Epidemiological Study of Sarin Poisoning in Matsumoto City, Japan

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On the night of June 27, 1994, about 12 liters of sarin were released by terrorists in Matsumoto City, Japan. In order to investigate the epidemic, community-based questionnaire surveys were conducted.

The subjects were all inhabitants (2052 people) living and staying in an area of 1050 meters from north to south and 850 meters from east to west including the sarin release site. Participants included 1743 people who answered the questionnaire at the first survey; those with symptoms were contacted for follow-up at four months and one year after the episode.

The number of sarin victims were 471 persons. Muscarinic signs were common to all victims; nicotinic signs were only seen in severely affected victims. The geographical distribution of sarin victims was closely related to the direction of the wind. Three weeks after the intoxication, 129 victims still had some symptoms such as dysesthesia of the extremities. At that time, many victims had begun to experience asthenopia, which was even more frequent at four months. Although victims who felt sarin-related symptoms had decreased by a year, some still had symptoms such as asthenopia.

Sarin released in a suburban area affected approximately 500 inhabitants living nearby; some still had symptoms a year after the intoxication. J Epidemiol, 1998; 8: 33-41.

Sarin (isopropyl methylphosphonofluoridate), an organophosphate nerve agent, is highly toxic and is considered to be a lethal chemical warfare agent. When dispersed as a vapor, it is readily absorbed through the respiratory tract or any body surface. The intoxicating manifestations of exposure include all those that can be expected from the inhibition of acetylcholinesterase (AChE) resulting in acetylcholine excess.

Hitherto, many sarin exposure experiments have been conducted using laboratory animals. A few human cases of sarin poisoning have also been reported; these were military accidents or experimentally investigated sarin miosis using volunteers. There is no report of mass poisoning with sarin in a suburban area.

On the night of June 27, 1994, about 12 liters of sarin were released by terrorists using a heater and fan in Matsumoto City, Japan (according to a police office report), causing harm to many inhabitants in the surrounding areas, including seven deaths (five men, and two women). The identification of the toxic vapor was made from air or water samples collected near the sarin release site by gas chromatograph-mass spectrometer at the Nagano Research Institute for Health and Pollution. A second attack with sarin vapor later occurred in the Tokyo subway on March 20, 1995.

In order to clarify the details of the epidemic of the sarin poisoning in Matsumoto, we surveyed inhabitants of the area...
where the sarin was released. We determined the time of onset, geographic location, and evolution of symptoms in those affected by the exposure.

**MATERIALS AND METHODS**

**Condition of release of toxic substance**

Twelve liters of sarin were released by terrorists using a heater and fan from a truck between 22:40 and 22:50 on 27th, June, 1994 (according to a police office report). The weather at that time was rainy at 20.5°C with a 0.6-1.7 meter per second wind from the southwest and 93 % humidity.

**Subjects**

In order to clarify the characteristics of sarin victims and the observed effects, three questionnaire surveys were conducted by the Health Research Subcommittee of the Medical Committee for the Toxic Gas Intoxication of the Matsumoto City Regional Comprehensive Medical Council. In each survey, informed consent was obtained from all subjects: the purpose of the survey was also included in the questionnaire. In a preliminary survey by interview, we confirmed that the sarin victims were distributed within an area of 1050 meters from south to north and 850 meters from east to west, consisting of nine town districts. The subjects of this study were all inhabitants (2052 people) who lived or stayed in the area, between the 27th and 28th of June, 1994 in Matsumoto City, Japan. In Japan, the addresses of all the inhabitants are registered at the regional office. As the district was a residential areas and there were no hotels or lodging facilities, it was estimated that there were no or very small number of victims, if any, who were excluded from this study. All inhabitants in Japan can consult doctors using medical insurance with minimal or free of charge.

**The first survey**

The first survey was conducted three weeks after the deliberate release of sarin. The questionnaire consisted of five items as follows: questions about personal information such as name, age, sex and address; 23 questions on symptoms (sneezing, rhinorrhea, nasal voice, sore throat, coughing, dyspnea, darkness of visual field, narrowing of visual field, flickering of vision, ocular pain, increase of lacrimation, blurriness of vision, diplopia, headache, nausea, vomiting, dizziness, dysesthesia of the extremities, muscle cramp, gait disturbance, paresis of peripheral muscle, dysphagia and fatigue) that subjects experienced immediately after sarin intoxication and those remaining three weeks after the intoxication; questions regarding hospitalizations and consultations with doctors; questions about when and where they experienced the symptoms; and questions concerning their location in their house and whether windows were open. The questionnaire was distributed to all subjects and recovered by the leader of each town district according to the notification of Matsumoto City Office. The questions were completed by the inhabitants at their homes. When subjects could not answer by themselves (e.g. infants), the questions were answered by another member of the family. The recovery of the questionnaire was 84.9 percent (1743 subjects, 847 men, 877 women and 19 sex non-specified), and the addresses of these respondents were registered.

**The Second Survey**

Four months after the release of sarin, we conducted a second survey of the health status of those victims who still had symptoms associated with the vapor three weeks after the episode (129 persons). The questionnaire consisted of only two sections: questions about personal information; 23 questions as shown in the first survey plus 8 additional questions (insomnia, difficulty in reading and writing, asthenopia, shoulder stiffness, feeling of heaviness in the head, husky voice and slight fever). These additional items were those complained of by sarin victims at three weeks after the episode. The questionnaires were sent to the victims and returned by mail; 105 people (18 people of the group hospitalized, 61 who consulted doctors, and 26 who did not) responded (81.4 percent of the injured victims who had subjective symptoms at three weeks).

**The third survey**

A year after the deliberate release of sarin, we again surveyed all victims (45 persons) who had reported symptoms four months after the episode. The questionnaire consisted of two sections: questions about personal information such as name, age, sex and address; 13 questions on symptoms (headache, fatigue, feeling of heaviness in the head, insomnia, shoulder stiffness, asthenopia, difficulty in reading and writing, blurriness of vision, husky voice, slight fever, palpitation, difficulty smoking and having bad dreams), which were constructed according to those reported at the second survey. The questionnaires were sent to the victims and returned by mail; all the people responded.

Along with the three surveys, health checks and laboratory examinations including erythrocyte AChE activity were encouraged without charge at four weeks after the episode for inhabitants who lived in the setting area; for inhabitants who showed lowered erythrocyte AChE activity at this time, the measurement was followed up until four months after the episode. The results were described elsewhere.

**Statistical analysis**

All of the data were analyzed at the Department of Hygiene, Shinshu University School of Medicine using the SPSS-X (SPSS Inc, Chicago) program on Hitachi (Tokyo) HITAC M240H at the Computer Center of Shinshu University. The victims were divided into three groups according to their
reports at the first survey; the victims requiring hospitalization; the victims who consulted doctors but did not require hospitalization; and the others with symptoms who did not consult a doctor. There were significantly different frequencies in the mean frequencies of symptoms immediately after sarin exposure among the three groups: 9.6 ± 6.4 for the group (40 people) who were hospitalized, 4.6 ± 2.9 for the group (156 people) who consulted doctors, and 2.5 ± 2.1 for the group (275 people) who did not consult doctors. The frequencies of symptoms were tested by analysis of variance. When there was significant difference among groups, the significance between the two groups was evaluated by the chi-square test.

RESULTS

Of the subjects who answered our questions (1743 people), 471 subjects (27.0 percent; the mean ± SD of age, 45.2 ± 21.6) had any of the listed symptoms. Of these subjects, the percentages of victims who had symptoms on June 27 and 28 in each age group were as follows: 11.1 percent in the 0-4 year old group, 10.2 percent in the 5-9 year old group, 34.1 percent in the 10-14 year old group, 39.0 percent in the 15-19 year old group, 34.6% in the 20-29 year old group, 27.1% in the 30-39 year old group, 25.8% in the 40-49 year old group, 32.3% in the 50-59 year old group, 28.0% in the 60-69 year old group, 23.4% in the 70-79 year old group, 20.0% in the 80-89 year old group and 15.4% in the unspecified group. Of these victims, 40 people were hospitalized, 156 people consulted physicians including internists, ophthalmologists or pediatricians, and 275 peoples did not.

The symptoms reported by all victims are listed in Table 1. More than half of the victims experienced rhinorrhea; more than 20% experienced sore throat, cough, dyspnea, darkness of visual field ("sunglass effect"), ocular pain and headache. The symptoms of sneezing, narrowing of vision, flickering and blurriness of vision were also reported by many victims. Although almost all the frequencies were less than 10%, victims experienced nasal voice increase of lacrimation, diplopia, nausea, vomiting, dizziness, dysesthesia of the extremities, muscle cramp, gait disturbance, paresis of perioral muscle, dysphagia and fatigue.

The frequencies of all the symptoms were significantly different among the groups. Of the group requiring hospitalization (admitted patient group), most victims (92.5%) experienced darkness of visual field; more than 70% of the victims experienced rhinorrhea, blurriness of vision and headache; more than 50% of the victims experienced coughing, dyspnea, narrowing of visual field and ocular pain; 30 to 40% of the victims experienced fatigue, dizziness, dysesthesia of extremities, gait disturbance, nausea and flickering of vision. Although the frequency was relatively small, some victims complained of increased lacrimation, diplopia, vomiting, dysphagia or muscle cramp more frequently than those in the other groups. Some of the victims also had incontinence of urine or feces, nosebleed and bloodshot eyes.

The most common symptom in the group who consulted doctors but who was not admitted (out patient group) was rhinorrhea, and its frequency was not significantly lower than that of the group requiring hospitalization. Sore throat was the single symptom that was more common in this group compared to the group requiring hospitalization. The out patient group also experienced sneezing, coughing and flickering of vision at a rate similar to that of the group requiring hospitalization, whereas all other symptoms were less common.

The most common complaint of the victims who did not consult doctors was rhinorrhea, though it was at a lower rate than those of the admitted patient and out patient groups. The other symptoms in this group were less than 20%, which were at a similar or lower rate than those of the out patient group.

Distribution by time of onset of sarin symptoms is shown in Fig 1. The earliest experience of symptoms was from 20:00 to 21:00 on the 27th of June. The number of victims experiencing onset of symptoms reached a maximum from 23:00 to 24:00. The number then decreased with time, but again increased after 5:00 the next morning and reached a second maximum from 8:00 to 9:00.

The sarin victims who felt the symptoms during the night or the next morning had the following characteristics. Compared to the latter, the former group was characterized by younger victims with more severe symptoms: all victims required hospitalization, a higher percentage of victims consulted doctors (the mean ± SD of age, 40.9 ± 19.5), and a half of victims who did not consult a doctor. In the former group, the most prominent symptom was rhinorrhea (67.8% of the former victims), followed by dyspnea (49.2%), darkness of visual field (46.7%), nasal voice (37.8%), headache (35.7), ocular pain (31.1%), sore throat (29.8%), flickering of vision (27.3%), narrowing of visual field (25.6%), sneezing (19.3%), nausea (15.1%), coughing (12.6%), fatigue (12.2%) and dizziness (11.9%). The frequencies of the other symptoms were under 10%. The latter group included most victims who did not consult a doctor and victims who were elderly (the mean ± SD of age, 49.7 ± 21.2). The most prominent symptom in this group was also rhinorrhea (66.9% of the latter victims), followed by headache (29.9%), sore throat (26.0%), ocular pain (22.0%), nasal voice (12.6%), flickering of vision (12.6%) and dyspnea (11.8%). The frequencies of the other symptoms were rare. In the latter group, no significant difference was seen between the numbers of victims and the distance of their home from the site where the sarin was released.

Locations of those victims suffering from the sarin exposure were mapped by their postal code. Fig. 2 shows suffering rates of sarin for inhabitants (the percentage of the population at risk that became ill) in each block by the postal code. In the block
### Table 1. Time course of reported symptoms after sarin poisoning.

| Symptoms                        | A      | B      | C      | D      | A      | B      | C      | D      |
|---------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| Number of people with symptoms/subjects participating | 471/1743 | 129/1743 | 45/105 | 20/45 | 40/1743 | 25/1743 | 10/105 | 7/45  |
| Sneezing                        | 73     | 2(2.7)* | 0(0)* | -      | 5      | 0(0)*  | 0(0)* | -      |
| Rhinorrhea                      | 297    | 25(7.4) | 10(2.8) | 2(0.6)* | 30     | 1(3.3) | 1(1.7) | 0(0)*  |
| Nasal voice                     | 38     | 3(7.9)  | 2(4.3) | -      | 8      | 0(0)   | 0(0)   | -      |
| Sore Throat                     | 115    | 13(11.3)| 2(1.4) | -      | 7      | 0(0)   | 0(0)   | -      |
| Coughing                        | 123    | 8(6.5)  | 9(5.9)  | 1(0.7) | 20     | 0(0)   | 1(3.6) | -      |
| Dyspnea                         | 147    | 7(4.8)  | 3(1.6)  | -      | 24     | 4(16.7)| 0(0)   | -      |
| Darkness of visual field        | 135    | 22(16.3)| 3(1.8)  | -      | 37     | 4(10.8)| 0(0)   | -      |
| Narrowing of visual field       | 75     | 14(18.7)| 1(1.1)  | 1(1.1) | 23     | 4(17.4)| 0(0)   | 1(3.1) |
| Flickering of vision            | 93     | 15(16.1)| 5(4.4)  | -      | 14     | 2(14.3)| 1(5.1) | -      |
| Ocular pain                     | 114    | 24(21.1)| 4(2.8)  | -      | 21     | 5(23.8)| 0(0)   | -      |
| Increase of lacrimation         | 35     | 8(22.9) | 5(11.6) | -      | 9      | 1(11.1)| 0(0)   | -      |
| Blurriness of vision            | 87     | 22(25.3)| 5(4.6)  | 13(12.1)| 28     | 3(10.7)| 2(5.1) | 5(12.9)|
| Diplopia                        | 18     | 3(16.7) | 3(13.6) | -      | 8      | 1(12.5)| 1(9.0) | -      |
| Headache                        | 147    | 4(2.7)  | 4(2.2)  | 0(0)   | 29     | 0(0)   | 1(2.4) | 0(0)   |
| Nausea                          | 49     | 4(8.2)  | 0(0)    | -      | 17     | 1(5.9) | 0(0)   | -      |
| Vomiting                        | 16     | 1(6.3)  | 0(0)    | -      | 11     | 1(9.1) | 0(0)   | -      |
| Dizziness                       | 38     | 7(18.4) | 1(2.1)  | -      | 14     | 4(28.6)| 0(0)   | -      |
| Dysesthesia of the extremities  | 26     | 30(115.4)| 7(21.9)| -      | 13     | 8(61.5)| 0(0)   | -      |
| Muscle cramp                    | 6      | 1(16.7) | 0(0)    | -      | 5      | 1(20.0)| 0(0)   | -      |
| Gait disturbance                | 15     | 0(0)    | 0(0)    | -      | 13     | 0(0)   | 0(0)   | -      |
| Paresis of perioral muscle      | 11     | 2(18.2) | 0(0)    | -      | 6      | 0(0)   | 0(0)   | -      |
| Dysphagia                       | 16     | 1(6.3)  | 0(0)    | -      | 5      | 0(0)   | 0(0)   | -      |
| Fatigue                         | 39     | 17(43.6)| 2(4.2)  | 17(35.5)| 17     | 9(52.9)| 2(8.5) | 7(29.7)|
| Insomnia                        | -      | 2b      | 4       | 3      | -      | 0b     | 0      | 1      |
| Difficulty reading and writing  | -      | 2b      | 13      | 1      | -      | 2b     | 4      | 0      |
| Asthenopia                      | -      | 14b     | 23      | 14     | -      | 8b     | 5      | 6      |
| Palpitation                     | -      | 1b      | 1       | 4      | -      | 1b     | 1      | 1      |
| Shoulder stiffness              | -      | 6b      | 2       | 9      | -      | 3b     | 2      | 2      |
| Feeling of heaviness in the head| -      | 4b      | 0       | 0      | -      | 1b     | 0      | 0      |
| Husky voice                     | -      | 4b      | 4       | 6      | -      | 2b     | 0      | 0      |
| Slight fever                    | -      | 2b      | 2       | 2      | -      | 2b     | 2      | 1      |
| Difficulty smoking              | -      | 2b      | 2b      | 3      | -      | 2b     | 2b     | 3      |
| Asthenia                        | -      | -       | 11      | -      | -      | -      | -      | 6      |
| Having bad dreams               | -      | -       | 2       | -      | -      | -      | -      | 1      |

A. immediately after the poisoning; B. three weeks after the poisoning; C. four months after the poisoning; D. a year after the poisoning

Figures represent numbers complaining of each symptom

a. Figures in the parentheses represent percentages based on the numbers who had symptoms immediately after exposure to sarin and the recovery

b. Additional symptoms reported by some, but not included in the questionnaire

-, Symptoms excluded in the questionnaire

*, **, ***. Significant differences were noted between the groups hospitalized and those who consulted doctors, or between groups who consulted doctors and those who did not at p<0.05. P<0.01 and p<0.001, respectively.
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where sarin was released (● in Fig 2), 76 % of all inhabitants experienced some symptoms. All of the seven persons who died, and 68 % of the hospitalized victims were also in this same block.

The majority (80 %) of all victims were located in an elliptical area (within the shadow in Fig 2) with a 400 meter long axis north east of the site. Other victims were distributed outside of the elliptical area, but all of them experienced only minimal symptoms not requiring medical consultation. All sarin victims were located in an area estimated to be 800 meters from south to north and 570 meters from west to east. A sarin victim who consulted a doctor was located at an area 500 meters west of the site where sarin was released.

The places where victims were exposed to sarin were also investigated in the first questionnaire survey. Over 80 % of the victims were exposed inside of their houses, and of these vic-

| Symptoms                        | Victims consulted doctors | Victims not consulted doctors |
|---------------------------------|---------------------------|-------------------------------|
|                                 | A  156/174 | B  66/174 | C  16/105 | D  11/45 | A  275/174 | B  38/174 | C  19/105 | D  2/45 |
| Sneezing                        | 35( 2.9)a | 1( 0.0)a | -         | -       | 33         | 1( 3.0)a | 0( 0)a    | -       |
| Rhinorrhea                      | 102(10.8) | 7( 0.6)  | 1( 0.9)a | -       | 165        | 1( 7.9)  | 1( 0.4)   | 1( 0.4)a|
| Nasal voice                     | 15         | 1         | 1( 6.7)  | 1( 4.6) | -          | -         | -         | -       |
| Sore Throat                     | 54         | 1( 1.7)  | -         | -       | 54         | 7( 13.0) | 1( 1.3)   | -       |
| Coughing                        | 52         | 4( 7.1)  | 4( 7.1)  | 1( 1.1)a| 51         | 4( 7.8)  | 4( 5.3)   | -       |
| Dyspnea                         | 66         | 3( 4.5)  | 3( 4.1)  | -       | 57         | 0( 0)    | 0( 0)     | -       |
| Darkness of visual field        | 72         | 16( 22.2)| 3( 3.9)  | -       | 26         | 2( 7.7)  | 0( 0)     | -       |
| Narrowing of visual field       | 34         | 7( 20.6) | 1( 2.7)  | -       | 18         | 3( 16.7) | 0( 0)     | -       |
| Flickering of vision            | 41         | 8( 19.5) | 3( 6.7)  | -       | 38         | 5( 13.2) | 1( 1.8)   | -       |
| Ocular pain                     | 48         | 11( 22.9)| 3( 5.8)  | -       | 45         | 8( 17.8) | 1( 1.5)   | -       |
| Increase of lacrimation         | 10         | 0( 0)    | 3( 27.6) | -       | 16         | 7( 43.8) | 2( 8.5)   | -       |
| Blurriness of vision            | 34         | 10( 29.4)| 3( 8.1)  | 6( 16.2)| 25         | 9( 32.0) | 0( 0)     | 2( 5.4) |
| Diplopia                        | 6          | 2( 33.3) | 2( 30.6) | -       | 4          | 0( 0)    | 0( 0)     | -       |
| Headache                        | 59         | 4( 6.8)  | 3( 4.7)  | 0( 0)   | 55         | 0( 0)    | 0( 0)     | 0( 0)   |
| Nausea                          | 16         | 2( 12.5) | 0( 0)    | -       | 15         | 1( 6.7)  | 0( 0)     | -       |
| Vomiting                        | 2          | 0( 0)    | 0( 0)    | -       | 3          | 0( 0)    | 0( 0)     | -       |
| Dizziness                       | 15         | 2( 13.3) | 1( 6.2)  | -       | 9          | 1( 11.1) | 0( 0)     | -       |
| Dysesthesis of the extremities  | 9          | 13( 14.4)| 7( 7.2)  | -       | 4          | 9( 22.5) | 0( 0)     | -       |
| Muscle clamp                    | 1          | 0( 0)    | 0( 0)    | -       | 0          | 0( 0)    | 0( 0)     | -       |
| Gait disturbance                | 1          | 0( 0)    | 0( 0)    | -       | 1          | 0( 0)    | 0( 0)     | -       |
| Paresis of perioral muscle      | 3          | 2( 66.7) | 0( 0)    | -       | 2          | 0( 0)    | 0( 0)     | -       |
| Dysphagia                       | 7          | 1( 14.3) | 0( 0)    | -       | 4          | 0( 0)    | 0( 0)     | -       |
| Fatigue                         | 13         | 5( 38.5)| 0( 0)    | 10( 70.7)| 9          | 3( 33.3)| 0( 0)     | 0( 0)   |
| Insomnia                        | -          | 1b        | 3         | 2       | -          | 1b        | 1         | 0       |
| Difficulty reading and writing  | -          | 0b        | 7         | 1       | -          | 0b        | 2         | 0       |
| Asthenopia                      | -          | 5b        | 15        | 6       | -          | 1b        | 3         | 2       |
| Palpitation                     | -          | 0b        | 0         | 3       | -          | 0b        | 0         | 0       |
| Shoulder stiffness              | -          | 3b        | 0         | 5       | -          | 0b        | 0         | 2       |
| Feeling of heaviness in the head| -          | 3b        | 0         | 0       | -          | 0b        | 0         | 0       |
| Husky voice                     | -          | 1b        | 3         | 4       | -          | 0b        | 1         | 2       |
| Slight fever                    | -          | 0b        | 0         | 1       | -          | 0b        | 0         | 0       |
| Difficulty smoking              | -          | 0b        | 0b        | 0       | -          | 0b        | 0         | 0       |
| Asthenia                        | -          | -         | -         | 4       | -          | -         | -         | 1       |
| Having bad dreams               | -          | -         | -         | 1       | -          | -         | -         | 0       |
Figure 1 Distribution by time of onset of symptoms of sarin-exposed victims. Abscissa and spindle axes represent time of onset of symptoms and the number of victims reporting first onset of symptoms, respectively.

Three weeks after the exposure to sarin, the day when this survey started, 129 victims (27.4% of the first victims; the mean ± SD of age, 44.3 ± 18.4) still had sarin-related symptoms (25 of the victims who were hospitalized, 66 who consulted doctors and 38 who did not consult doctors) (Table 2). The frequencies of all symptoms except dysesthesia of the extremities and fatigue decreased to under 25% at this time. However, the decrease of symptoms of fatigue was only half; that of dysesthesia of the extremities was not seen. In the group hospitalized, the most common symptoms were fatigue, dysesthesia of the extremities and ocular pain. In the group who consulted doctors, symptoms included darkness of visual field, dysesthesia of extremities, rhinorrhea, and ocular pain. In the group who did not consult doctors, the primary symptom was rhinorrhea. At three weeks, some people also reported asthenopia (8 people (20%) of the group hospitalized, 5 (3.2%) who consulted doctors and 1 (0.4%) who did not require consultation), which was not seen at the early stage of sarin intoxication. Of people with this complaint, erythrocyte AChE activity of ten measured at four weeks after the deliberate release was significantly lower (1.18 ± 0.36 unit, normal range 1.2 to 2.0) than 142 people of those without the symptom (1.57 ± 0.30 unit) [6]. Although the symptoms were not included on the questionnaire sheet, some victims newly complained of shoulder stiffness, insomnia, husky voice, difficulty reading and writing, feeling of heaviness in the head, slight fever, palpitations, difficulty smoking, abnormal taste, diarrhea, abdominal pain, dizziness, nasal congestion, ocular itch, perioral and lingual paresis or chest pain.

At four months, 45 victims (10 people of the group who were hospitalized, 16 who consulted doctors and 19 who did not consult doctors, the mean ± SD of age, 47.5 ± 18.0) still complained of symptoms, and four of them continued to consult a doctor. Thus, the percentage of victims with complaints was largest among the hospitalized people, followed by those who consulted doctors. All symptoms observed immediately after the intoxication, except increase of lacrimation, diplopia and dysesthesia of extremities, had decreased to under 10 percent. The most common complaint was asthenia, which doubled in frequency from three weeks to four months. Other complaints included difficulty in reading and writing, insomnia, husky voice, slight fever, shoulder stiffness and difficulty in smoking. There were no victims with lowered erythrocyte AChE activity at this point.

At a year after the accident, 20 victims (7 people of the group who were hospitalized, 11 who consulted doctors and 2 who did not consult doctors, respectively; the mean ± SD of age, 44.3 ± 18.1) still felt some symptoms. The most common complaint was fatigue, followed by asthenia, blurriness of vision, asthenia, shoulder stiffness and husky voice. The frequencies of these symptoms, except asthenia, seemed to be greater at one year than at four months. In contrast, some symptoms seen at four months, such as headache, feeling of heaviness in the head and difficulty in reading and writing, had disappeared by one year after the intoxication. Although the frequency was very low, four victims felt palpitation, three felt insomnia, two felt slight fever and two had bad dreams. All these victims were included in those requiring hospitalization.
Figure 2 Geographical distribution of sarin victims in Matsumoto City. Areas were divided by postal code of the address. Each figure represents the percentage of inhabitants who complained of sarin-related symptoms in the acute stages. ●, the point where sarin was released. The majority (80%) of victims were located in an area within the shadow which showed areas where more than 20% of the inhabitants had symptoms. The symbol (•) means the direction of wind at the point of the deliberate release of sarin.

DISCUSSION

From our survey, the prevalence of sarin poisoning was estimated to be 27.0%. At the time when the sarin was released, it was rainy with a 0.6-1.7 meter per second wind from the southwest in the area. The majority of the victims were concentrated in an elliptical area with a 400 meter long axis north east from the site where the sarin was released, suggesting that the geographical distribution was closely related to the wind direction. Within the elliptical area, the air in the block where the sarin was released was severely polluted as shown by the large number of victims who died or were hospitalized.

It is interesting that the onset of the symptoms attributable to sarin occurred with two peaks in number during the first 12 hours. The first peak was immediately after the sarin was released; this group had a high percentage of severely affected victims. The second peak appeared 8 hours later, after many inhabitants began to leave their homes in the morning; this group predominantly experienced mild symptoms. The victims in the second peak were situated both inside and outside of the highly polluted elliptical area (in Fig 2), suggesting that low levels of sarin vapor inducing mild intoxication still occurred both near the release site and polluted areas wider than the area with immediate intoxication. Indeed, samples taken at 11:00 in the morning found sarin in the air inside of the nearest house north of the release site, and also in the water samples from a pond outside. Since most people were sleeping between 24:00 and 6:00, those with symptoms might be simply small
during the period. These results suggest that in the event of a similar exposure, inhabitants should remain inside their homes with all windows and doors closed as long as they remain asymptomatic; if symptoms develop, they should vacate the premises as quickly as possible. It is unknown why some subjects reported symptoms before the sarin release. The symptoms were closely related to those reported thereafter, suggesting that misunderstanding of the time reported may be denied because three weeks had passed when the first survey was done. A small amount of the agents might be leaked before the release of sarin.

Symptoms of nerve-agent poisoning were first summarized by Grob et al. and Gunderson et al. and later by WHO and Sidell and Boak. Symptoms in the present case were consistent with these previous reports. The major symptom in those of accidental or experimental exposure to sarin was miosis, a finding which is slightly different from those in the present report. The symptom of rhinorrhea was most prominent in the Matsumoto exposure, but not in these previously described cases.

The typical profile in sarin poisoning is a lowered erythrocyte AChE activity, which may result in primarily muscarinic, but also nicotinic symptoms. Erythrocyte AChE activity measured at four weeks after the intoxication of victims requiring hospitalization was significantly lower than that of those who consulted doctors or other victims who had symptoms but did not consult a doctor, suggesting that the group of victims requiring hospitalization was more severely affected than the others. Symptoms of rhinorrhea, cough, dyspnea, darkness of visual field, narrowing of visual field, ocular pain, flickering of vision, dimness of vision and headache were predominant in the present case; these symptoms were caused by the muscarinic effects of sarin. In victims requiring hospitalization, however, the symptoms of dysesthesia of extremities, gait disturbance and fatigue were also present, suggesting that nicotinic effects were additionally seen in the severely affected.

Since the effects of sarin are related to the inhibition of AChE, atropine and oxime have been used as primary therapy. Erythrocyte AChE activity is considered a good indicator for when to initiate oxime therapy. In the present case, erythrocyte AChE activity measured at four weeks after the intoxication was lower in victims experiencing rhinorrhea, dyspnea, darkness of visual field, narrowing of visual field, ocular pain, increase of lacrimation, blurriness of vision, headache, nausea, vomiting, dysesthesia of extremities, convulsion, gait disturbance, paresis of perioral muscle or fatigue than those without these symptoms, suggesting that these symptoms are also a good indicator for starting therapy.

The frequencies of early symptoms associated with sarin poisoning decreased with time. At three weeks after the exposure, the most prominent complaint was dysesthesia of the extremities. In rodents, sarin is thought not to cause neuropathy except after sublethal repeated exposure. Our data showing that dysesthesia in the extremities was most prominent at three weeks suggests that sarin has an effect on the peripheral nervous system. However, this symptom was not seen four months after intoxication, and none of these victims showed any abnormality in nerve conduction studies.

The complaint of asthenopia occurred in victims with lowered erythrocyte AChE activity at three weeks after the intoxication. It is noteworthy that the frequency of this complaint further increased at four months after the intoxication and was still present after one year, although erythrocyte AChE activity returned to normal in all victims studied. In addition, among victims still having symptoms a year after the intoxication, more than 50% felt symptoms such as fatigue, asthenia, and blurriness of vision, and 40% felt shoulder stiffness. The severer the symptoms sarin victims experienced after the sarin intoxication, the greater the symptoms they retained. The mean age of these victims was not different from those whose symptoms had resolved, suggesting that further follow-up study including people without symptoms should be done to evaluate whether the symptoms reported a year after the intoxication are a later sequelae of acute exposure to sarin. Since some victims requiring hospitalization still had bad dreams, slight fever and symptoms of palpitation, these should also be followed.

In the present survey, people whose symptoms were solved at early stage were not included afterward. Therefore, the numbers of people who had symptoms four months and a year after sarin incident might be estimated low. Although the validity of results might be pointed because of the nature of questionnaire, that was partially covered by the measurement of AChE activity.

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