and the number of dead oysters increased sharply compared to June. However, by setting cheesecloth in early August, the surface seawater temperature on the cheesecloth-set raft was approximately 1°C lower than the normal raft that wasn't set cheesecloth, and the number of dead oysters was significantly reduced. Finally, we report on the Minamata Fisheries Cooperative Association using

a final report containing outcomes on this theme over five years.

[9] Outreach activities related to science and technology research for elementary and junior high school students

Masumi Marumoto

(Department of Basic Medical Sciences).

Researchers and research institutes are expected to disseminate scientific knowledge and results to the public.

Kumamoto Prefecture, where NIMD is located, is known both domestically and internationally as the area where Minamata disease occurs, but elementary and junior high school students' knowledge of Hg is limited. Therefore, we will provide accurate knowledge about Hg by conducting classes at elementary and junior high schools in Minamata City and beyond. To emphasize interactivity rather than one-way transmission from the researcher, a question box was set up before the delivery class, and a questionnaire was administered to answer questions in advance of the presentation. Contributing to the community by proactively responding to requests for cases other than delivery classes for Hg. One of the achievements this year is that the 2nd and 3rd year students of Minamata High School, whom we taught last year, presented their research to the Environmental Science Society and received an excellent presentation award and a high school student poster award at the Metal Bioscience Research Meeting. In addition, as in the previous year, work experience for second-year junior high school students in Minamata City and the "Minamata" calligraphy and painting competition were also organized.

5. International Contribution · Information Group

The Minamata Convention on Mercury, which came into force in 2017, aims to reduce the adverse effects of mercury use on the environment and human health. In support of the implementation of the Convention, the International Contribution and Information Group at NIMD has advanced collaborative projects with international organizations such as the WHO and UNEP. These efforts include support for the organization of the International Conference on Mercury as a Global Pollutant (ICMGP), planning the NIMD Forum, and strengthening networks among mercury researchers worldwide.

To address mercury pollution issues in developing countries, the National Institute for Minamata Disease (NIMD) has provided expertise, technology, and experience in collaboration with organizations such as JICA. In line with the Japanese government's MOYAI Initiative, NIMD has also promoted the development of simplified mercury analysis methods, analytical training programs, interlaboratory proficiency testing, and reference materials for quality control. In regions lacking analytical capacity, the Institute supports biomonitoring by providing analytical and evaluation techniques. These achievements were disseminated through academic publications and conference presentations.

[Research theme and summary]

[1] Development of a simple method for the determination of mercury and reference materials

(Project research)

Koichi Haraguchi

(Department of International Affairs and Research).

This project focused on three main areas with the aim of enhancing the international mercury analysis capacity in support of the Minamata Convention: (1) simplified and efficient exposure assessment methods, (2) improved analysis of mercury in skin lighting

products (SLPs), and (3) international proficiency testing programs.

(1) Simplification and Efficiency

A novel approach for mercury exposure assessment independent of conventional biological samples was introduced through real-time on-site measurements and the use of wearable masks for personal exposure monitoring. These methods enable the rapid assessment of mercury concentrations in field settings. Further validation will be conducted by comparing these results with conventional biomonitoring data.

(2) Mercury in SLPs

The screening performance of X-ray fluorescence (XRF) analysis was assessed to ensure rapid and accurate evaluation of mercury content in cosmetics. Mercury content was analyzed in whitening creams and overseas products obtained through e-commerce platforms to reveal the current state of mercury-containing cosmetic products.

(3) Effectiveness Evaluation of the Minamata Convention

The NIMD conducts regular proficiency testing programs and online training sessions to improve the analytical capabilities of laboratories in the participating countries. These efforts have contributed to strengthening international analytical networks and provided the scientific support necessary to evaluate the implementation of the Convention.

[Activity theme and summary]

[2] Examination of hair mercury in areas concerned with mercury pollution around the world

Masatake Fujimura

(Department of International Affairs and Research).

(1) Hair Hg measurements in areas concerned with Hg pollution

Hair Hg concentrations were measured in 27 males and 51 females from the Maroni River basin, French

Guiana, and relatively high MeHg exposure (6.9 ppm on average for both sexes) was observed. MeHg levels were also measured for the 16 samples that showed total Hg levels of 10 ppm or higher, and the MeHg/total Hg ratio was 92.8%, indicating that the Hg exposure was an internal exposure to MeHg. In addition, three papers on the results of hair Hg analysis of residents living near e-waste dumping areas in Bangladesh were accepted for publication in international journals as co-authors.

(2) Hair Hg levels were measured at the International Conference on Hg as a Global pollutant in 2024 (ICMGP2024). We measured 100 males and 105 females from 42 countries worldwide and found that the average hair Hg level was less than 1 ppm in each case. In addition, as a member of the ICMGP steering committee, I organized a special session on a Minamata disease storyteller lecture and presented a paper as the first author on the results of hair Hg measurements.

[3] NIMD forum and international workshop

Masatake Fujimura

(Department of International Affairs and Research).

This year's NIMD forum was held as a workshop for ICMGP 2024 in Cape Town, South Africa.

Group in charge: International contribution and information group

Theme: Strengthening the mercury research capacity in low-and middle-income countries: Focusing on vulnerable populations

Presentations: 11 abstracts

(Japanese researchers: four; international researchers: seven)

Venue: Cape Town international convention center

Date: July 21, 2024

Number of participants: Approx. 40 people

[4] Promotion of international collaborations

Masatake Fujimura

(Department of International Affairs and Research).

(1) Dispatch of NIMD staff

- Participated in the 2nd WHO Western Pacific Regional Network Meeting Environmental and Occupational Health Subcommittee (one person)
- Organization of NIMD forum 2024 and participation in the ICMGP2024 (6 persons)
- Participation in the 13th partners' meeting of the Asia-Pacific Mercury Monitoring Network (one person).
- Working environment survey on metallic mercury (1 person).

(2) Invitation of foreign researchers

- Participated in the NIMD Forum 2024:Bangladesh, Nigeria, Brazil, Nepal, Singapore, Thailand, and the Maldives (7 people).
- Research on art event at Minamata memorial : France (2 persons).

(3) Training for foreign researchers

Face-to-face implementation:

- DrPH Program, Graduate School of Planetary Health, Nagasaki University Minamata Field Training (9 persons).
- Training for analysis of total Hg in urine (4 persons).
- Provision of technology for Hg analysis in biological samples (4 persons).
- Provision of technology for Hg analysis in biological samples (2 persons).

On-line implementation:

- Strengthening of cooperation and communication among Hg analysis laboratories (87 persons).

(4) International joint research and operations

- Exposure assessment of metallic Hg to gold plating factory workers in Nepal.
- Joint work with UNEP: Proficiency test for Hg analysis (total Hg and MeHg in fish meat).
- Supply of blood-certified reference materials (total Hg and MeHg levels in whole blood).
- Joint work with JICA: Training program for Hg analysis in six Central American countries (Uruguay, Belize, Honduras, Guatemala, Panama,

and Costa Rica).

- ICMGP2024: Special session related to hair mercury and the joint organization of a Minamata storyteller lecture in Kumamoto Prefecture.
- Exposure assessment of MeHg in pregnant women in Hanoi, Vietnam.

[5] Transmission of information on Minamata Disease and organization of documents and materials in the Minamata Disease Archives

Rie Harada

(Department of International Affairs and Research).

This fiscal year, the Q&A corner was redesigned and new quiz content was added, completing the renewal of the permanent exhibition. A new special exhibition, 'NIMD's Global Monitoring, ' was added to the 'Expanding NIMD's Activities' section of the ground floor exhibition room. The introduction of research activities at the special exhibition has also been updated. The posters and brochures were updated to coincide with these changes.

Additionally, NIMD actively exchanged information with organizations such as the Minamata Disease Museum, Minamata Disease Centre Soshisha, Kumamoto University Archives, and Photographer's Eye to strengthen cooperation.

An additional committee member was appointed to strengthen the project structure and promote the hearing project in the 'Minamata Disease History Preservation Project.'

The results of collaboration with other institutions in the Unk 'Study Group on the Maintenance and Use of Minamata Disease Materials' were presented at the Forum for Cooperation between Pollution Museums and Archives.

[6] Activities as a WHO Collaborating Center

Megumi Yamamoto

(Department of Environment and Public Health)

The NIMD was designated as a WHO Collaborating

Center (CC) for "Studies on the Health Effects of Mercury Compounds" (World Health Organization Western Pacific Regional Office: WPRO) in September 1986 (Ref. # JPN-49). We have been conducting surveys and research on the health effects of mercury with the following objectives:

1. to support the improvement of public health related to the health effects of mercury in developing countries
2. to respond to WHO-related work, including ad hoc matters, and issues related to the health effects of mercury.

In this fiscal year, we mainly carried out the following tasks:

- (1) At the joint meeting of the Joint Conference of the International Society of Environmental Epidemiology-Asia and Western Pacific Chapter (ISEE-AWPC) and International Society for Exposure Science (ISES)-Asia Chapter (Malaysia; June 2024), as a WPRO (Western Pacific Regional Office) Regional Network Meeting on Environment and Occupational Health, a session "WHO and WHO Collaboration in Addressing Climate Change and Environmental Health Risks in the Western Pacific Region" was organized with Hokkaido University (WHO CC: JPN-91). In this session, we presented the Activities of the National Institute for Minamata Disease as a WHO Collaborating Center," and exchanged information.
- (2) Training and technology transfer of mercury analysis to researchers and technicians in developing countries with environmental problems related to mercury and discussions on surveys were conducted (Diponegoro University [Indonesia], University of Jember [Indonesia], University of Ibadan [Nigeria], and Universidad Nacional Autonoma de Nicaragua [Nicaragua]).
- (3) Joint work with the UNEP Regional Office for Asia and the Pacific: Proficiency tests for mercury analysis (total mercury and methylmercury in soil) were conducted.

- (4) Preparation and processing of the annual report (January-December 2024) on activities as a WHO Collaborating Center.
- (5) The application was prepared and processed for re-designation as a WHO Collaborating Center for the next quadrennial period (January 2025 to December 2028) and was approved.

6. publications and scientific meetings

[International Journals]

Underline: NIMD staff, *: first author, #:corresponding author

Fujimura M^{##}: Gabapentin improves neuropathic pain in Minamata disease model rats. *Environ Health Prev Med*, 2024; 29: 31.

Sakamoto M^{##}, Marumoto M, Haraguchi K, Toyama T, Saito Y, Balogh SJ, Tohyama C, Nakamura M. Assessing the role of selenium in Minamata disease through reanalysis of historical samples. *Environ Int*, 2025; 195:109242.

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Sakuragi T, Shibata E, Yamamoto M, Shimajiri S, Kondo E, Mori H, Tajiri R, Nakayama T, Yoshino K, Tsuji M. Evaluation of expression of amino acid and fatty acid metabolic transporters in the placenta of pregnant women with glucose intolerance. *J Obstet Gynaecol Res*, 2025; 51: e16163.

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[International meetings]

Underline: NIMD staff,

Matsuyama A, Yano S, Tada Y: Time course variation of seawater characteristics by environmental incubation experiments using Minamata Bay sediment and seawater. 16th International Confidence on Mercury as a Global Pollutant, Cape Town. 2024. 7.

Fujimura M, Usuki F, Unoki T: Decreased plasma thiol antioxidant capacity precedes neurological signs in a rat methylmercury intoxication model. 16th International Confidence on Mercury as a Global Pollutant, Cape Town. 2024. 7.

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