A Central Nervous System Disease of Unknown Cause That Occurred in the Minamata Region: Results of an Epidemiological Study

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Recently, a series of cases of a central nervous system disease of unknown cause with extrapyramidal tract abnormalities as the most prominent feature occurred, mainly in fishermen’s communities, on the periphery of Minamata City. Because the symptoms of the disease were unique and severe, and its prognosis was extremely poor, the disease caught immediate attention.

In response to the request from the local Minamata Strange Disease Countermeasures Committee to investigate this disease, we visited this area many times since September 1956 and conducted a detailed epidemiological study, including face-to-face interviews of 40 households with patients and 68 adjacent households without patients as control households. The results of the study are described below.

GEOGRAPHICAL AND METEOROLOGICAL CONDITIONS OF THE AREA WHERE CASES OCCURRED AND LIVING CONDITIONS OF LOCAL RESIDENTS

The cases occurred at the periphery of Minamata City, which is located in the southernmost part of Kumamoto Prefecture, a scenic waterfront and bay district neighboring Hyakken Port. In particular, a large number of cases occurred in four communities: Myojin, Tsukinoura, Dezuki, and Yudo (see Figure 1, Figure 2, Figure 3, and Figure 4).

These communities are fishing villages located in strips stretching from the seashore to relatively steep hills. Many villagers engage in fishing in the sea and in the bay. Their standards of living are low. Their living environments, including housing, are substandard and unhygienic (see Figure 3). The fresh water supply is poor. Their dietary staples are rationed rice, wheat, and sweet potatoes. They raise some of their own wheat and sweet potatoes. Besides these staples, they consume a large amount of seafood caught locally, while their intake of vegetables and fruits is low.

The meteorological conditions of this area according to the Minamata City handbook (1956) are shown in Table 1. The area is warm and rainy. Its predominant wind direction is northwest. There are no other noteworthy findings.

Figure 1. Yudo community

Figure 2. Tsukinoura community

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NUMBER OF CASES THAT OCCURRED BY YEAR AND MONTH

The number of patients with this disease identified based on interviews with local hospitals and clinics is shown chronologically in Table 2.

Confirmed cases of this disease first occurred at the end of 1953 and, as shown in the table, increased suddenly in 1956. The number of patients by month shows marked seasonal variation. The number is high in the period from April to September and low in winter.

DISTRIBUTION OF PATIENTS BY SEX AND AGE

There are no unusual findings regarding the population composition by age and sex (Table 3). Cases have generally occurred irrespective of sex or age, except that cases have tended to occur a little more frequently in children aged 10 years or younger. The youngest patient is a girl who was 1 year and 10 months of age at onset. There have been no infant cases, although diagnosis of this disease in infants is difficult.

Table 1. Weather in Minamata City (from the 1956 Minamata City handbook)

|                | 1954  | 1955  |
|----------------|-------|-------|
|                | June  | July  | August| September| October| November| December| January| February| March| April| May |
| **Temperature, °C** | 22.6  | 26.6  | 27.3  | 24.4  | 18.8  | 14.2  | 9.6  | 6.8  | 7.5  | 9.7  | 13.9 | 18.8  |
| Mean           | 30.1  | 32.4  | 35.2  | 32.3  | 27.1  | 24.8  | 21.2 | 13.9 | 20.0 | 26.1 | 23.6 | 26.8  |
| Minimum        | 11.0  | 19.9  | 21.7  | 12.0  | 6.8   | 6.5   | 0.6  | −2.5 | −3.6 | 2.0  | 2.4   | 10.5  |
| Mean humidity, %| 77    | 90    | 73    | 30    | 64    | 52    | 57   | 58   | 60   | 64   | 66    | 69    |
| Rainfall, mm   | 756.3 | 747.8 | 255.2 | 327.0 | 61.4  | 40.4  | 21.0 | 73.9 | 113.1| 183.0| 345.3 | 153.4 |
| Maximum daily  | 140.7 | 98.7  | 164.5 | 132.6 | 27.7  | 19.6  | 4.5  | 34.8 | 38.3 | 22.4 | 129.8 | 17.4  |
| Number of days | Clear | 7     | 5     | 27    | 17    | 20    | 18   | 19   | 11   | 16   | 10    | 14    |
|                | Cloudy| 15    | 19    | 2     | 9     | 8     | 10   | 15   | 8    | 13   | 9     | 14    |
|                | Rainy | 8     | 7     | 2     | 4     | 3     | 2    | 2    | 3    | 3    | 8     | 7     |
|                | Snowy | 0     | 0     | 0     | 0     | 0     | 0    | 0    | 2    | 1    | 0     | 0     |
|                | Most frequent wind direction| NW | SE | NW | NW | E | SE | N | NW | SE | NW | NW | NW |
|                | Mean wind speed, m/s | 2.1 | 3.2 | 4.6 | 2.4 | 2.2 | 1.9 | 2.3 | 2.7 | 2.8 | 2.5 | 3.2 | 3.1 |
|                | Maximum wind speed, m/s | 7.0 | 6.5 | 7.0 | 5.5 | 4.8 | 7.5 | 6.0 | 7.0 | 7.5 | 5.5 | 6.0 | 5.5 |
INCIDENCE PROPORTION, CASE FATALITY RATE, AND PROGNOSIS OF THIS DISEASE

The total population of these districts is 10,119. The 3-year incidence rate up to the present is 51.3 per 10,000 people. When exclusively examining fishermen’s communities by excluding the Marushima, Hyakken, and Tatara districts, the incidence proportion doubles to 102 per 10,000 people (Table 4).

Seventeen patients have died from this disease. The case fatality rate is extremely high at 32.8%. Time from onset to death is, as shown in Table 5, as short as 20 days and as long as 2 years and 3 months. Only 3 of the 52 patients were able to return to work, and still have sequelae. There are 23 patients who remain bedridden after onset. The amount of time for which they have been confined to bed up to the present is, as shown in Table 5, 1 year or longer for 6 patients. One of these patients has been bedridden for 2 years and 3 months. Prognosis is extremely poor.

GEOGRAPHICAL DISTRIBUTION, ORDER OF ONSET, AND FAMILIAL AGGREGATION OF PATIENTS

Figure 4 is a sketch of a map of the area, with sites where cases occurred plotted using numbers in the order of occurrence (the seashore district to the east of Sannengaura in the figure, where no cases have occurred, has no houses). As shown in Table 6, relatively more cases occurred in the Tsukinoura and Yudo districts in 1956 (site number 23 and higher). However, overall, there is no tendency for the distribution of cases to gradually expand or move. Intervals between the dates of onset within the same household, as shown in Table 7, vary widely from as short as 6 days to as long as 1 year and 5 months. Based on these observations, it is highly unlikely that this disease was transmitted through a chain of infection.

The familial aggregation rate (the proportion of patients from families with at least two patients) is 21/52, that is, approximately 40%, which is much higher than that for other infectious central nervous system diseases.

While most patients are permanent residents in this area, two patients developed the disease 6 months after migrating from remote areas.

DISTRIBUTION OF THE OCCUPATIONS OF HOUSEHOLDS WITH PATIENTS

Table 8 compares the occupations of householders between households with patients and control households. Although it is expected that this area would contain a large number of fishermen’s households, there was a marked difference in the proportion of fishermen’s households between households with patients and control households. A finding that was particularly noteworthy was that of the 14 non-fishermen’s households with patients, 10 households contained at least one person, either the householder or a family member, who engaged in fishing in one way or another, while the remaining 4 households did not contain anyone who engaged in fishing but are adjacent to fishermen’s households and could obtain seafood caught locally. No similar findings were found in the control households without patients.

The single case in the Tatara district, which occurred away from the seashore (number 6 in Figure 4), is an office worker who enthusiastically engaged in fishing. A patient in Hyakken (number 50 in Figure 4) is a barber but engaged in fishing for one-third of a month. These examples explain the circumstances by which cases occurred.

| Table 2. Number of cases by month and year |
|------------------------------------------|
| Month | 1953 | 1954 | 1955 | 1956 | Total |
|---|---|---|---|---|---|
| January | 1 | 1 | | | 2 |
| February | | | | | |
| March | 2 | 1 | 3 | 6 | 12 |
| April | 1 | 2 | 5 | 8 | 16 |
| May | 1 | 8 | 11 | 20 |
| June | 2 | 1 | 5 | 8 |
| July | | | | | |
| August | 4 | 1 | 1 | 6 |
| September | 1 | 1 | 5 | 7 |
| October | 1 | 1 | 2 | 4 |
| November | 2 | 1 | 2 | 5 |
| December | 1 | | | 1 | 3 |
| Total | 13 | 8 | 30 | 52 |

| Table 3. Distribution of patients by sex and age |
|-----------------------------------------------|
| Age | ≤9y | ≥10y | ≥19y | ≥20y | 29y | ≥30y | 49y | 59y | ≥60y | ≥79y | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Males | 4 | 6 | 3 | 4 | 5 | 4 | 1 | 0 | 0 | 31 |
| Females | 6 | 4 | 4 | 2 | 0 | 2 | 0 | 0 | 0 | 21 |
| Total | 10 | 10 | 7 | 5 | 4 | 6 | 1 | 0 | 0 | 52 |

| Table 4. Number of households, population, and number of cases that occurred by district |
|-------------------------------------------|
| District | Number of households | Population | Number of patients |
|---|---|---|---|
| Tsukinoura | 100 | 498 | 16 |
| Yudo | 121 | 649 | 11 |
| Dezaki | 96 | 453 | 7 |
| Myojin | 104 | 491 | 5 |
| Mategata | 70 | 343 | 3 |
| Hyakken | 243 | 1,192 | 3 |
| Umedo | 172 | 978 | 2 |
| Marushima | 775 | 3,839 | 2 |
| Tatara | 125 | 586 | 1 |
| Sakaguchi | 94 | 513 | 1 |
| Modo | 119 | 577 | 1 |

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DEATH OF DOMESTIC ANIMALS RAISED LOCALLY

A fact that is related to the development of this disease and is extremely specific to this disease is that many cats, and domestic animals raised locally, developed symptoms similar to those of patients and died.

### Table 5.1. Patient outcomes

| At work | Improved | Not improved | Dead | Total |
|---------|----------|--------------|------|-------|
| 3       | 9        | 23           | 17   | 52    |

### Table 5.2. Time from onset to death

| 0–1 month | ≤2 months | ≤6 months | ≤1 y and 6 months | ≤2 y | 2–3 y | Total |
|-----------|-----------|-----------|-------------------|------|-------|-------|
| 2         | 6         | 3         | 4                 | 1    | 0     | 17    |

### Table 5.3. Time of confinement to bed up to present in patients who have not improved

| 0–6 months | 7–12 months | ≤2 y | ≤3 y | Total |
|------------|-------------|------|------|-------|
| 13         | 4           | 5    | 1    | 23    |

### Table 6. Number of cases that occurred by district and year

| District   | Tsukinoura | Sakaguchi | Yudo | Dezuki | Modo | Myojin | Hyakken | Mategata | Unedo | Marushima | Tatara | Total |
|------------|------------|-----------|------|--------|------|--------|---------|----------|-------|-----------|--------|-------|
| 1953       | 0          | 0         | 0    | 1      | 0    | 0      | 0       | 0        | 0     | 0         | 0      | 1     |
| 1954       | 2          | 0         | 2    | 2      | 0    | 2      | 1       | 3        | 0     | 0         | 1      | 13    |
| 1955       | 1          | 0         | 1    | 0      | 1    | 0      | 0       | 0        | 1     | 0         | 0      | 8     |
| 1956       | 8          | 1         | 8    | 5      | 1    | 2      | 2       | 0        | 1     | 2         | 0      | 30    |
| Total      | 11         | 1         | 12   | 1      | 5    | 3      | 3       | 2        | 2     | 1         | 0      | 52    |

### Table 7. Intervals between the dates of onset within the same family

| District   | Relationship with the householder and age of onset | Date of onset | Interval between the dates of onset |
|------------|---------------------------------------------------|---------------|------------------------------------|
| Myojin     | Eldest son Householder                            | 20 June 1955  | 1 year, 4 months, and 20 days      |
|            |                                                   | 10 November 1956 |                                           |
|            | Eldest son Householder                            | 25 April 1954 | 1 month and 15 days                 |
|            |                                                   | 10 June 1954  |                                                   |
| Mategata   | Eldest daughter Householder                       | 10 August 1954| 6 days                              |
|            |                                                   | 16 August 1954|                                                   |
| Yudo       | Eldest daughter of the eldest son                 | 24 September 1956| 2 months and 18 days              |
|            | Eldest son of the eldest son                      | 12 November 1956|                                           |
|            | Third son                                         | 26 May 1955   | 1 year, 1 month, and 19 days        |
|            |                                                   | 14 July 1956  |                                                   |
| Dezuki     | Third son                                         | September 1955| Approximately 1 year                |
|            | Householder                                       | 15 September 1956| 7 days                          |
|            |                                                   | 22 September 1956|                                           |
|            | Wife                                              | 27 August 1954| 1 year, 2 months, and 20 days       |
|            |                                                   | 15 November 1955|                                           |
| Tsukinoura | Nephew Younger brother                            | End of April 1956| Approximately 2 weeks             |
|            |                                                   | May 1956       |                                           |
|            | Fourth daughter                                   | May 1956       | Approximately 2 weeks              |
|            | Fourth son                                        | 26 May 1956    |                                           |
|            | Wife                                              | 26 May 1956    |                                           |
|            | Fifth son                                         | June 1956      |                                           |

Editorial note: the original paper had the column showing “name of householder” in this table, but the editor of the Journal of Epidemiology omitted it to prevent potential ethical issues.

Deaths of cats by district and year confirmed through interviews are shown in Table 9. Most cats that were raised in households with patients have died. The cats generally died 1–2 months before the case deaths in the same household. The number of cat deaths by year was 1, 18, 25, and 30 since 1953, demonstrating a similar pattern to the increase in the number of human patients by year.

The number of deaths of dogs and domestic animals is shown in Table 10. The circumstances of these deaths are not clear. Among these, however, 5 pigs and 1 dog ingested seafood, developed symptoms similar to those of cats, and died, according to the interviews.

Based on the results of bacteriological and virological examinations and clinical and pathological findings, this disease is slightly different from known infectious or familial/hereditary central nervous system diseases. As described above, the distribution of cases did not expand or move chronologically or geographically, and intervals between the dates of onset within the same household varied widely. These findings suggest that a person-to-person chain of infection is unlikely. Moreover, considering that the familial aggregation rate is extremely high, the complete cure rate is equal to 0, the disease course can be very long, the prognosis is very poor, and cases have occurred irrespective of the sex or age of patients, conventional infectious central nervous system diseases, including Japanese encephalitis, epidemic meningitis, and acute poliomyelitis, can be ruled out.
Pathological and clinical findings suggest that this disease is caused by a toxic substance or substances rather than an infectious disease. Epidemiological findings show that cases occurred sporadically in space and continuously in time. It is also impossible to identify a starting point from which the disease developed for each patient. Therefore, if the disease is the result of poisoning, it develops after long-term continuous exposure to a common cause specific to these districts.

Deaths of domestic cats may suggest that cats are an animal source of infection to humans. However, it can also suggest that both cats and humans were exposed to a common cause and developed poisoning. The results of the search for this common cause are described below.

### INTAKE OF DRINKING WATER AND FARM PRODUCE

Residents of this area generally drink well water. Because the water supply is limited, quite a few households use wells that are shared among many other households. The usage of wells is shown in Table 11. Table 12 shows that, even among households using the same shared well, there are households with patients and without patients. Moreover, as shown in Table 11, four cases occurred in households that used the Minamata City’s water supply. This clearly demonstrates that contamination of drinking water is not the cause of this disease.

This area contains acid soil composed of pyroxene andesite and is a narrow plain along the seashore. Therefore, even farmers’ households have limited farm produce. Almost no rice is cultivated. Many people purchase rationed rice for consumption.

### Table 8.1. Occupations of households with patients and control households

|                | Fishing | Farming and fishing | Farming | Other | Total |
|----------------|---------|---------------------|---------|-------|-------|
| Households with patients | 22 (55%) | 4 (10%) | 2 (5%) | 12 (30%) | 40   |
| Control households      | 10 (14.7%) | 3 (4.4%) | 15 (22.1%) | 40 (58.8%) | 68   |

### Table 8.2. Households with and without patients according to employment in fishing

| Employment in fishing | Households with patients | Control households |
|-----------------------|--------------------------|--------------------|
| Employment in fishing | 36 (90%)                 | 20 (29.4%)         |
| No employment in fishing | 4 (10%)               | 48 (70.6%)         |
| Total                 | 40                       | 68                 |

### Table 9. Number of cat deaths

|                      | Tsukinoura | Dezuki | Yudo | Myojin | Mategata | Hyakken | Umedo | Marushima | Tataru | Total |
|----------------------|------------|--------|------|--------|-----------|---------|-------|------------|--------|-------|
| Number of cats raised| 14         | 15     | 18   | 4      | 4         | 2       | 3     | 1          | 61     |       |
| Number of deaths     | 13         | 10     | 15   | 4      | 4         | 1       | 2     | 1          | 50     |       |
| 1953                 | 3          | 6      | 1    | 3      | 3         | 1       | 1     | 1          | 15     |       |
| 1954                 | 4          | 5      | 3    | 2      | 1         |         |       |            | 15     |       |
| 1956                 | 6          | 5      | 6    | 1      | 1         | 1       |       |            | 20     |       |

### Table 10. Status of raised domestic animals

|                      | Households with patient(s) | Control households |
|----------------------|----------------------------|-------------------|
| Number of domestic animals currently being raised | Number of deaths in recent years | Number of domestic animals currently being raised | Number of deaths in recent years |
| Rabbit               | 8                          | 0                 | 29                              | 2                               |
| Dog                  | 10                         | 0                 | 6                               | 1                               |
| Goat                 | 1                          | 3                 | 3                               | 1                               |
| Horse                | 1                          | 0                 | 1                               | 0                               |
| Cattle               | 0                          | 0                 | 3                               | 0                               |
| Pig                  | 26                         | 5                 | 53                              | 3                               |
| Chicken              | 85                         | 2                 | 313                             | 0                               |

Traditional unit of volume, 1 to = approximately 18 liters.
Self-sufficient use of wheat and sweet potato as substitutes for the staple is not different between households with patients and those without patients (Table 13). Households with patients in Tatara and Hyakken purchase farm produce from the Minamata market. Based on these facts, farm produce is not worth considering as a potential source of contamination. Rather, the poorer conditions of households with patients, which can be presumed by the number of tatami mats per person (Table 14), along with no or little area for dry field farming indicate that households with patients may have imbalanced nutrient intake or a lack of vitamins and minerals.

**INTAKE OF SEAFOOD AND FISHING METHODS**

Many local residents are fishermen and, as expected, consume a large amount of seafood. Compared to other areas, this area is unique in that the residents mainly consume seafood caught in the bay. There are similar fishing villages on the seashore immediately northeast and southwest of this area. However, no cases occurred in these communities, and fishermen in these communities do not fish in Minamata Bay because their fishing zones are different. In contrast, fishermen’s households in this area, from Marushima to Mado, engage in fishing mainly in this bay.

In general, most fishing methods used by local fishermen are very small in scale and can be broadly divided into gill net fishing, dragnet fishing, pole-and-line fishing, octopus fishing, torch fishing, and shellfish harvesting. Gill net fishing uses a vinyl net and was started in 1952. This method is similar to that using mist nets on land. Usually, a net is set in the sea the previous day and is dragged in the next morning. Fishing grounds are located in Minamata Bay. In particular, the coasts of Myojin and Tsukinoura are good fishing grounds. Fish species caught by gill net fishing include gizzard shad, sillaginoid, spotnape ponyfish, flatfish, white croaker, flathead, redlip mullet, flounders, black rockfish, marbled rockfish, prawn, crab, and mantis shrimp. Some fishermen engage in gill net fishing all year round, while many fishermen switch to the pole-and-line fishing of striped mullets in the summer. In winter, the frequency of gill net fishing and the catch decreases slightly. In the Yudo district, where the number of cases increased in fiscal year 1956, cases occurred in 5 of the 7 households that engaged in gill net fishing in the same fiscal year.

At the end of 1955, these households moved their gill net fishing location from a southern part of the bay, in the vicinity of Fukuro Bay, to the northern parts, Myojin and Tsukinoura.

Fishing grounds for dragnet fishing are Fukuro Bay and the seashore of Tsukinoura. The fishing season is year-round, but the frequency of dragnet fishing is low. The main catch is Japanese anchovies. Sometimes gizzard shad and other small fish are also caught.

Fishing grounds for pole-and-line fishing and octopus fishing are in the bay. The main catch by pole-and-line fishing is striped mullets. Other fish caught are lizardfish and cutlassfish. Catching striped mullets is the main contribution to the high catch of fish in summer.

Torch fishing, also called harpooning, is mainly used to catch sea cucumbers, abalones, octopuses, marbled rockfish, and others using carbide lamps at night on the coast. Fishing grounds comprise the entire coast of the bay and the fishing season is year-round.

Shellfish, specifically oysters, small snails, and Manila clams, are mainly harvested from November to March. Because of the tidal rhythm, they are caught for a week per month. In recent years, seaweed has not been harvested in the bay.

**Table 12. Households with patients and without patients using shared wells**

| Shared well | A | B | C | D | E | F |
|-------------|---|---|---|---|---|---|
| Number of households using a shared well | 12 | 4 | 6 | 6 | 9 |
| Number of households with patients | 3 | 2 | 2 | 1 | 1 |
| (number of patients) | (3) | (4) | (2) | (1) | (1) |
| Number of households without patients | 9 | 2 | 4 | 5 | 8 |

**Table 13. Self-sufficiency of staples**

| | Self-sufficient | Partially self-sufficient | Purchasing all staples | No access to rationed food |
|-----------------|-----------------|---------------------------|-----------------------|--------------------------|
| **Rice** | | | | |
| Households with patients (40) | 1 (2.5%) | 1 (2.5%) | 36 (90%) | 2 (5.0%) |
| Control households (68) | 3 (4.4%) | 0 (0%) | 59 (86.8%) | 6 (8.8%) |
| **Wheat/Sweet potato** | | | | |
| Households with patients (40) | 13 (32.5%) | 12 (30.0%) | 15 (37.5%) | — |
| Control households (68) | 22 (32.3%) | 19 (27.9%) | 27 (39.8%) | — |

| Land under cultivation | None | ≤1 “tan” | ≤2 “tan” | ≤5 “tan” | >5 “tan” |
|----------------------|------|---------|---------|---------|---------|
| **Rice field** | | | | | |
| Households with patients (40) | 38 | 0 | 1 | 1 | 0 |
| Control households (68) | 65 | 0 | 1 | 2 | 0 |
| **Dry field** | | | | | |
| Households with patients (40) | 13 | 12 | 6 | 8 | 1 |
| Control households (68) | 18 | 24 | 14 | 10 | 2 |

Traditional unit of area, 1 tan = approximately 1000 m².

**Table 14. Number of tatami mats per person**

| | 0–0.9 | 1.0–1.9 | 2.0–2.9 | 3.0–3.9 | 4.0–4.9 | 5.0–5.9 | ≥6.0 | Total |
|-----------------|-------|--------|--------|--------|--------|--------|------|-------|
| Households with patients | 8 | 12 | 11 | 4 | 4 | 4 | 0 | 40 |
| Control households | 4 | 14 | 20 | 16 | 9 | 4 | 1 | 68 |

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Comparison of these fishing methods between households with patients and control households is shown in Table 15. Even after accounting for the difference in the number of fishermen’s households, the proportion of households that engaged in gill net fishing, octopus fishing, torch fishing, and shellfish harvesting was larger among households with patients than control households.

We identified the seafood species ingested by season through interviews and found marked differences between households with patients and control households (Table 16). That is, patients predominately consumed fish caught using the methods described above in the bay, while most control households consumed fish caught outside the bay; specifically, horse mackerel, mackerel, sardines, sea bream, and others purchased from the Minamata market or through peddlers from Komenotsu, Kagoshima Prefecture. The seafood classification and intake, which were investigated by identifying the frequency of consumption per month, are shown in Table 17 and demonstrate that households with patients consumed a very large amount of fish and shellfish from the bay.

The species of fish and shellfish from the bay that were consumed in large amounts included gizzard shad, striped mullet, crabs, oysters, and small snails. No particular type of fish or shellfish was commonly consumed in large quantities by patients. There was no association between the fish and shellfish consumed and development of the disease. The fish and shellfish were either eaten raw or cooked; there was no preference in cooking method.

### Table 15. Fishing methods

| Fishing methods         | Households with patients (40) | Control households (68) |
|-------------------------|-------------------------------|-------------------------|
|                         | Number of households using the method | % | Number of households using the method | % |
| Gill net fishing        | 15                            | 37.5                     | 8.8 |
| Dragnet fishing         | 2                             | 5.0                      | 2   |
| Pole-and-line fishing   | 20                            | 50.0                     | 19  |
| Octopus fishing         | 8                             | 20.0                     | 2   |
| Torch fishing           | 8                             | 20.0                     | 2   |
| Shellfish/oyster harvesting | 16                    | 40.0                     | 6   |

### Table 16. Seafood ingested

| Species                 | Fishing Location | Method                  | Households with patients (40) | Control households (68) |
|-------------------------|------------------|-------------------------|-------------------------------|-------------------------|
|                         |                  |                         | Spring | Summer | Fall | Winter | Total | Spring | Summer | Fall | Winter | Total |
| Lizardfish              | In the bay       | Gill net fishing, Fishing | 3      | 4      | 2    | 0      | 9     | 2      | 0      | 1     | 1     | 4     |
| Gizzard shad            |                  | Gill net fishing        | 20     | 10     | 16   | 12    | 58    | 9      | 5      | 6      | 9     | 34    |
| Sillagnoid              |                  | Fishing                 | 10     | 7      | 10   | 8     | 35    | 4      | 3      | 4     | 1     | 12    |
| Spottednape ponyfish    |                  | Gill net fishing        | 10     | 3      | 6    | 6     | 25    | 4      | 3      | 1     | 1     | 9     |
| Flatfish                |                  | Gill net fishing        | 9      | 3      | 6    | 7     | 25    | 2      | 3      | 5     | 1     | 11    |
| White croaker           |                  | Gill net fishing        | 9      | 2      | 9    | 6     | 26    | 2      | 1      | 2     | 1     | 6     |
| Flathead                |                  | Gill net fishing        | 10     | 4      | 9    | 6     | 29    | 1      | 0      | 1     | 1     | 3     |
| Redlip mullet           |                  | Gill net fishing        | 11     | 3      | 8    | 9     | 31    | 1      | 0      | 1     | 1     | 3     |
| Skullfish               |                  | Gill net fishing        | 6      | 0      | 6    | 9     | 21    | 4      | 3      | 4     | 3     | 14    |
| Black rockfish          |                  | Gill net fishing        | 2      | 0      | 0    | 1     | 3     | 0      | 0      | 0     | 0     | 0     |
| Marbled rockfish        |                  | Torch fishing           | 3      | 1      | 0    | 1     | 5     | 0      | 1      | 0     | 0     | 1     |
| Striped mullet          |                  | Fishing                 | 8      | 24     | 21   | 2     | 55    | 5      | 23     | 22    | 1     | 51    |
| Cutslassfish            |                  | Fishing                 | 4      | 14     | 16   | 5     | 39    | 6      | 13     | 18    | 6     | 43    |
| Black sea bream         |                  | Fishing                 | 2      | 4      | 2    | 1     | 9     | 2      | 1      | 2     | 0     | 5     |
| Japanese anchovy         |                  | Dragnet fishing         | 2      | 3      | 3    | 2     | 10    | 4      | 2      | 1     | 3     | 10    |
| Puffer fish             |                  | Fishing                 | 0      | 0      | 0    | 1     | 1     | 0      | 0      | 0     | 0     | 0     |
| Prawn                   |                  | Gill net fishing        | 10     | 1      | 8    | 7     | 26    | 4      | 4      | 3     | 0     | 11    |
| Crab                    |                  | Gill net fishing        | 16     | 11     | 12   | 9     | 48    | 4      | 4      | 3     | 2     | 13    |
| Mantis shrimp           |                  | Torch fishing           | 7      | 0      | 8    | 6     | 21    | 1      | 0      | 1     | 1     | 3     |
| Sea cucumber            |                  | Torch fishing           | 3      | 0      | 0    | 8     | 11    | 1      | 0      | 0     | 1     | 2     |
| Octopus                 |                  | Torch fishing, Octopus fishing | 9 | 13     | 2    | 4     | 28    | 6      | 8      | 6     | 2     | 22    |
| Squid                   | Outside the bay   | Gill net fishing, Fishing | 3      | 4      | 1    | 2     | 10    | 3      | 0      | 1     | 3     | 7     |
| Oyster                  | In the bay        | Shellfish harvesting    | 17     | 3      | 1    | 26    | 47    | 8      | 1      | 2     | 23    | 34    |
| Small snails            |                  | Shellfish harvesting    | 13     | 10     | 5    | 13    | 41    | 11     | 4      | 2     | 9     | 26    |
| Manila clam             |                  | Shellfish harvesting    | 5      | 2      | 3    | 2     | 12    | 6      | 2      | 2     | 4     | 14    |
| Abalone                 |                  | Torch fishing           | 2      | 0      | 0    | 4     | 6     | 1      | 0      | 1     | 1     | 3     |
| Horse mackerel          | Outside the bay   | Gill net fishing        | 16     | 11     | 18   | 12    | 57    | 35     | 28     | 39    | 45    | 147   |
| Mackerel                |                  | Gill net fishing        | 15     | 6      | 12   | 11    | 44    | 29     | 19     | 37    | 35    | 120   |
| Sardine                 |                  | Gill net fishing        | 17     | 7      | 14   | 14    | 52    | 46     | 30     | 36    | 39    | 151   |
| Saury                   |                  | Gill net fishing        | 0      | 0      | 0    | 1     | 1      | 0      | 0      | 2     | 0     | 2     |
| Silver-stripe round herring |                | Gill net fishing        | 0      | 0      | 0    | 1     | 1      | 0      | 0      | 2     | 0     | 2     |
| Sea bream               |                  | Gill net fishing        | 0      | 2      | 1    | 0     | 3     | 1      | 3      | 2     | 0     | 6     |
| Wakame seaweed          |                  | Gill net fishing        | 0      | 0      | 0    | 1     | 1      | 0      | 0      | 0     | 0     | 0     |

### Table 17. Intake of seafood

| Species                | Bay fish | Oysters and other shellfish | Non-bay fish |
|------------------------|----------|----------------------------|--------------|
|                        | Eat almost every day | Eat 2–3 times a week | Eat 2–3 times a month | Eat almost every day | Eat 2–3 times a week | Eat 2–3 times a month |
| Households with patients (40) | 25 | 5 | 2 | 10 | 11 | 2 |
| Control households (68) | 3 | 6 | 6 | 4 | 4 | 2 | 28 | 39 | 45 | 147 |
|                        | 19 | 12 | 25 | 23 | 22 | 151 | 36 | 39 | 151 | 36 | 39 | 151 |
Some of the patients had never eaten raw seafood. In addition, pigs, which usually do not eat raw food, also died. The fact that development of the disease is not associated with any particular fish or shellfish, or the consumption of raw fish or shellfish may rule out the possibility that this disease is caused by a biological toxin present in specific fish or shellfish or that it is a parasitic disease mediated by fish or shellfish, even if ingestion of fish and shellfish from the bay is the cause of this disease.

A noteworthy fact about the species of fish and shellfish inhabiting the bay is that a few of these species contain aneurinase and were consumed in relatively large quantities.

Table 18 shows the change in catch of fish in the bay by month in a year for households with patients, which was investigated at the fishermen’s union office in Marushima. The catch of fish decreases in the rainy season and in winter. When this change is compared with the change in the number of cases that occurred by month (Figure 5), the two changes appear similar with a slight lag.

The results described above indicate that, if this disease is a poisoning, fish and shellfish in the bay are contaminated for some reason, and relatively long-term ingestion of these fish by local residents and domestic animals leads to development of this disease. That is, the common cause for entry of a toxic substance into the body is conceivably fish and shellfish from the bay. This explains the seasonal change in the development of the disease, the absence of the disease in infants, and the predominance of cats among the dead pets and domestic animals.

However, if this is the case, the details of individual seafood intake suggest that the predisposition of an individual plays a significant role in the development of this disease. If the fish and shellfish in this bay are contaminated, it is unknown why the contamination started near the end of 1953. Lastly, we will present the results of our investigation into special environments that may have caused the contamination.

**SPECIAL ENVIRONMENTS OF THE AREA WHERE CASES OCCURRED**

Special environments in the area where cases occurred that could have contaminated the bay are the Minamata factory of a fertilizer corporation, a municipal slaughterhouse in the Tsukinoura district, springs in the sea in the Yudo district (shown in Figure 4), and the former Japanese navy ammunition depot and high-angle gun position in the Modo district.

Wastewater from the fertilizer factory is released into the Hyakken Port entrance. Analytical values of inorganic salts contained in the wastewater (measured by the engineering department of the factory) are shown in Table 19. Toxic gases contained in exhaust gas from the factory are sulfurous acid gas and nitrogen oxide, which are usually produced at sulfuric acid plants.

The slaughterhouse is located at the top of a hillock facing the Tsukinoura coast, and its wastewater is released into the sea. The number of domestic animals slaughtered in recent years is shown in Table 20.

No changes in the water from the springs in the sea in the Yudo district have been detected in recent years. Similarly, there has been no change in the farming of young sweetfish, which has been performed for some time.

The ammunition stored in the Modo district was removed by stationed troops after World War II and the remaining parts were purchased and transported by ship. These were not dumped into the sea.

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**Table 18. Catch of fish in the bay by month**

| Month    | Catch of fish ("kan") | Index compared to the monthly mean catch (100) | Proportion of the annual catch (%) |
|----------|-----------------------|-----------------------------------------------|-----------------------------------|
| January  | 48                    | 42.1                                          | 3.4                               |
| February | 91                    | 79.7                                          | 6.6                               |
| March    | 80                    | 70.2                                          | 5.8                               |
| April    | 376                   | 330.0                                         | 27.4                              |
| May      | 86                    | 75.5                                          | 6.3                               |
| June     | 30                    | 26.3                                          | 2.2                               |
| July     | 77                    | 67.3                                          | 5.6                               |
| August   | 164                   | 144.0                                         | 12.0                              |
| September| 160                   | 140.0                                         | 11.7                              |
| October  | 127                   | 111.0                                         | 9.3                               |
| November | 86                    | 75.5                                          | 6.3                               |
| December | 47                    | 41.2                                          | 3.4                               |

*Traditional unit of weight, 1 kan = approximately 3.75 kg.

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**Table 19. Analytical values of wastewater from a fertilizer factory**

| Parameter | Value |
|-----------|-------|
| pH        | 3.5   |
| Total residue on evaporation | 9.900 mg/L |
| KMnO4 consumption | 155 |
| SiO2 | 23 |
| FeCl3 | 2 |
| Al2O3 | 19 |
| CaO | 163 |
| MgO | 436 |
| K2O | 114 |
| Na2O | 2.700 |
| NH3 | 24 |
| Cu | 5 |
| Pb | 0.13 |
| As | 0.001 |
| Mn | 0.17 |
| Cl | 3.950 |
| P2O5 | 9 |
| SO3 | 676 |

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**Figure 5. Relationship between the catch index in the bay and the number of cases that occurred by month**

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The results of the epidemiological study on this central nervous system disease of unknown cause occurring in the Minamata region are as follows:

1. Cases started to occur at the end of 1953. The number of patients was 13 in 1954, 8 in 1955, and dramatically increased to 31 in 1956 (as of the end of November), resulting in a total of 52 patients in 3 years.
2. The number of cases that occurred per month was higher in April–September and lower in winter, demonstrating marked seasonal change.
3. Case numbers are similar, irrespective of age and gender. However, there have been no infant cases.
4. The case fatality rate of this disease is 33%. Most patients’ symptoms have not changed for a long time, and no patient has been cured completely. The prognosis of this disease is extremely poor.
5. The area where cases occurred is limited to farmers’ and fishermen’s communities on the seashore of Hyakken Port in Minamata City and is not expanding. In particular, many patients are from fishermen’s households, and the familial aggregation rate is extremely high at 40%. Moreover, many cats raised in the same area had similar symptoms and have died.
6. It has been found that this disease develops after long-term continuous exposure to a common cause, which is conceivably contaminated fish and shellfish inhabiting the bay.

We acknowledge the Minamata Strange Disease Countermeasures Committee for their enthusiastic support and cooperation in this study.

### Table 20. The number of domestic animals slaughtered recently in Minamata City

| Fiscal year | Species | Cattle | Pig | Horse | Goat | Total | Remarks |
|-------------|---------|--------|-----|-------|------|-------|---------|
| 1946        |         | 211    | 62  | 40    | 0    | 313   | April-March in every fiscal year |
| 1947        |         | 207    | 26  | 14    | 0    | 247   |         |
| 1948        |         | 294    | 41  | 14    | 0    | 349   |         |
| 1949        |         | 178    | 166 | 8     | 0    | 352   |         |
| 1950        |         | 364    | 167 | 18    | 0    | 549   |         |
| 1951        |         | 268    | 266 | 9     | 10   | 553   |         |
| 1952        |         | 323    | 975 | 6     | 0    | 1,304 |         |
| 1953        |         | 362    | 758 | 129   | 0    | 1,249 |         |
| 1954        |         | 608    | 562 | 101   | 0    | 1,271 |         |
| 1955        |         | 1,554  | 643 | 30    | 0    | 2,227 |         |
| 1956        |         | 984    | 555 | 31    | 0    | 1,570 | In April 1, 1956 to November 30, 1956 |
| Total       |         | 5,353  | 4,221 | 400 | 10 | 9,984 |         |