Annex 1

Report on Surveys of the Toxic Gas Poisoning in Matsumoto City

Date: March, 1995

Matsumoto City Council of Community-Based Integrated Care

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2. Progression and outline of explanatory meetings for residents, questionnaires, medical checkups

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* VI. Causative substance analysis results: Matsumoto Healthcare Center, Environment Pollution Section, Living Environment Department, Nagano Prefecture

VII. Presentations to the various associations.

VIII. Concluding remarks: Shohei Mimura, Nobuo Yanagisawa

* partially translated.

I. Introduction

Nobuo Yanagisawa
Chair of Expert Committee on Medical Cares Against Toxic Gas Poisoning Attack

I. Introduction

Nobuo Yanagisawa

(Chair of Expert Committee on Medical Cares Against Toxic Gas Poisoning Attack)

Late at night on June 27, 1994, an unprecedented toxic gas attack occurred in a quiet residential area of Matsumoto City. Since it was very stuffy, many windows were open, for sleep or for study purposes, in the medium-rise tenements where students and unmarried individuals lived. Therefore, the most severely affected victims were young people. The immediately responding emergency vehicles included a doctor car of the Matsumoto Regional Fire Bureau. The doctor car in Matsumoto city was the nation's first equipment that was stationed in the local government. In the system, physicians from the Shinshu University Hospital and several regional hospitals had been working in alternate shifts with regular rotations. That night, several physicians from the Shinshu University Hospital were on duty and travelled to affected areas. Of the seven deceased victims, two were transported to the hospital via ambulance and were pronounced dead on arrival (DOA). One victim, with cardo-respiratory arrest, was transported to the hospital and was declared vegetative. The other victims were saved because the on-duty physicians of the doctor car evaluated the victims in a level-headed manner and dealt with them appropriately.

Each of the six hospitals that received victims via ambulance independently diagnosed organic phosphorus compound poisoning based on the markedly constricted pupils, as well as respiratory and gastrointestinal symptoms, presented by the victims. The victims were appropriately treated with atropine sulfate administration (among others), which saved all the remaining victims, including patients with persistent systemic convulsions and lethargy, with no notable aftereffects. The actions of the medical staff were noteworthy because the residents were exposed to sarin, an extremely poisonous substance.

The widespread sarin poisoning gave some indefinable anxieties to residents, especially because the cause remained unknown for a while. On June 28, the Matsumoto City government immediately recommended that affected residents receive medical checkups, decided to provide aid regarding initial medical consultation fees, and initiated explanatory meetings, circulating documents, and health consultations.

At the time when, excepting the one patient who arrived at the hospital with cardio-respiratory arrest and was declared vegetative, the other inpatients recovered within one week of treatment, a liaison meeting among the physicians in charge of actual medical care at the involved hospitals was held, and subsequent strategies were considered by the Matsumoto City Council of Community-Based Integrated Care.

The Council planned and implemented questionnaires and medical checkups by specialized physicians for the residents who had various complaints and anxieties but did not consult a physician

at medical facilities, and measurement of red blood cell cholinesterase levels that are an objective index of the effects of organic phosphorus, with the significant support of Matsumoto City. Monthly medical checkups were continued for victims who presented symptoms and abnormalities at the examinations until their conditions normalized. By three months after the attack, red blood cell cholinesterase levels had become normalized in all patients, and their neurological symptoms disappeared. However, slight fevers and subjective symptoms remained in some patients. The purpose of these regular medical checkups and clinical examinations were to accurately understand the reality of sarin poisoning and generate reference documentation by which appropriate treatment can be provided whenever any affected resident shows aftereffect symptoms. The questionnaire results were analyzed in detail at the Department of Public Health, Shinshu University School of Medicine, and precious knowledge was obtained.

Sarin is a strong organophosphorus toxic substance that rapidly combines with cholinesterase and quickly ages. Sarin thus inhibits acetylcholine (excitatory transmitter)-degrading enzymes, resulting in excessive acetylcholine within the body. Skeletal muscle symptoms include contracting of the fiber fascicle and hyposthenia induced by excessive excitation of the muscle fibers. Autonomic nervous symptoms include constricted pupils, sweating, salivation, respiratory tract supersecretion, bronchial convulsions, vomiting, diarrhea, bradycardia, and urinary/fecal incontinence. Central neurological symptoms include headache, restlessness, impaired consciousness, and systemic convulsions.

As the fact of its use as a chemical weapon has shown, sarin has a more potent effect than organophosphate pesticides, and because it combines with cholinesterase strongly and ages quickly, we have no treatments other than symptomatic therapy with atropine and whole-body management with fluid replacement. Although sarin has been present since the World War II, there are almost no publications regarding medical knowledges of sarin poisoning. Based on the victim clinical symptoms and mass spectrometry results, it was considered with certainty that the toxin used in the Matsumoto City poisoning attack was sarin. Therefore, the information contained within this report is very rare and important. Medically, although there were several victims who died during the hyperacute stage, the victims who exhibited lethargy with systemic convulsions recovered rapidly after treatment, and were unexpectedly deemed cured approximately one week later, which brought us joy. Constricted pupil was a feature in victims, and is a marked and sensitive symptom, which persists for a long period of time. Many victims said that their field of vision suddenly and unexpectedly became dark, indicating that constricted pupil occurred almost instantaneously. Apart from these observations, much new knowledges have been presented in medical reports and questionnaire result analysis.

Although it is highly regrettable that the cause of the attack still remains unknown nine months hence, their correspondences by the public administration and medical agencies have completed for

now. The fatal victims included a final-year medical student with whom we studied, and many ordinary young people were snuffed out their lives unexpectedly and suddenly. This is very upsetting.

This report is the fruit of efforts of those involved. We have written this report in mourning for the victims.

IV. Reports related to medical care

Mikio Shimizu: Chair of the Hospital/Clinic Liaison Conference

1. Outline of activities

Mikio Shimizu and Hidemitsu Hirabayashi

2. Emergency activities of the doctor cars

Hiroshi Okudera and Tomomi Iwashita

3. Medical care summary and result analysis for individuals who consulted at medical facilities

Mikio Shimizu and Hidemitsu Hirabayashi

4. Outline of medical care for severely affected victims

Physicians in charge of each hospital

5. Analysis of ocular symptoms

Masahiko Nohara and others

IV. Reports related to medical care

Mikio Shimizu and Hidemitsu Hirabayashi (The Hospital/Clinic Liaison Conference)

1. Outline of activities

On June 27, on the night of the toxic gas attack, the victims were transferred in emergency vehicles or doctor cars to medical facilities. The patients presented common symptoms of poisoning by organic phosphorus compounds, including constricted pupils. Blood examinations revealed markedly reduced plasma cholinesterase levels, again indicating that the poisoning was caused by organic phosphorus compounds. However, there were many aspects that be unexplained by existing organic phosphorus poisoning caused by pesticide. This, in combination with the fact that the causative substance was not immediately identified, resulted in difficulties at medical facilities in dealing with the victims.

Accordingly, we considered it necessary that physicians in charge of treating the victims shared information to deduce the causative substance and discussed treatment directions. On June 30, we notified each medical facility in the city where the victims were hospitalized that a liaison conference regarding the victims of the toxic gas poisoning was held at the Nagano Prefectural Cancer Detection and Emergency Care Center on July 4. However, on July 3, the police notified that a substance presumed to be sarin was detected at the Nagano Research Institute for Health and Pollution, and was likely the causative substance. Immediately, although medical facilities made efforts to collect documents related to nerve gas, only two previous cases were available, since very few sarin poisoning cases were reported worldwide.

On July 4, the first liaison conference regarding the victims of toxic gas poisoning was held with many physicians in charge of each medical facility, as well as board members in charge of emergency of the Matsumoto City Medical Association, in attendance. The physicians in charge reported on each case, and shared information and discussed treatment directions. An introduction of sarin references was also conducted. It was confirmed that the treatments at each medical facility commenced at the time of the attack were appropriate.

Participating physicians at the liaison conference

Name of hospital	Attendance
Aizawa Hospital	Hirotaka Kawakami, Kazuko Hirabayashi
Shironishi Hospital	Ken Seki, Manabu Seki, Touwa Seki, Naosuke Usui
Matsumoto Kyoritsu Hospital	Toshihiko Furuhata, Jun Suzuki, Masaki Tsukakoshi, Kyohei Yamazaki
Marunouchi Hospital	Shinobu Sato, Eiichi Gomi, Toru Kakazu
Department of Emergency and Critical Care, Shinshu University Hospital	Hiroshi Okudera
Intensive Care Unit, Shinshu University Hospital	Tatsuhiko Shibata
First Department of Internal Medicine, Shinshu University Hospital	Keishi Kubo, Kenji Tsushima, Miyoko Suzawa
Second Department of Internal Medicine, Shinshu University Hospital	Takeshi Sodeyama, Shigeyuki Kawa
Third Department of Internal Medicine, Shinshu University Hospital	Hiroshi Morita, Yoshiki Sekijima
Nagano Prefectural Cancer Detection and Emergency Care Center	Mikio Shimizu, Hidemitsu Hirabayashi, Toshiki Aoki, Shuichi Oshima
Matsumoto City Medical Association	Sadayoshi Kubota, Haruo Ogawa

Moreover, on July 19, the second liaison conference was held with experts in hygieiology and pharmacology, as well as the physicians in charge of each hospital and members of the Matsumoto City Medical Association. At this conference, the participants reported on and discussed subsequent symptoms and treatments in inpatients and outpatients, and the necessity of sharing information and establishing a follow-up system for longitudinal patient observation was brought up. We therefore decided to establish the Hospital/Clinic Liaison Conference as a department of the Expert Committee in the Council of Community-Based Integrated Care and to continue current activities.

In September, we requested that the medical facilities submit clinical survey sheets that summarized patient symptoms, examination results, and gross outcomes, etc. In October, we also implemented questionnaires using these clinical survey sheets by mailing them to individuals with unknown gross outcomes, as well as patients treated in outpatient sections.

The emergency medical services in Matsumoto City have been supported by physicians on call, the network connecting secondary emergency hospitals with Shinshu University Hospital having advanced functionalities, and the Matsumoto Regional Fire Bureau. This attack, which involved a large number of victims in a concentrated area over a very short time, presented aspects of a mass

disaster, and it could therefore be used as an indicator of the effectiveness of the local emergency medical system. Because of unknown causative substance, although it could not be strictly said that there was no confusion at attack locations on June 27 and 28, it must be noted in the records that the physicians in the doctor cars and the emergency crews conducted victim triage and transfer in an appropriate and effective manner, and that the medical facilities made utmost efforts to treat the victims and minimize the number of deaths. We firmly believe that the records of these activities will strengthen the collaboration and relationship between the local hospitals and clinics, and contribute to the improvement of emergency medical service.

We could have only managed the conferences with the cooperation with many individuals, including Mr. Mimura, the Chair of the Matsumoto City Medical Association, Mr. Kubota, the Vice-Chair of the Matsumoto City Medical Association, and Dr. Yanagisawa, Director of the Shinshu University Hospital. We deeply thank those individuals, as well as the many people who took time out of their busy lives to attend the conferences, and the secretariat of the Matsumoto City Medical Association for distribution and collection of the clinical survey sheets and questionnaire sheets.

3. Medical care summary and result analysis for individuals who consulted at medical facilities

Mikio Shimizu and Hidemitsu Hirabayashi (Hospital/Clinic Liaison Conference)

A. Purpose

The purpose was to conduct medical surveys for the victims of organic phosphorus gas (sarin) poisoning attack on June 27, 1994, who visited hospitals in Matsumoto City.

B. Survey methods and duration

1. The Hospital/Clinic Liaison Conference mailed clinical survey sheets regarding the toxic gas attack to the six hospitals involved.

2. Various symptoms, examination results, and gross outcomes occurring or obtained from June 27 onwards were noted on these survey sheets, which were collected by September 20 and tallied.

1) Survey-cooperating hospitals

Aizawa Hospital

Shironishi Hospital

Matsumoto Kyoritsu Hospital

Marunouchi Hospital

Shinshu University Hospital

- First Department of Internal Medicine
- Second Department of Internal Medicine
- Third Department of Internal Medicine
- Department of Ophthalmology

Department of Emergency, Nagano Prefectural Cancer Detection and Emergency Care Center

2) Breakdown of surveyed cases (Table 1)

Name of Hospital	Outpatients	Inpatients	Total
Aizawa Hospital	19	8	27
Marunouchi Hospital	134	13	147
Shironishi Hospital	8	11	19
Matsumoto Kyoritsu Hospital	26	18	44
Prefectural Emergency Care Center	1	2	3
Departments of Internal Medicine, Shinshu University Hospital	15	4	19
Department of Ophthalmology, Shinshu University Hospital	5	0	5
Total	208	56	264

3) Test procedures

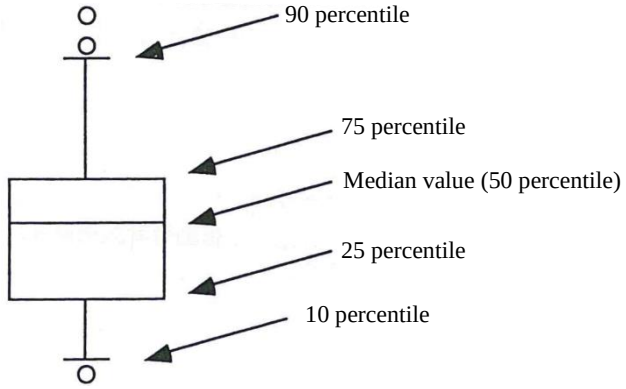
① The correlation between subjective/objective symptoms and each examination finding was investigated using plasma cholinesterase values as an index of gas poisoning severity (refer to D-3, Document 16).

② Homoscedastic/variance uniformity tests were conducted. Because these tests revealed non-normal distribution or uneven variance of data, a Freedman test was conducted. In the event that analysis of variance detected a significant difference, a Scheffé F test was used for multiple comparisons.

③ For statistic processing and producing graphs, Stat View 4.0J, Delta Graph Pro3, CANVAS3.5J, and Excel 4.0J were used on a Macintosh Power Book 540c.

4) How to use a box plot

Since the tested data was not normally distributed (non-parametric data), a box plot was added to the conventional mean ± standard deviation (error) to show the data trends.



C. Subjects: persons consulting at hospitals, sex, age demographics, living district, gross outcomes

1. The total number of persons consulting at hospitals was 264 (147 males and 117 females). The mean age (mean ± standard deviation) was 33.4±17.8 years (ages 33–86 years).

Document 1: age and sex in persons consulting at hospitals

2. The number of the outpatients was 208 and the number of the inpatients was 56.

3. The gross outcomes of the 264 cases at the time of the survey (September 20) included two cases of death, 163 cases of cure, one case of hospitalization, seven cases of outpatient status, 90 unknown cases, and on case of hospital change/discontinuation.

In the 98 persons who reported outpatient status, hospital change/discontinuation, or unknown gross outcomes, questionnaires regarding “presence or absence of symptoms” and “presence or absence of medical facility visit” were conducted on October 25 of the same year (54 respondents).

As of September 20, among the seven outpatients, three continued hospital visits and four did not

answer. Among the 90 persons with unknown gross outcomes, 31 reported that they were cured, 40 did not respond, 14 reported the continued presence of symptoms, two did not answer the question, and three responded unknown. The one individual who had changed hospitals or discontinued visitations had been cured. In addition, among the persons who were originally classified as cured, two individuals were attending hospitals regularly again, and five now reported as outpatients (Table 2).

Gross outcomes as of October 25 (Table 2)

Death	2
Hospitalization	1
Regular hospital visitation	5
Cured	196
Discontinued regular hospital visitation; still symptomatic	14
Unknown	46
Total	264

4. The date of initial medical visit ranged widely from June 27 to August 4. Visitation numbers were the highest on June 28 (139 individuals), with 54 and 34 individuals visiting medical facilities on June 29 and 30, respectively. Of the total surveyed population, 86% made their initial consultations on one of these three days.
Document 2: outpatient and inpatient initial hospital visit date and the gross outcomes

5. The mean hospitalization duration was 9.8 ±14.8 days (range 11–84) and the mean duration of regular visitation of a hospital or other medical facility was 9.6 ±15.7 days.
Document 3: gross outcomes for individuals consulting at hospitals at the time of the survey (September, 1994)
Document 4: hospitalization duration and gross outcomes

6. Regarding the location of residence for individuals consulting with medical authorities, the highest number of patients (180) was from the Kitafukashi area, followed by the Kaichi (29) and Asahimachi areas (17). Both individuals who died at hospital lived in the Kitafukashi area. On the questionnaire, due to privacy concerns, the results were tabulated in accordance with addresses present in the medical records, rather than the actual physical locations of the patients on June 27. Indeed, many cases were recorded at places which were distant from the epicenter of the attack.
Document 5: gross outcomes and addresses of persons consulting at hospitals

D. Subjective symptoms and findings in persons consulting at hospitals

As for subjective symptoms, survey items included headache, fatigue, heat sensation, visual field abnormalities, reduced visual acuity, and subjective sensory abnormalities, such as numbness and tingling, and the correlation between symptom frequency and plasma cholinesterase value (ChE%, where the lower normal limit was set at 100%) was investigated.

Document 6: subjective symptoms and findings in persons consulting at hospitals

1. Headache

Sixty persons complained of headaches (average duration: seven days). Patients with headaches (60 cases) showed significantly lower plasma cholinesterase values than patients who did not complain of headaches (201 cases, $P<0.0001$).

Document 7: headache

2. Fatigue

Thirty-three persons complained of fatigue (average duration: 12 days). Patients with fatigue (33 cases) showed significantly lower plasma cholinesterase values than patients who did not complain of fatigue (228 cases, $P<0.0001$).

Document 8: fatigue

3. Heat sensation

Sixteen persons complained of heat sensations (average duration: 9 days). Patients with heat sensations (16 cases) showed significantly lower plasma cholinesterase values than patients who did not complain of heat sensation (245 cases, $P<0.0001$).

Document 9: heat sensation

4. Visual field abnormalities

Eighty-three persons responded concerning visual field abnormalities, with 39 cases of its presence and 44 cases of its absence. In 76 cases whose plasma cholinesterase value was measured, the patients with visual field abnormalities showed significantly lower plasma cholinesterase values ($P<0.0007$). However, plasma cholinesterase values did not decrease in 18 patients who reported visual field abnormalities. In addition, five patients did not report symptoms despite plasma cholinesterase values under 50% of the normal range.

Document 10: visual field abnormalities

5. Reduced visual acuity

Two-hundred forty-seven patients responded regarding the symptom of reduced visual acuity, with

124 cases of its presence and 123 cases of its absence. In 209 cases and were found to be decreased in the patients exhibiting whose plasma cholinesterase value was measured, the patients with reduced visual acuity showed significantly lower plasma cholinesterase values (P=0.0002). However, plasma cholinesterase values did not decrease in 82 cases who reported reduced visual acuity.
Document 11: reduced visual acuity

6. Subjective sensory abnormalities (numbness, pain, hypoesthesia, etc.)
Two-hundred twenty persons responded regarding subjective sensory abnormalities, with 20 cases of its presence. Patients with subjective sensory abnormalities showed significantly lower plasma cholinesterase values than patients who did not complain of subjective sensory abnormalities (P<0.0001).
Document 12: subjective sensory abnormalities

E. Objective findings: electrocardiographs, pupil diameter, plasma cholinesterase values, etc. (Most parameters were measured on the initial examination day)

1. Electrocardiographs
a. Electrocardiography (ECG) was conducted in 39 individuals, with five cases of abnormal findings. Those findings consisted of 1) supraventricular arrhythmia, flattering of the T wave (V5–6), 2) stand still, 3) atrial fibrillation, 4) ventricular extrasystole, and 5) 2:1 A-V block. No significant difference in plasma cholinesterase values were identified between patients with and without ECG abnormalities. However, both groups presented decreased plasma cholinesterase values (40.7% of the normal lower limit in the group with the abnormalities, 72.0% in the group without the abnormalities), indicating that ECG was conducted in severe cases.
Document 13: abnormal electrocardiographic findings

2. Pupil diameter
a. Pupil diameter was measured in 219 patients. Twenty-one cases of diameter less than 1 mm (markedly constricted), 93 cases of 1–2 mm (intermediately constricted), 38 cases of 2–4 mm (mildly constricted), and 67 cases of 4 mm or greater (no constriction, normal) were observed. No patients with pupil diameter of 2.5 mm or greater presented plasma cholinesterase values less than 50% of the normal lower limit. In the group with 1 mm or smaller pupil diameter (21 cases), the plasma cholinesterase value was normal in 10 cases. The value was also normal in 59 cases for patients with pupil diameter between 1–2 mm (93 cases).

Statistically, the correlation between pupil diameter and plasma cholinesterase value was investigated. In the comparison among the severe group with plasma cholinesterase values less than

50% of the normal lower limit (17 cases, mean pupil diameter: 0.9 mm), the mild group with 50 – less than 100 % (30 cases, mean pupil diameter: 1.3 mm), and the normal group with 100% or more (140 cases, mean pupil diameter: 2.2 mm), although no significant difference in pupil diameter was found between the severe group and mild group, significant differences were found between the severe and normal groups and between the mild and normal groups (P=0.0013, P=0.0037, respectively).

Document 14: pupil dimeter (1)

b. We investigated how the plasma cholinesterase value differed in accordance with the degree of pupil constriction. The mean ChE% value was 84.3% in the group with markedly constricted pupils and exceeded 100% in the groups with intermediately constricted pupils, mildly constricted pupils, and normal pupil dilation. The correlation between pupil constriction and plasma cholinesterase value among the four groups was investigated. No significant difference in ChE% was found between the mildly constricted pupil and the normal groups, whereas significant differences were found among the other groups ($P<0.05$). In cases where pupil diameter was less than 4 mm, it was demonstrated that a correlation between plasma cholinesterase value decrease and pupil diameter was present.

Document 15: pupil diameter (2)

3. Plasma cholinesterase values

a. ChE%: division of severity according to plasma cholinesterase values

Since the definition of plasma cholinesterase normal range differs among medical facilities, in order to compare data obtained from multiple facilities, it was expressed as ChE% (case plasma ChE% value / facility normal lower limit × 100).

Severity was classified as follows: 100% or higher ChE% was “normal,” 50–100% was “mild,” and less than 50% was “severe.”

b. Frequency distribution: plasma cholinesterase values were measured in 222 cases. A “normal” result was obtained in 169 cases, “mild” in 33 cases, and “severe” in 20 cases.

c. Gross outcomes: as of September 15, the ChE% at initial examination of the seven outpatients was severe in six cases and normal in one case.

Documents 16, 17, and 18: plasma cholinesterase values (1), (2), (3).

4. Erythrocyte true cholinesterase values

a. Measurement date: performed almost once monthly, measured three times in total.

First time: July 23–24, 1994

Second time: August 19–25, 1994

Third time: September 29–30, 1994

Facility: measurement was conducted at the Otsuka Assay Laboratories of Diagnostic Division, Otsuka Pharmaceutical Co., Ltd.
Criterion value: 1.2–2.0 U
Subjects: 64, 58, and 15 individuals in the first, second, and third measurements, respectively.
b. Frequency distribution: at the first measurement, 15 cases were under the criterion value. Five cases were under the criterion value at the second measurement, and all samples were within the normal range at the third measurement.
c. Transition: mean ± standard deviation was 1.40 ± 0.40 U at the first measurement and 1.56 ± 0.27 U at the second measurement; these groups were significantly different ($P<0.05$). The results indicated that the erythrocyte true cholinesterase values recovered over a period of one to two months after the initial injury from the attack
Documents 19, 20, 21: transition of the erythrocyte true cholinesterase values (1) (2) (3)

5. Serum creatine kinase (CK)
a. CK%: Since the definition of serum creatine kinase normal range differs among medical facilities, in order to compare data obtained from multiple facilities, it was expressed as CK% (case plasma CK% value / facility normal lower limit × 100).
b. Frequency distribution: CK was measured in 155 cases. Thirty-three cases showed values of 100% or higher.
c. Correlation with ChE% decrease (classification of the severity): The mean CK% value was 73.7 ± 56.1% in the ChE% "normal group" (n = 112), 74.9 ± 59.4% in the "mild group" (n = 24), and 138.9 ± 175.8% in the "severe group" (n = 18). Significant differences in CK values were present between the "severe group" and the "mild group," and between the "severe group" and the "normal group" ($P<0.05$). The "severe group" had higher values than the other groups did.
Document 22: correlation between serum CK and plasma ChE decrease

6. Erythrocyte count
a. Subjects: One-hundred seventy-three subjects were examined. The mean value ± standard deviation was 469 ± 46 ($\times 10^4/mm^3$).
b. Correlation with ChE% decrease (classification of the severity): No significant differences were present among the three groups.
Document 23: correlation between erythrocyte count at the initial examination and plasma ChE decrease

7. Leukocyte count
a. Subjects: One-hundred seventy-three subjects were examined.

b. Correlation with ChE% decrease (classification of the severity): The leukocyte count mean value ± standard deviation was 6,175 ± 1,590/mm^3 in the ChE% "normal group" (n = 124), 6,986 ± 1,781 in the "mild group" (n = 29), and 10,972 ± 4,075 in the "severe group" (n = 18). Significant differences were present between the "severe group" and the "mild group," and between the "severe group" and the "normal group." In the "severe group," leukocyte count increased significantly ($P<0.0001$).

Document 24: correlation between leukocyte count at the initial examination and plasma ChE decrease

8. Serum BUN

a. Subjects: One-hundred ninety-one subjects were examined. The mean value ± standard deviation was 14.4 ± 4.2 mg/dL.

b. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 25: correlation between serum BUN at the initial examination and plasma ChE decrease

9. Serum creatinine

a. Subjects: One-hundred eighty-seven subjects were examined. The mean value ± standard deviation was 0.8 ± 0.2 mg/dL.

b. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 26: correlation between serum creatinine at the initial examination and plasms ChE decrease

10. Serum Na

a. Subjects: One hundred eighty-eight subjects were examined. The mean value ± standard deviation was 142 ± 2 mEq/L.

b. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 27: correlation between serum Na at the initial examination and plasma ChE decrease

11. Serum K

a. Subjects: One-hundred eighty-eight subjects were examined. The mean value ± standard deviation was 4.0 ± 0.4 mEq/L.

b. Correlation with ChE% decrease (classification of the severity): The mean value ± standard deviation was 4.1 ± 0.3 mEq/L in the ChE% "normal group" (n = 132), 4.0 ± 0.3 mEq/L in the "mild

group" (n = 32), and 3.6 ± 0.6 mEq/L in the "severe group" (n = 20). Significant differences were present between the "severe group" and the "mild group," and between the "severe group" and the "normal group." In the "severe group," serum K values decreased significantly (P<0.001).
Document 28: correlation between serum K at the initial examination and plasma ChE decrease

12. Serum Cl

a. Subjects: One-hundred eighty-eight subjects were examined. The mean value ± standard deviation was 107 ± 3 mEq/L.

b. Correlation with ChE% decrease (classification of the severity): The mean value ± standard deviation was 107 ± 3 mEq/L in the ChE% "normal group" (n = 132), 106 ± 4 mEq/L in the "mild group" (n = 32), and 104 ± 3 mEq/L in the "severe group" (n = 20). A significant difference was present between the "severe group" and the "normal group." The "severe group" showed significantly lower Cl values than the" normal group" did (P=0.0019).
Document 29: correlation between serum Cl at the initial examination and plasma ChE decrease

13. Serum total Ca (criterion value: 8.6–10.1 mg/dL)

a. Subjects: Thirty-six subjects were examined. The mean value ± standard deviation was 8.8 ± 0.6 mg/L.

b. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.
Document 30: correlation between serum total Ca at the initial examination and plasma ChE decrease

14. Arterial blood gas analysis

a. pH

i. Subjects: Twenty-nine subjects were examined. The mean value ± standard deviation was 7.41 ± 0.09.

ii. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 31: correlation between arterial blood gas pH and plasma ChE decrease

b. $PaCO_2$

i. Subjects: Twenty-nine subjects were examined. The mean value ± standard deviation was 34.8 ± 6.5 mmHg.

ii. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 32: correlation between arterial blood gas ($PaCO_2$) and plasma ChE decrease

c. PaO_2

i. Subjects: Twenty-nine subjects were examined. Although the oxygen concentration administered was not constant, the mean value ± standard deviation was 86.6 ± 30.9 mmHg.

ii. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 33: correlation between arterial blood gas (PaO_2) and plasma ChE decrease

d. Hydrogen carbonate (HCO_3)

i. Subjects: Twenty-seven subjects were examined. The mean value ± standard deviation was 22.4 ± 3.7 mEq/L.

ii. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 34: correlation between arterial blood gas HCO_3 and plasma ChE decrease

e. BE

i. Subjects: Twenty-five subjects were examined. The mean value ± standard deviation was -1.1 ± 4.2 mEq/L.

ii. Correlation with ChE% decrease (classification of the severity): No significant differences were found among the three groups.

Document 35: correlation between arterial blood gas base excess and plasma ChE decrease

F. Follow-up investigations

Although the questionnaire mailed on October 25 has been mentioned previously, the symptoms in the five outpatients were as follows:

Subjective symptoms in outpatients

Age	Sex	Symptoms
44	Female	Runny nose, difficulty breathing, eye pain, numbness in the hands and feet, exhaustion, sleeplessness, dazzling, and eye fatigue
44	Male	Headache, exhaustion, sleeplessness, and slight fever
47	Male	Decrease in arterial blood oxygen partial pressure
46	Male	Heavy head, sleeplessness, eye fatigue, and eye adjustment abnormality
85	Female	Eye discharge

Summary

A. The number of persons who consulted at hospitals was 264 and the mean age was 33.4 years. Most residents (180) lived in the Kitafukashi area. As of September 20, the gross outcomes comprised two cases of death, 163 cases of cure, one case of hospitalization, seven cases of regular hospital visits, 90 unknown cases, and one case of hospital change/discontinuation.

The questionnaire of October 25 updated this information to: two cases of death, 196 cases of cure, one case of hospitalization, five cases of regular hospital visits, 46 unknown cases, and 14 cases of possessing symptoms but not consulting hospitals.

B. When the correlation between subjective symptoms and plasma cholinesterase values was investigated, the plasma cholinesterase values decreased significantly in patients who complained of "headache," "fatigue," "heat sensation," "visual field abnormalities," "reduced visual acuity," and "subjective sensory abnormalities" ($P<0.01$).

C. Objective findings

1. Plasma cholinesterase values: There were 169 "normal cases (normal lower limit or greater)," 33 cases of "mild reduction (50%–100% of the normal lower limit)," and 20 cases of "severe reduction (less than 50% of the normal lower limit)."
2. Erythrocyte true cholinesterase values: In the examination conducted three months after the onset, all cases showed recovery to normal values.
3. Pupil diameter: A significant correlation was present between constricted pupil (pupil diameter less than 4 mm) and plasma cholinesterase value decrease. However, there were 10 cases in which plasma cholinesterase values remained within the normal range despite markedly constricted pupil.
4. Blood examination results: A significant correlation with severity, as classified according to plasma cholinesterase values, was found for increasing serum creatinine kinase (CK), leukocytosis, decreasing serum K, and decreasing serum Cl.

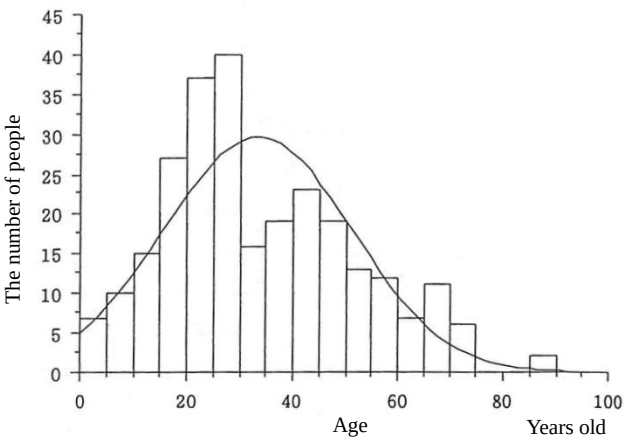
Document 1

Age and sex in persons consulting at hospitals

Frequency distribution: Age

Lower limit (≥)	Upper limit (<)	Frequency of the total	Female	Male
0	5	7	4	3
5	10	10	2	8
10	15	15	4	11
15	20	27	10	17
20	25	37	13	24
25	30	40	16	24
30	35	16	7	9
35	40	19	12	7
40	45	23	15	8
45	50	19	4	15
50	55	13	6	7
55	60	12	7	5
60	65	7	6	1
65	70	11	7	4
70	75	6	2	4
75	80	0	0	0
80	85	0	0	0
85	90	2	2	0
90	95	0	0	0
95	100	0	0	0
	Total	264	117	147

Histogram



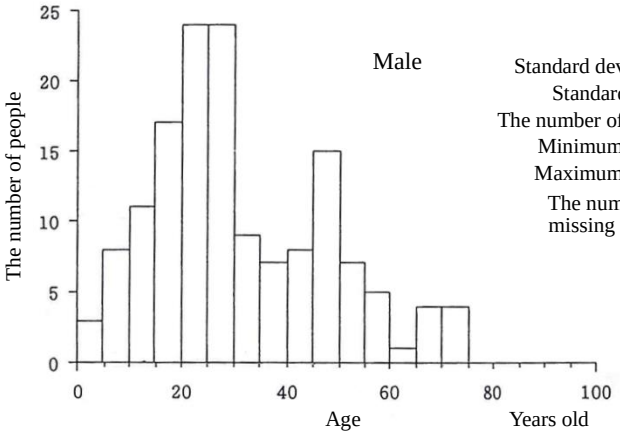
Descriptive statistics – Continuous variables

	Age
Mean	33.4
Standard deviation	17.8
Standard error	1.1
The number of cases	264
Minimum value	3.0
Maximum value	86.0
The number of missing values	0

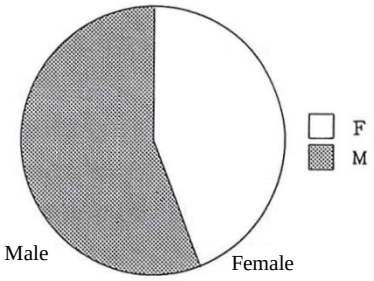
Frequency distribution: Sex

	Frequency	Percent
F	117	44.3
M	147	55.7
Total	264	100.0

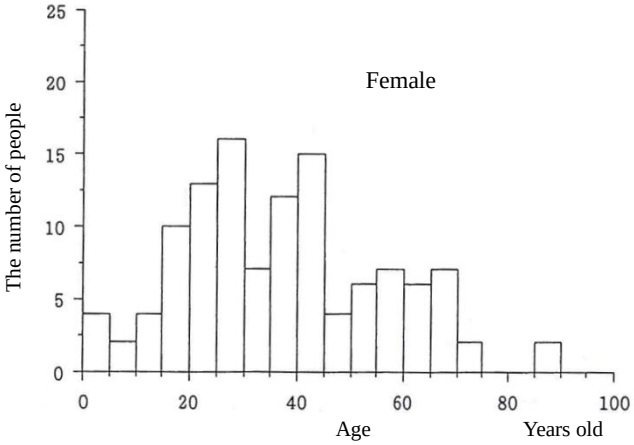
Male



Circular graph: Sex



Female



Initial hospital visit date of inpatients and outpatients and the gross outcomes

Frequency distribution: Initial hospital visit date

	The total number of people	Death / inpatient	Cure / outpatient	Cure / inpatient	Regular hospital visit / inpatient	Unknown / outpatient	Unknown / inpatient	Discontinuation because of changing to another medical facility / inpatient	Hospitalization / inpatient
94. 6.27	2	0	0	1	0	1	0	0	0
94. 6.28	139	2	26	34	7	62	6	1	1
94. 6.29	54	0	38	2	0	14	0	0	0
94. 6.30	34	0	28	1	0	5	0	0	0
94. 7. 1	4	0	3	1	0	0	0	0	0
94. 7. 2	1	0	1	0	0	0	0	0	0
94. 7. 3	2	0	2	0	0	0	0	0	0
94. 7. 4	8	0	7	0	0	1	0	0	0
94. 7. 5	9	0	9	0	0	0	0	0	0
94. 7. 6	3	0	3	0	0	0	0	0	0
94. 7. 8	2	0	2	0	0	0	0	0	0
94. 7.12	1	0	1	0	0	0	0	0	0
94. 7.13	1	0	0	0	0	1	0	0	0
94. 7.14	1	0	1	0	0	0	0	0	0
94. 7.15	1	0	1	0	0	0	0	0	0
94. 7.27	1	0	1	0	0	0	0	0	0
94. 8. 4	1	0	1	0	0	0	0	0	0
Total	264	2	124	39	7	84	6	1	1

Death / inpatient: died during hospitalization
Cure / outpatient: Cure in the outpatients
Cure / inpatient: Cure in the inpatients
Regular hospital visit / inpatient: Regular hospital visit by the victims who had been hospitalized
Unknown / outpatient: Unknown gross outcomes of the outpatients
Unknown / inpatient: Unknown gross outcomes of the inpatients
Discontinuation because of changing to another medical facility / inpatient: Changing to another hospital as an inpatient
Hospitalization / inpatient: Hospitalization at the time of the survey

Gross outcomes of the people who consulted with hospitals at the time of the survey (September, 1994)

Final hospital visit date and gross

	The total number of people	Cure	Regular hospital visit	Unknown	Discontinuation because of changing to another medical facility
94. 6.28	39	2	0	37	0
94. 6.29	25	16	0	9	0
94. 6.30	35	20	0	15	0
94. 7. 1	4	4	0	0	0
94. 7. 2	6	5	0	1	0
94. 7. 3	1	1	0	0	0
94. 7. 4	10	7	0	3	0
94. 7. 5	7	7	0	0	0
94. 7. 6	9	8	0	1	0
94. 7. 7	3	3	0	0	0
94. 7. 8	6	5	0	1	0
94. 7. 9	2	2	0	0	0
94. 7.11	6	4	0	2	0
94. 7.12	5	5	0	0	0
94. 7.13	4	2	0	2	0
94. 7.14	6	4	0	2	0
94. 7.15	3	1	0	2	0
94. 7.16	4	1	0	3	0
94. 7.18	4	3	0	1	0
94. 7.20	4	4	0	0	0
94. 7.21	2	2	0	0	0
94. 7.23	2	2	0	0	0
94. 7.26	1	1	0	0	0
94. 7.27	1	1	0	0	0
94. 7.28	2	1	0	0	1
94. 7.29	1	0	0	1	0
94. 8. 1	2	2	0	0	0
94. 8. 2	1	0	1	0	0
94. 8. 4	1	1	0	0	0
94. 8.11	1	1	0	0	0
94. 8.17	1	1	0	0	0
94. 8.19	1	1	0	0	0
94. 8.21	1	1	0	0	0
94. 8.23	4	3	0	1	0
94. 8.26	1	1	0	0	0
94. 8.27	2	2	0	0	0
94. 8.29	1	1	0	0	0
94. 9.13	1	0	1	0	0
94. 9.19	2	0	2	0	0
94. 9.20	2	0	2	0	0
Total	213	125	6	81	1

Hospital visit duration (including the hospitalization)

Lower limit (≥)	Upper limit (<)	Frequency
0	5	135
5	10	35
10	15	21
15	20	14
20	25	6
25	30	3
30	35	2
35	40	4
40	45	0
45	50	0
50	55	2
55	60	5
60	65	3
65	70	0
70	75	1
75	80	1
80	85	2
85	90	0
90	95	0
95	100	0
	Total	234

Hospitalization duration

Mean	9.8
Standard deviation	14.8
Standard error	2.0
The number of cases	55
Minimum value	1.0
Maximum value	84.0
The number of missing values	209

Regular hospital visit duration

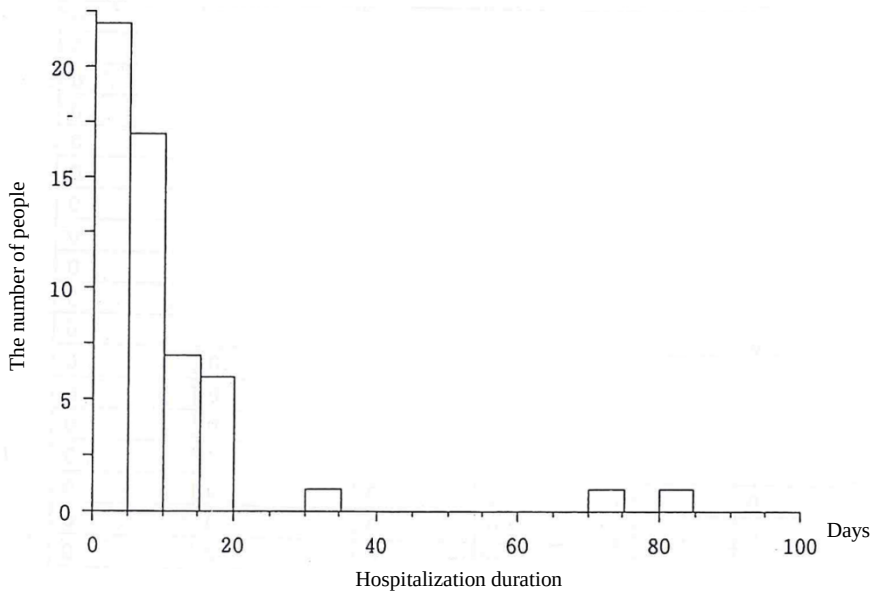
Mean	9.6
Standard deviation	15.8
Standard error	1.0
The number of cases	234
Minimum value	1.0
Maximum value	84.0
The number of missing values	30

Document 4

Hospitalization duration and gross outcomes

Lower limit (≥)	Upper limit (<)	The total number of people	Death	Cure	Regular hospital visits	Unknown	Discontinuation because of changing to another medical facility	Hospitalization
0	5	22	2	14	2	4	0	0
5	10	17	0	15	0	1	1	0
10	15	7	0	7	0	0	0	0
15	20	6	0	2	4	0	0	0
20	25	0	0	0	0	0	0	0
25	30	0	0	0	0	0	0	0
30	35	1	0	0	1	0	0	0
35	40	0	0	0	0	0	0	0
40	45	0	0	0	0	0	0	0
45	50	0	0	0	0	0	0	0
50	55	0	0	0	0	0	0	0
55	60	0	0	0	0	0	0	0
60	65	0	0	0	0	0	0	0
65	70	0	0	0	0	0	0	0
70	75	1	0	1	0	0	0	0
75	80	0	0	0	0	0	0	0
80	85	1	0	0	0	0	0	1
85	90	0	0	0	0	0	0	0
90	95	0	0	0	0	0	0	0
95	100	0	0	0	0	0	0	0
	Total	55	2	39	7	5	1	1

Histogram



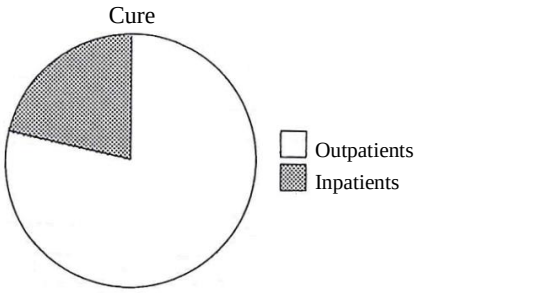
Gross outcomes and addresses of people who consulted with hospitals

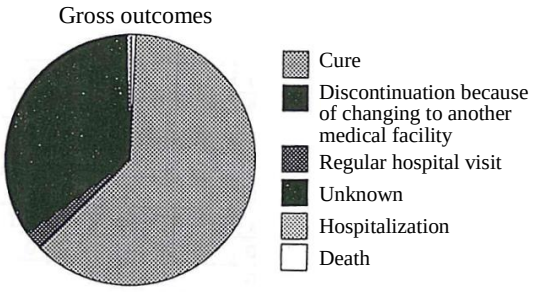
Sex (outpatient/inpatient)

	The total frequency	Females	Males
Outpatients	208	90	118
Inpatients	56	27	29
Total	264	117	147

Gross outcomes

	Frequency	Percent
Death	2	0.76
Cure	163	61.7
Regular hospital visit	7	2.7
Unknown	90	34.1
Discontinuation because of changing to another medical facility	1	0.38
Hospitalization	1	0.38
Total	264	100.0





	The total number of people	Death	Cure	Regular hospital visits	Unknown	Discontinuation because of changing to another medical facility	Hospitalization
Kitafukashi	180	2	106	6	64	1	1
Omura	2	0	2	0	0	0	0
Joto	2	0	2	0	0	0	0
Sawamura	3	0	2	0	1	0	0
Asama Onsen	1	0	1	0	0	0	0
Nagisa	1	0	1	0	0	0	0
Motomachi	2	0	2	0	0	0	0
Okadamatsuoka	1	0	1	0	0	0	0
Yoshikawanomizo	1	0	1	0	0	0	0
Kaichi	29	0	20	0	9	0	0
Asahimachi	17	0	11	0	6	0	0
Shiojirimachi	1	0	0	0	1	0	0
Metoba	2	0	2	0	0	0	0
Kiri	1	0	0	0	1	0	0
Yokota	1	0	0	0	1	0	0
Arigasaki	2	0	2	0	0	0	0
Mizukuma	1	0	0	0	1	0	0
Misuzu	1	0	1	0	0	0	0
Agata	1	0	0	0	1	0	0
Marunouchi	1	0	0	0	1	0	0
Chuo	4	0	0	0	4	0	0
Kotobukishirasebuchi	1	0	1	0	0	0	0
Hotakamachi	1	0	1	0	0	0	0
Tsukama	1	0	1	0	0	0	0
Satoyamabe	1	0	1	0	0	0	0
Igawajo	2	0	2	0	0	0	0
Akashinamachi	1	0	1	0	0	0	0
Miyata	1	0	0	1	0	0	0
Nakajo	1	0	1	0	0	0	0
Nomizo	1	0	1	0	0	0	0
Total	264	2	163	7	90	1	1

Subjective symptoms and findings in people who consulted with hospitals

Headache

	The total number of people	Females	Males
Presence	60	34	26
Absence	201	83	118
Total	261	117	144

Fatigue

	The total number of people	Females	Males
Presence	33	18	15
Absence	228	99	129
Total	261	117	144

Heat sensation

	The total number of people	Females	Males
Presence	16	8	8
Absence	245	109	136
Total	261	117	144

Reduced visual acuity

	The total number of people	Females	Males
Presence	124	54	70
Absence	123	57	66
Total	247	111	136

Visual field abnormalities

	The total number of people	Females	Males
Presence	39	17	22
Absence	44	19	25
Total	83	36	47

Subjective sensory abnormalities

	The total number of people	Females	Males
Presence	20	13	7
Absence	200	84	116
Total	220	97	123

Electroencephalogram abnormalities

	The total number of people	Females	Males
Presence	1	0	1
Absence	7	5	2
Total	8	5	3

Electrocardiographic abnormalities

	The total number of people	Females	Males
Presence	5	1	4
Absence	34	14	20
Total	39	15	24

- Supraventricular arrhythmia, T wave flattering (V5–V6)
- Standstill
- Atrial fibrillation
- 2:1 AV block
- Ventricular extrasystole

Abnormal tendon reflex

	The total number of people	Females	Males
Presence	2	0	2
Absence	16	11	5
Total	18	11	7

*Reduction in the patellar reflex and Achilles tendon reflex

Chest X-ray abnormalities

	The total number of people	Females	Males
Presence	1	0	1
Absence	49	24	25
Total	50	24	26

Headache

Frequency distribution: Duration of headache (days)

Lower limit (≥)	Upper limit (<)	Frequency
1	9	50
9	18	5
18	26	2
26	34	1
34	42	0
42	51	0
51	59	0
59	67	1
67	76	0
76	84	1
	Total	60

Descriptive statistics - Continuous variables

Duration of headache (days)

Mean	7.0
Standard deviation	13.8
Standard error	1.8
The number of cases	60
Minimum value	1.0
Maximum value	84.0
The number of missing values	204

Scheffe: ChE%
Effect: headache
Significance level: 5%

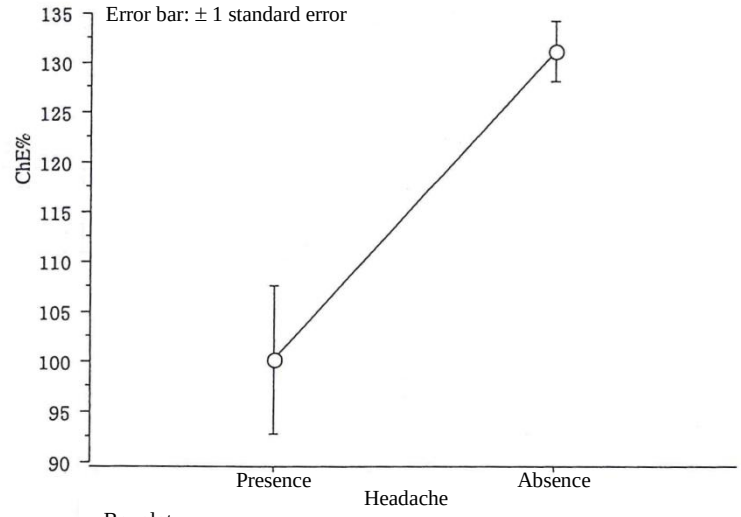
	Difference in the mean value	Critical value	p value	
Presence/ absence	-30.9	8.4	<0.0001	S

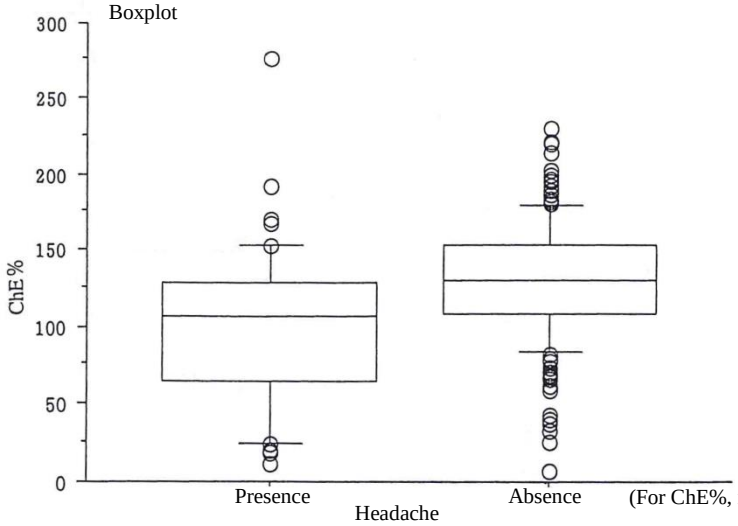
Frequency distribution: Headache
Division variable: Degree of reduction in ChE

	The total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	60	12	10	30
Absence	201	6	23	139
Total	261	18	33	169

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

Presence or absence of headache and ChE% value





(For ChE%, refer to Document 16.)

Fatigue

Frequency distribution: Duration of fatigue (days)

Lower limit (≥)	Upper limit (<)	Frequency
1	9	22
9	18	3
18	26	3
26	34	1
34	42	1
42	51	0
51	59	0
59	67	1
67	76	0
76	84	1
	Total	32

Descriptive statistics - Continuous variables

	Duration of fatigue
Mean	12.2
Standard deviation	18.7
Standard error	3.3
The number of cases	32
Minimum value	1.0
Maximum value	84.0
The number of missing values	232

Frequency distribution: Fatigue
Division variable: Degree of reduction in ChE

	The total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	33	14	10	8
Absence	228	4	23	161
Total	261	18	33	169

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

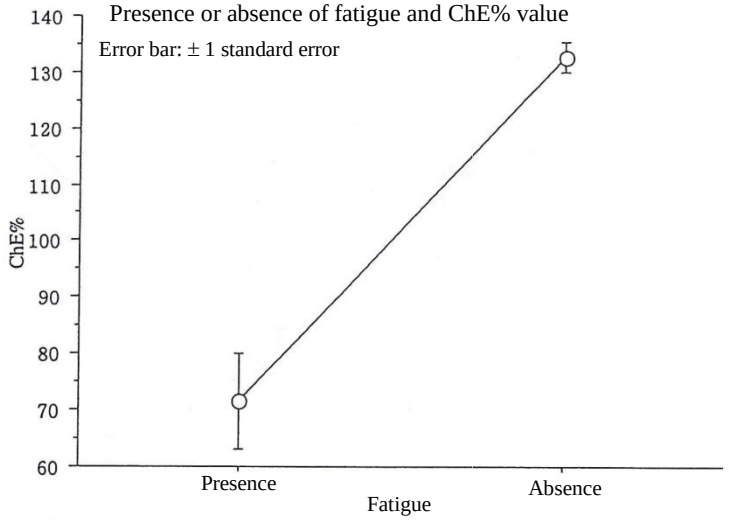
Basic statistical value: ChE%
Effect: Fatigue

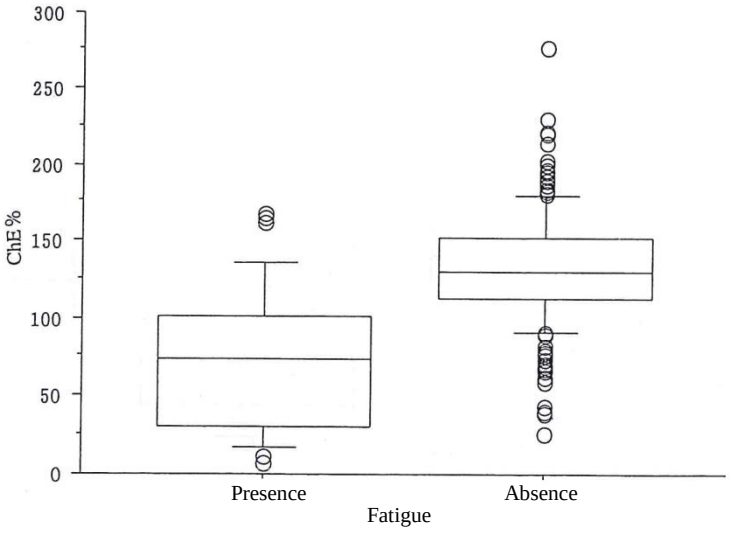
	The number of cases	Mean value	Standard deviation	Standard error
Presence	32	71.6	47.6	8.4
Absence	188	132.7	37.1	2.7

Scheffe: ChE%
Effect: Fatigue
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Presence/absence	−61.1	14.6	<0.0001	S

Presence or absence of fatigue and ChE% value





Heat sensation

Frequency distribution:
Duration of heat sensation (days)

Lower limit (≥)	Upper limit (<)	Frequency
1	9	14
9	18	3
18	26	0
26	34	0
34	42	0
42	51	0
51	59	0
59	67	0
67	76	0
76	84	1
	Total	18

Descriptive statistics -
Continuous variables

	Duration of heat sensation
Mean	9.1
Standard deviation	19.4
Standard error	4.6
The number of cases	18
Minimum value	1.0
Maximum value	84.0
The number of missing values	246

Frequency distribution: Heat sensation
Division variable: Degree of reduction in ChE

	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	16	9	3	4
Absence	245	9	30	165
Total	261	18	33	169

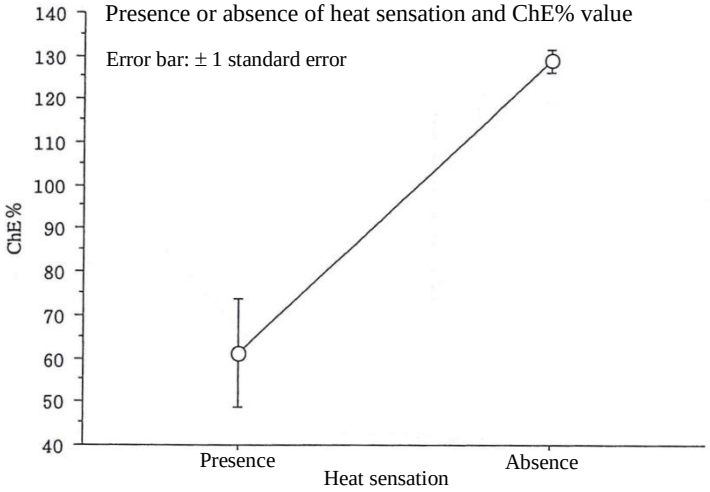
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

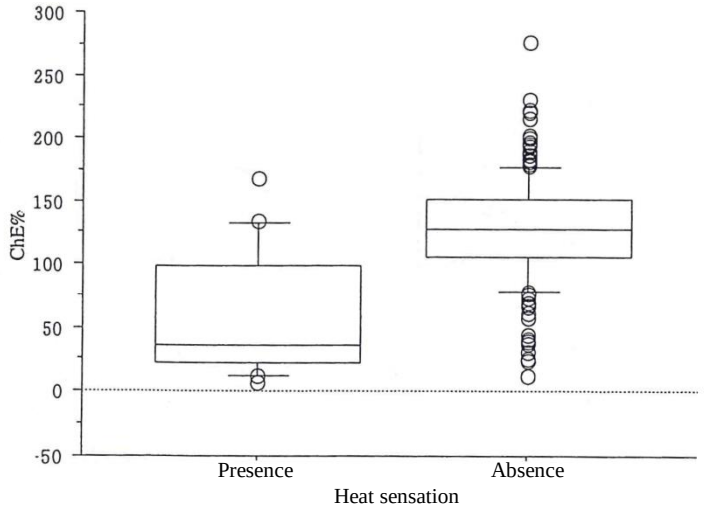
Basic statistical value: ChE%
Effect: Heat sensation

	The number of cases	Mean value	Standard deviation	Standard error
Presence	16	61.3	49.6	12.4
Absence	204	128.7	40.0	2.8

Scheffe: ChE%
Effect: Heat sensation
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Presence/absence	−67.5	20.8	<0.0001	S





Visual field abnormalities

Frequency distribution: Visual field abnormalities
Division variable: Degree of reduction in ChE

	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	39	10	10	18
Absence	44	5	3	30
Total	83	15	13	48

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

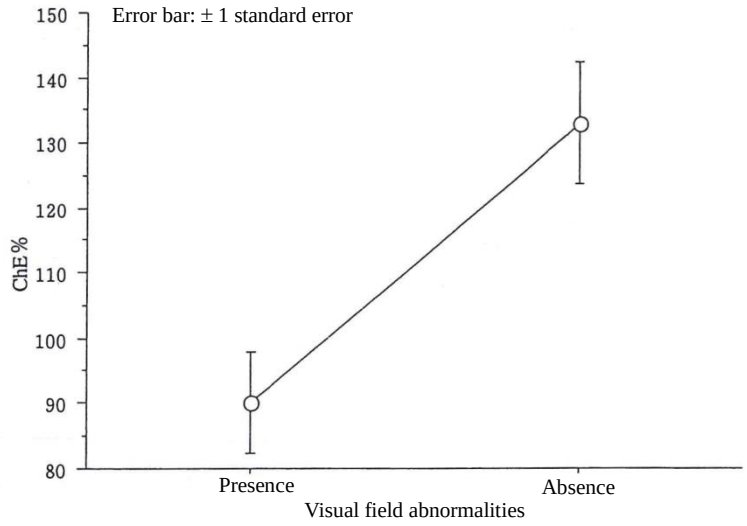
Basic statistical value: ChE%
Effect: Visual field abnormalities

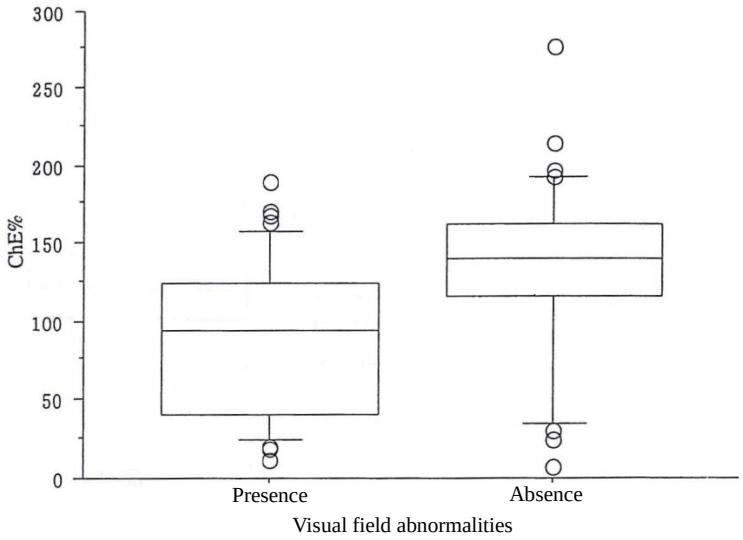
	The number of cases	Mean value	Standard deviation	Standard error
Presence	38	90.1	47.5	7.7
Absence	38	132.9	57.1	9.3

Scheffe: ChE%
Effect: Visual field abnormalities
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Presence/absence	−42.8	24.0	0.0007	S

Presence or absence of visual field abnormalities and ChE% value





Reduced visual acuity

Frequency distribution: Reduced visual acuity
Division variable: Degree of reduction in ChE

	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	124	10	26	82
Absence	123	7	7	77
Total	247	17	33	159

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

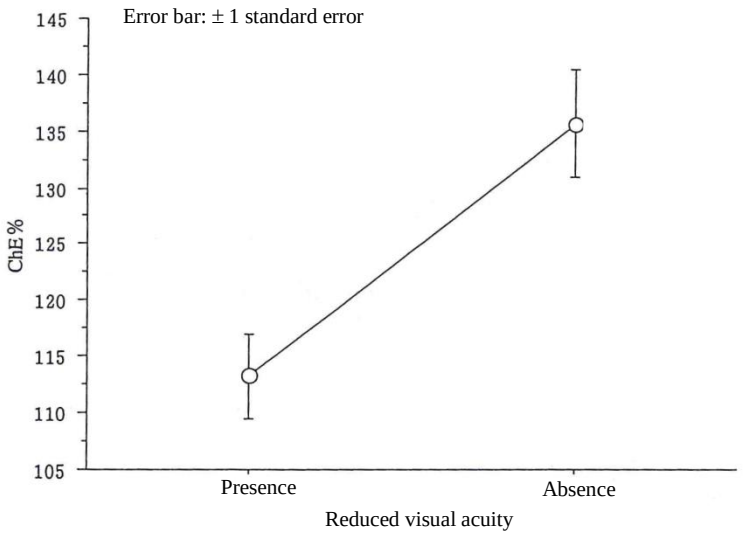
Basic statistical value: ChE%
Effect: Reduced visual acuity

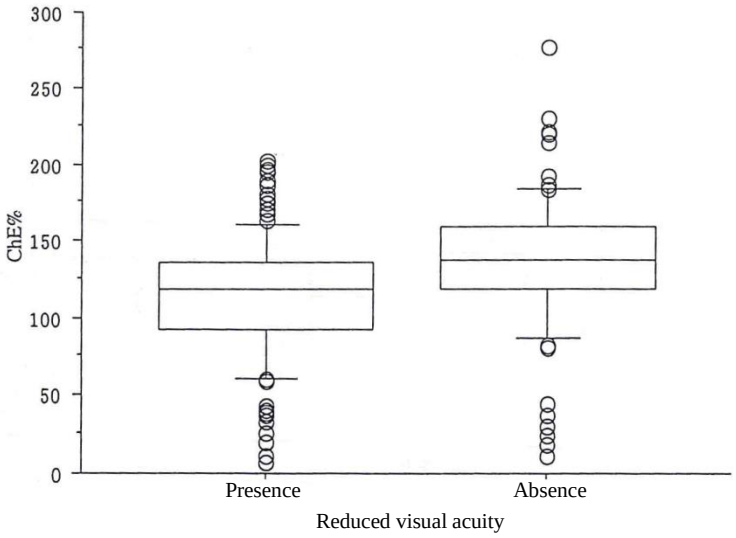
	The number of cases	Mean value	Standard deviation	Standard error
Presence	118	113.2	40.4	3.7
Absence	91	135.6	45.6	4.8

Scheffe: ChE%
Effect: Reduced visual acuity
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Presence/absence	−22.4	11.8	0.0002	S

Presence or absence of reduced visual acuity and ChE% value





Subjective sensory abnormalities

Frequency distribution: Subjective sensory abnormalities
Division variable: Degree of reduction in ChE

	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	20	6	3	7
Absence	200	5	23	139
Total	220	11	26	146

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

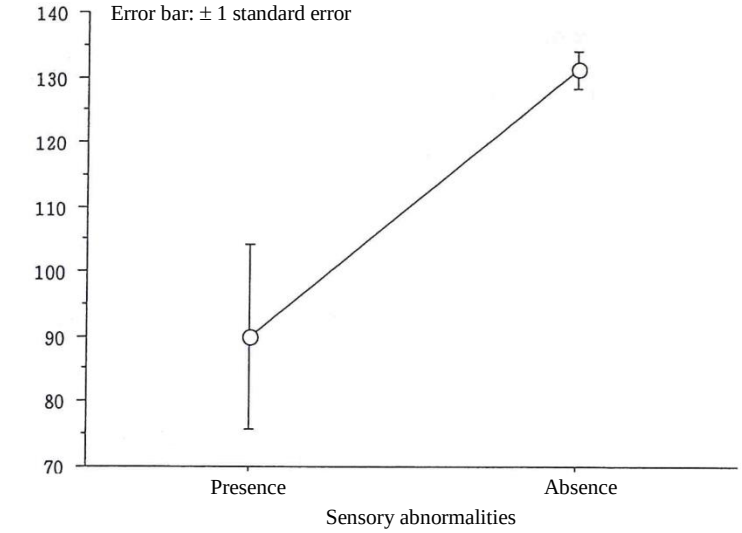
Basic statistical value: ChE%
Effect: Subjective sensory abnormalities

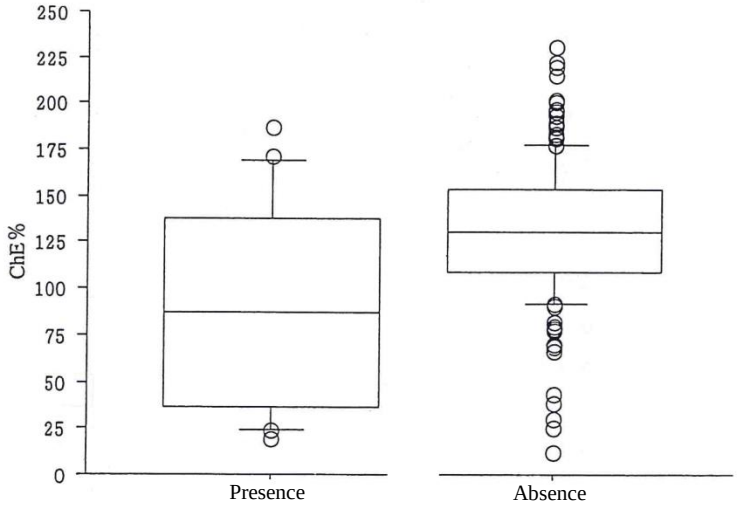
	The number of cases	Mean value	Standard deviation	Standard error
Presence	16	90.0	56.3	14.1
Absence	167	131.0	37.2	2.9

Scheffe: ChE%
Effect: Subjective sensory abnormalitie
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Presence/absence	−41.1	20.2	‹0.0001	S

Presence or absence of subjective sensory abnormalities and ChE% value





Electrocardiographic abnormalities

Frequency distribution: Electrocardiographic abnormalities
Division variable: Degree of reduction in ChE

	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
Presence	5	4	0	1
Absence	34	13	12	9
Total	39	17	12	10

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

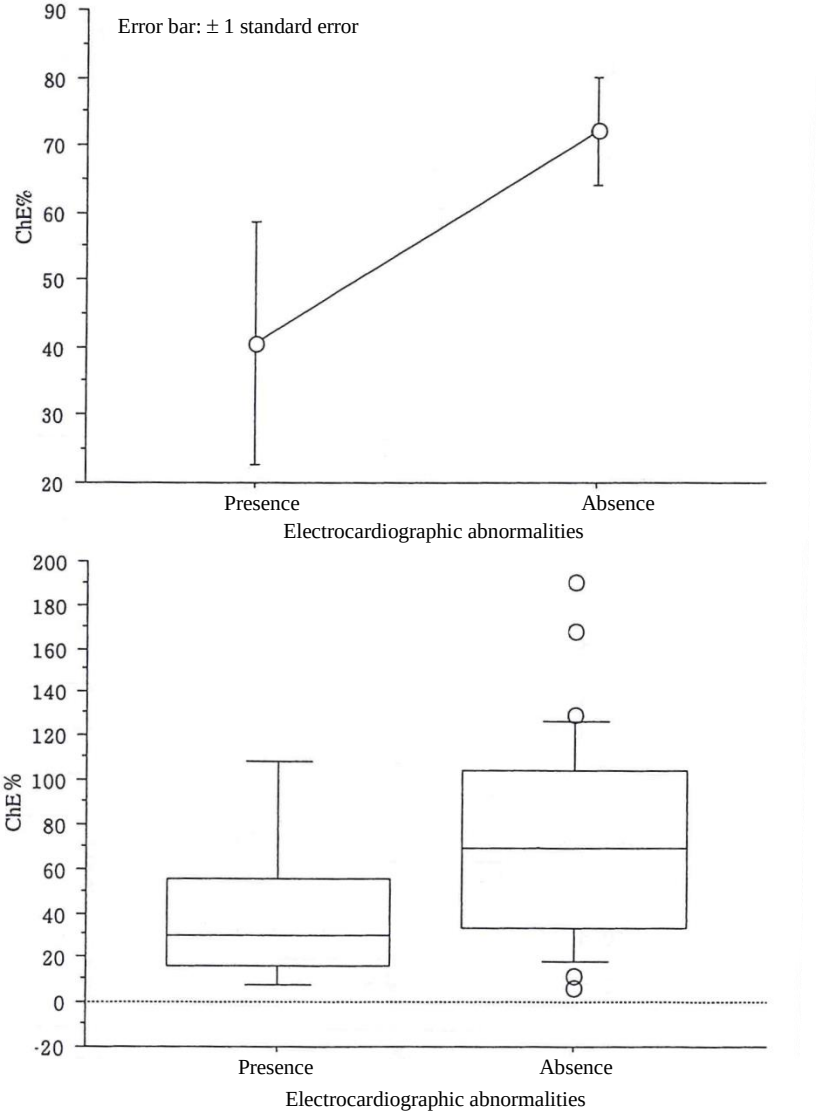
Basic statistical value: ChE%
Effect: Electrocardiographic abnormalities

	The number of cases	Mean value	Standard deviation	Standard error
Presence	5	40.7	39.8	17.8
Absence	34	72.0	46.1	7.9

Scheffe: ChE%
Effect: Electrocardiographic abnormalities
Significance level: 5%

	Difference in the mean value	Critical value	p value
Presence/absence	−31.3	44.1	0.1592

Presence or absence of electrocardiographic abnormalities and ChE% value



Pupil diameter (1)

Frequency distribution of the pupil diameter and the degree of reduction in plasma cholinesterase

Frequency distribution: Pupil diameter
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
0.0	0.5	0	0	0	0
0.5	1.0	21	5	6	10
1.0	1.5	87	11	18	56
1.5	2.0	6	0	0	3
2.0	2.5	32	1	4	25
2.5	3.0	0	0	0	0
3.0	3.5	5	0	0	5
3.5	4.0	1	0	0	0
4.0	4.5	40	0	1	31
4.5	5.0	27	0	1	10
	Total	219	17	30	140

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

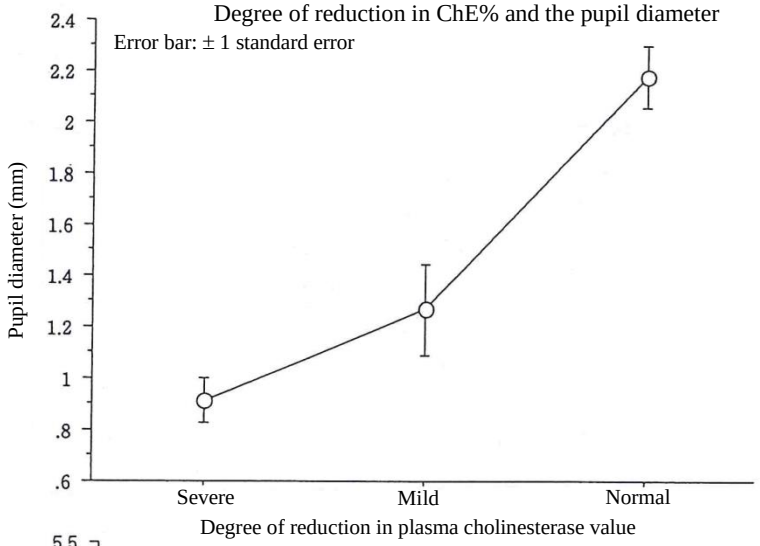
Basic statistical value: Pupil diameter
Effect: Degree of reduction in ChE

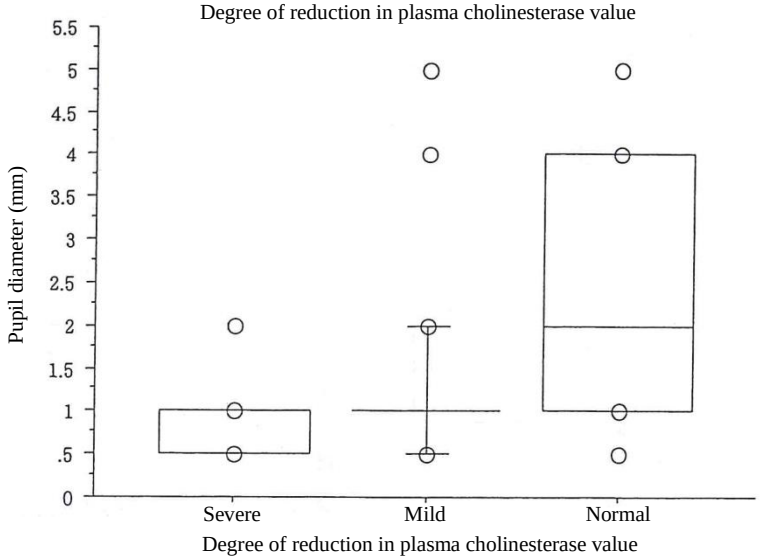
	The number of cases	Mean value	Standard deviation	Standard error
Severe	17	9.1E-1	3.6E-1	8.8E-2
Mild	30	1.3	9.9E-1	1.8E-1
Normal	140	2.2	1.5	1.2E-1

Scheffe: Pupil diameter
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Severe/mild	−3.5E-1	9.9E-1	0.6793	
Severe/normal	−1.3	8.4E-1	0.0013	S
Mild/normal	−9.1E-1	6.6E-1	0.0037	S

Degree of reduction in ChE% and the pupil diameter





Pupil diameter (2)

Classification of constricted pupil according to the pupil diameter (mm)

Marked: 0.0–1.0
Intermediate: 1.0–2.0
Mild: 2.0–4.0
Normal: 4.0 or more

Frequency distribution:
Degree of constricted pupil

	Frequency
Marked	21
Intermediate	93
Mild	38
Normal	67
Total	219

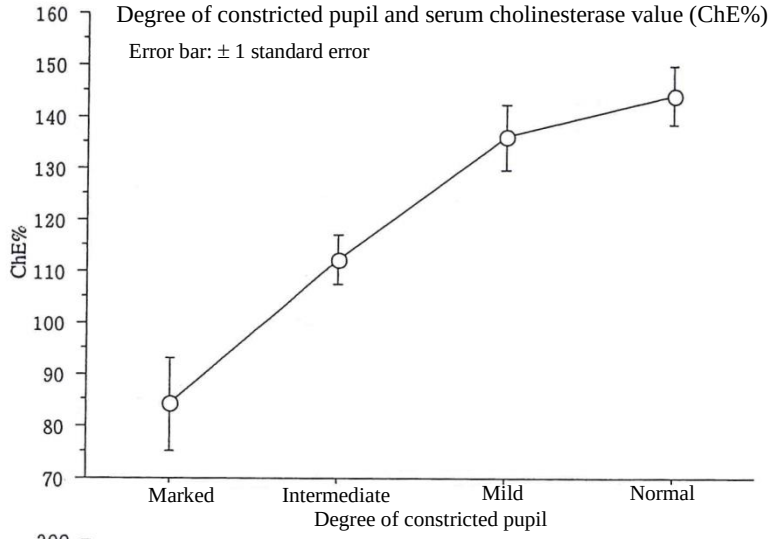
Basic statistical value: ChE%
Effect: Degree of constricted pupil

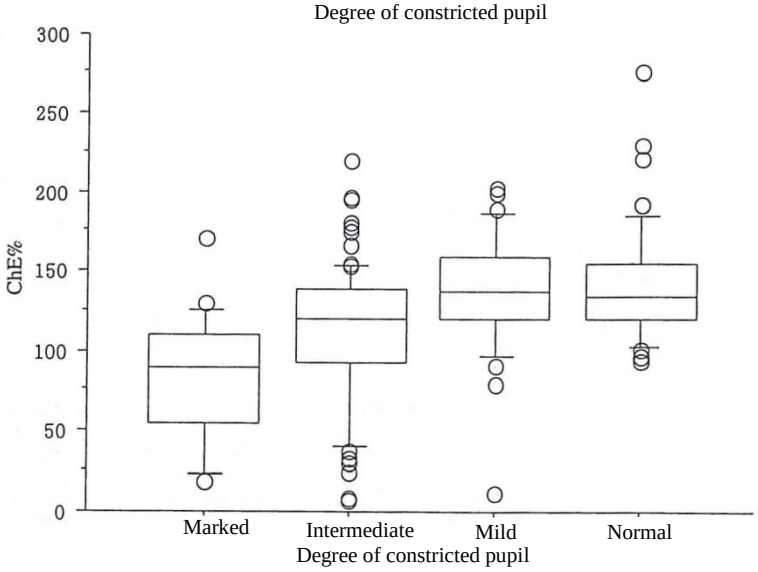
	The number of cases	Mean value	Standard deviation	Standard error
Marked	21	84.3	40.7	8.9
Intermediate	88	112.2	43.2	4.6
Mild	35	135.9	36.9	6.2
Normal	43	143.9	37.1	5.7

Scheffe: ChE%
Effect: Degree of constricted pupil
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Marked, intermediate	−27.9	27.7	0.0479	S
Marked, mild	−51.7	31.5	0.0001	S
Marked, normal	−59.6	30.4	‹0.0001	S
Intermediate, mild	−23.8	22.8	0.0375	S
Intermediate, normal	−31.7	21.2	0.0007	S
Mild, normal	−7.9	26.0	0.8637	

Degree of constricted pupil and serum cholinesterase value (ChE%)



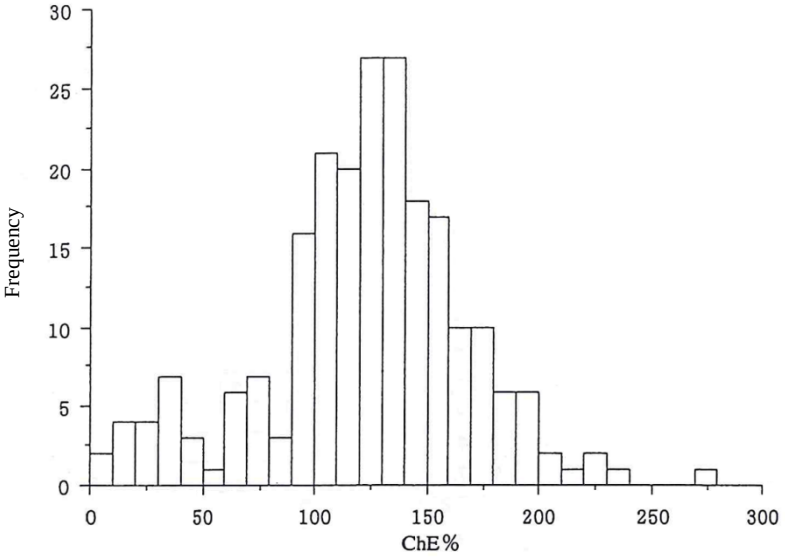


Plasma cholinesterase values (1)

Frequency distribution: ChE%

Lower limit (≥)	Upper limit (<)	The frequency
0	10	2
10	20	4
20	30	4
30	40	7
40	50	3
50	60	1
60	70	6
70	80	7
80	90	3
90	100	16
100	110	21
110	120	20
120	130	27
130	140	27
140	150	18
150	160	17
160	170	10
170	180	10
180	190	6
190	200	6
200	210	2
210	220	1
220	230	2
230	240	1
240	250	0
250	260	0
260	270	0
270	280	1
280	290	0
290	300	0
	Total	222

Histogram



Frequency distribution: Degree of reduction in ChE

	The frequency
Severe	20
Mild	33
Normal	169
Total	222

Classification of the severity according to plasma cholinesterase value

	ChE%
Normal	100% or higher
Mild	50%–100%
Severe	less than 50%

As the normal range differs among facilities, it was expressed as ChE% = ChE value / facility normal lower limit × 100.

Plasma cholinesterase values (2)

Degree of reduction in plasma ChE at initial examination dates

		Severe	Mild	Normal	Total (the number of people)
	Total	20	33	169	222
Initial examination date	94. 6.27	2	0	0	2
	94. 6.28	17	26	78	121
	94. 6.29	0	6	37	43
	94. 6.30	0	0	27	27
	94. 7. 1	1	0	1	2
	94. 7. 2	0	0	1	1
	94. 7. 3	0	0	1	1
	94. 7. 4	0	1	6	7
	94. 7. 5	0	0	8	8
	94. 7. 6	0	0	3	3
	94. 7. 8	0	0	2	2
	94. 7.12	0	0	1	1
	94. 7.13	0	0	1	1
	94. 7.15	0	0	1	1
	94. 7.27	0	0	1	1
	94. 8. 4	0	0	1	1

Degree of reduction in cholinesterase value and gross outcomes, initial examination date

			Death	Cure	Regular hospital visit	Unknown	Discontinuation because of changing to another medical facility	Hospitalization	Total (the number of people)
	Total		2	163	7	90	1	1	264
Initial examination date	94. 6.27,	Severe	0	1	0	1	0	0	2
	94. 6.28,	Severe	1	9	5	0	1	1	17
		Mild	0	18	0	8	0	0	26
		Normal	0	31	1	46	0	0	78
	94. 6.29,	Mild	0	5	0	1	0	0	6
		Normal	0	25	0	12	0	0	37
	94. 6.30,	Normal	0	23	0	4	0	0	27
	94. 7. 1,	Severe	0	1	0	0	0	0	1
		Normal	0	1	0	0	0	0	1
	94. 7. 2,	Normal	0	1	0	0	0	0	1
	94. 7. 3,	Normal	0	1	0	0	0	0	1
	94. 7. 4,	Mild	0	0	0	1	0	0	1
		Normal	0	6	0	0	0	0	6
	94. 7. 5,	Normal	0	8	0	0	0	0	8
	94. 7. 6,	Normal	0	3	0	0	0	0	3
	94. 7. 8,	Normal	0	2	0	0	0	0	2
	94. 7.12,	Normal	0	1	0	0	0	0	1
	94. 7.13,	Normal	0	0	0	1	0	0	1
	94. 7.15,	Normal	0	1	0	0	0	0	1
	94. 7.27,	Normal	0	1	0	0	0	0	1
	94. 8. 4,	Normal	0	1	0	0	0	0	1

The total result is not identical to the sum of the individual cells because of the missing values of the division variables.

Plasma cholinesterase values (3)

Distribution of plasma cholinesterase value (ChE%) at the initial examination date

Lower limit (≥)	0	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260	270	
Upper limit (<)	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260	270	280	Total
Total	2	4	4	7	3	1	6	7	3	16	21	20	27	27	18	17	10	10	6	6	2	1	2	1	0	0	0	1	222
94. 6.27	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
94. 6.28	2	2	4	7	2	1	6	6	2	11	15	13	14	11	9	4	2	4	1	3	0	1	1	0	0	0	0	0	121
94. 6.29	0	0	0	0	0	0	0	1	1	4	1	1	6	7	6	6	4	3	2	0	0	0	0	1	0	0	0	0	43
94. 6.30	0	0	0	0	0	0	0	0	0	0	3	3	4	4	1	3	2	1	1	2	2	0	1	0	0	0	0	0	27
94. 7. 1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
94. 7. 2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
94. 7. 3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
94. 7. 4	0	0	0	0	0	0	0	0	0	1	0	0	1	3	0	0	0	0	1	0	0	0	0	0	0	0	0	1	7
94. 7. 5	0	0	0	0	0	0	0	0	0	0	1	0	1	0	2	1	2	1	0	0	0	0	0	0	0	0	0	0	8
94. 7. 6	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	3
94. 7. 8	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
94. 7.12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
94. 7.13	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
94. 7.15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1
94. 7.27	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
94. 8. 4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1

Transition of the erythrocyte true cholinesterase values (1)

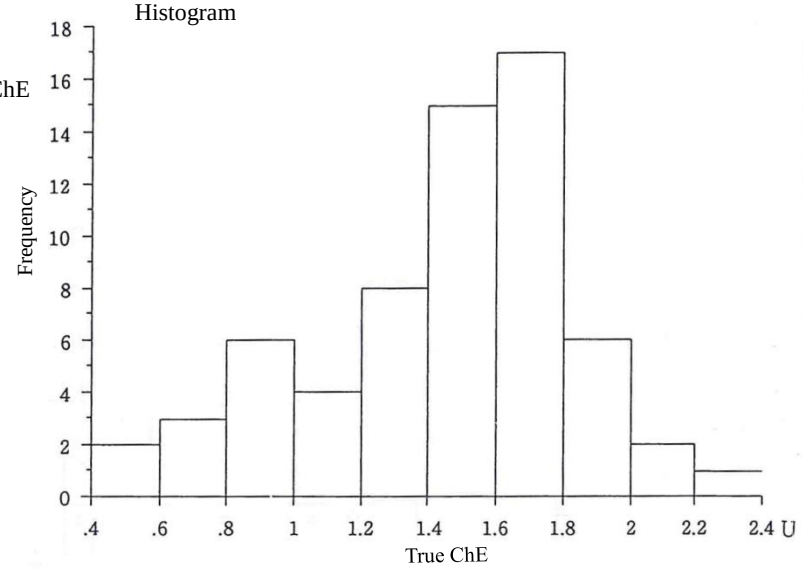
True (erythrocyte) cholinesterase
Criterion value: 1.2–2.0 U
Examination: Diagnostic Division, Otsuka Pharmaceutical Co., Ltd., Otsuka Assay Laboratories

Date of examination: July 23, 1994

Frequency distribution: True ChE

Lower limit (≥)	Upper limit (<)	Frequency
0.4	0.6	2
0.6	0.8	3
0.8	1.0	6
1.0	1.2	4
1.2	1.4	8
1.4	1.6	15
1.6	1.8	17
1.8	2.0	6
2.0	2.2	2
2.2	2.4	1
	Total	64

Histogram

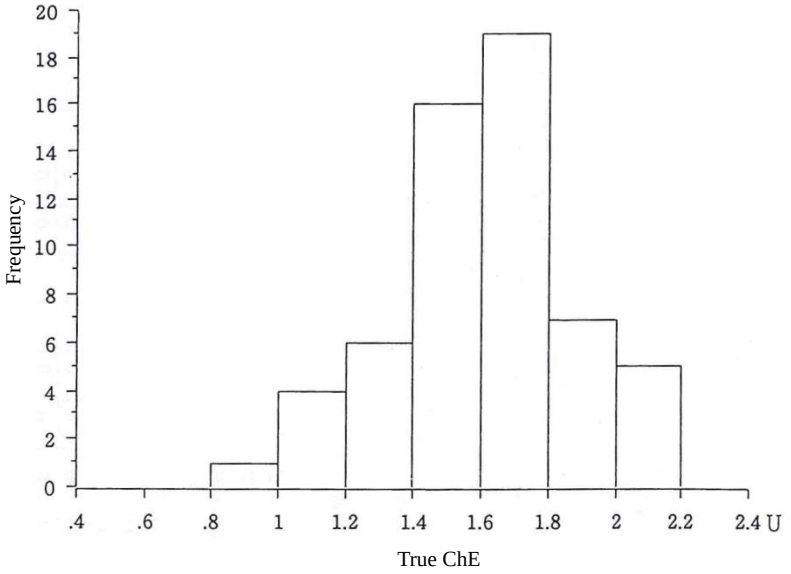


Date of examination: August 20, 1994

Frequency distribution: True ChE

Lower limit (≥)	Upper limit (<)	Frequency
0.8	1.0	1
1.0	1.2	4
1.2	1.4	6
1.4	1.6	16
1.6	1.8	19
1.8	2.0	7
2.0	2.2	5
2.2	2.4	0
2.4	2.6	0
2.6	2.8	0
	Total	58

Histogram



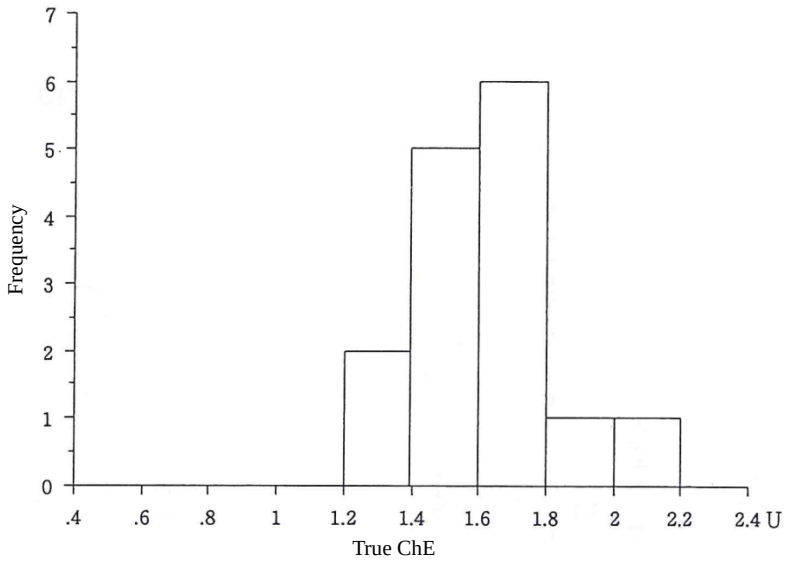
Transition of the erythrocyte true cholinesterase values (2)

Date of examination:
September 29, 1994

Frequency distribution: True ChE

Lower limit (≥)	Upper limit (<)	Frequency
0.4	0.6	0
0.6	0.8	0
0.8	1.0	0
1.0	1.2	0
1.2	1.4	2
1.4	1.6	5
1.6	1.8	6
1.8	2.0	1
2.0	2.2	1
2.2	2.4	0
	Total	15

Histogram



Transition of the erythrocyte true cholinesterase values (3)

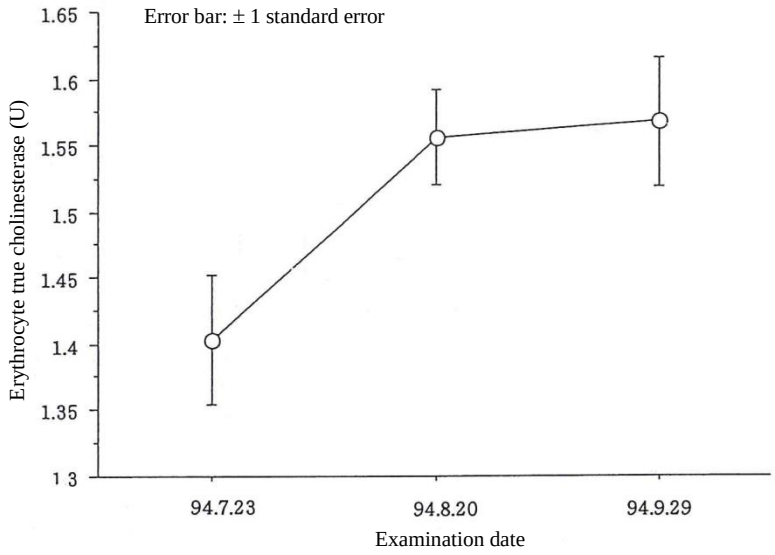
Basic statistical value: True ChE transition
Effect: Transition of category true ChE

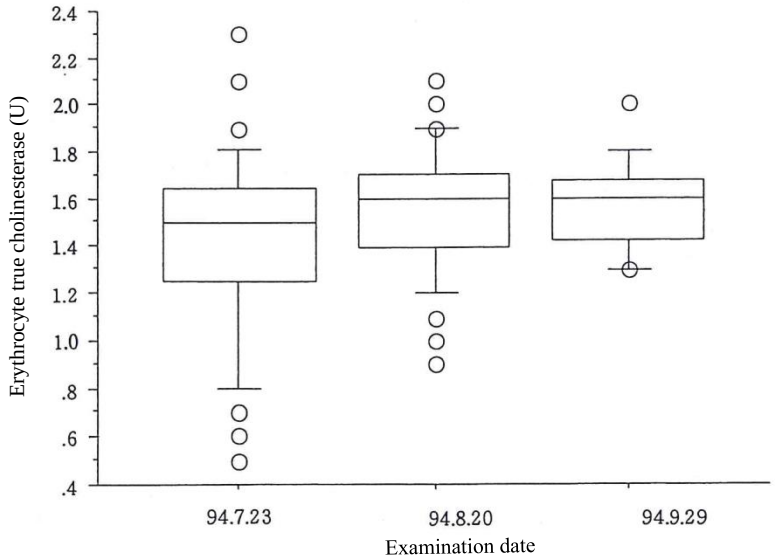
	The number of cases	Mean value	Standard deviation	Standard error
July 23	64	1.403	0.398	0.050
August 20	58	1.555	0.270	0.035
September 29	15	1.567	0.188	0.048

Scheffe: True ChE transition
Effect: Transition of category true ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value	
July 23–August 20	−0.152	0.148	0.0429	S
July 23–September 29	−0.164	0.235	0.2291	
August 20–September 29	−0.011	0.237	0.9928	

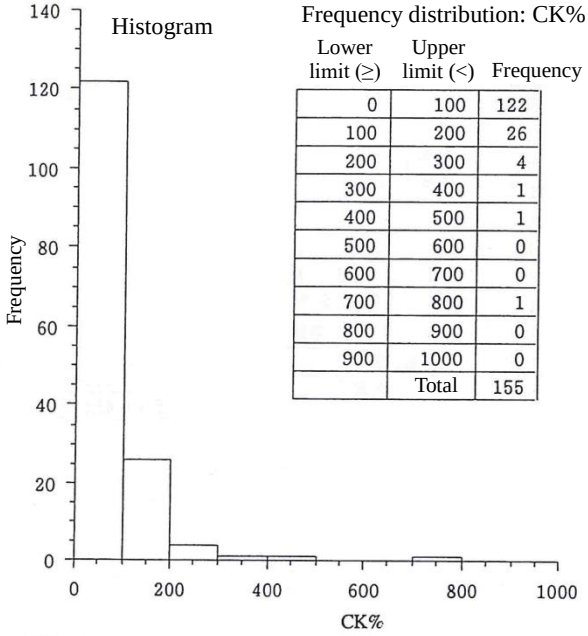
Variation over time of true cholinesterase value





Correlation between serum CK and plasma ChE decrease

As the criterion value of CK differs between the sexes and among facilities, it was expressed as CK% = case CK value / facility normal upper limit × 100



Frequency distribution: CK%

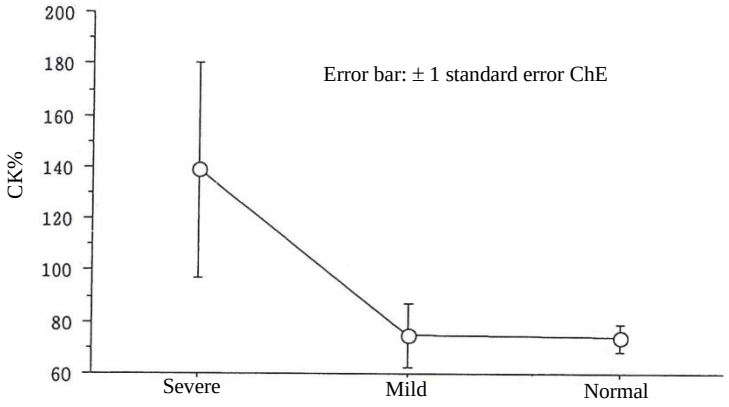
Lower limit (≥)	Upper limit (<)	Frequency
0	100	122
100	200	26
200	300	4
300	400	1
400	500	1
500	600	0
600	700	0
700	800	1
800	900	0
900	1000	0
	Total	155

Basic statistical value: CK%
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	18	138.9	175.8	41.4
Mild	24	74.9	59.4	12.1
Normal	112	73.7	56.1	5.3

Scheffe: CK%
Effect: Degree of reduction in ChE
Significance level: 5%

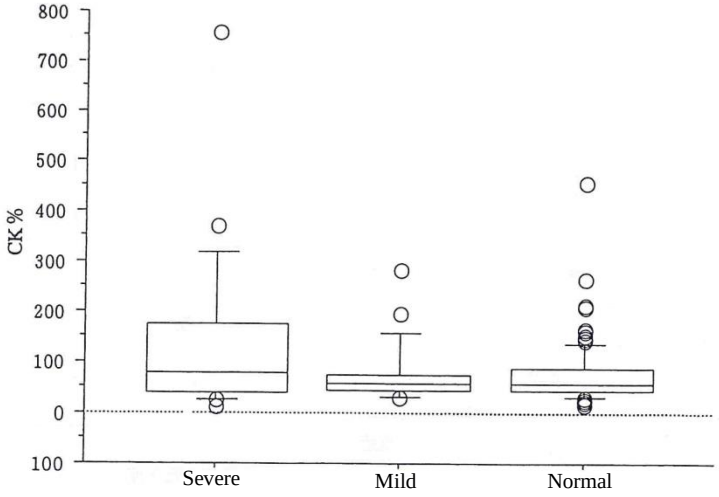
	Difference in the mean value	Critical value	p value	
Severe, mild	64.0	61.4	0.0386	S
Severe, normal	65.2	50.0	0.0065	S
Mild, normal	1.2	44.3	0.9977	



Divided groups according to the degree of reduction in plasma cholinesterase value

Descriptive statistics
Continuous variables

	CK%
Mean	82
Standard deviation	82
Standard error	7
The number of cases	155
Minimum value	14
Maximum value	755
The number of missing values	109



Correlation between erythrocyte count at the initial examination ($\times 10^4/mm^3$) and plasma ChE

Frequency distribution: RBC
Division variables: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
349	373	4	0	2	2
373	397	8	0	2	6
397	421	12	0	1	11
421	445	24	4	5	15
445	469	34	5	5	23
469	493	34	3	9	22
493	517	30	3	2	24
517	541	18	2	1	15
541	565	6	0	2	4
565	589	3	1	0	2
	Total	173	18	29	124

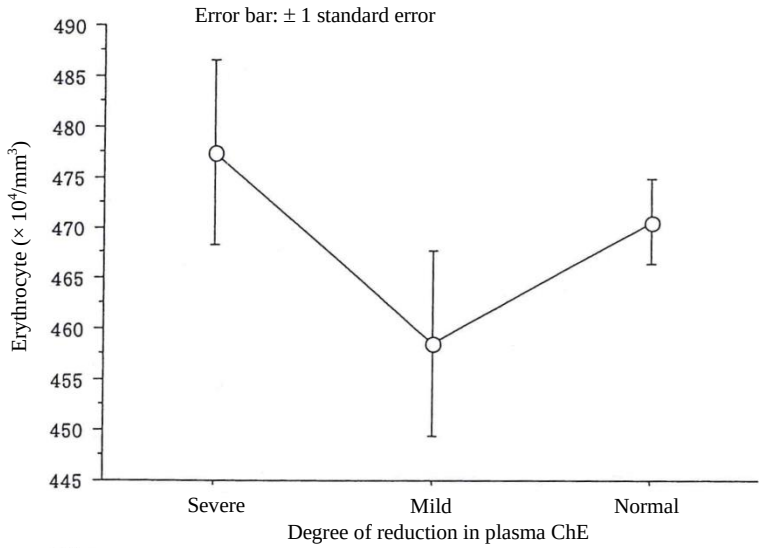
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

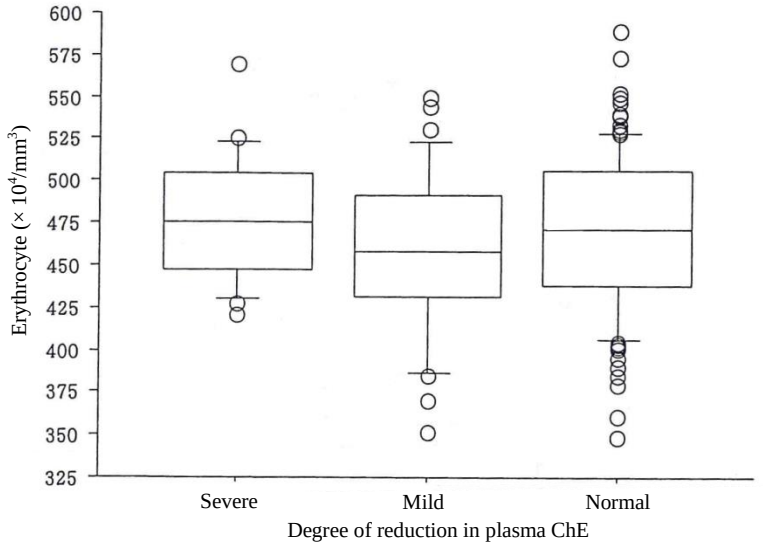
Basic statistical value: RBC
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	18	477	39	9
Mild	29	459	49	9
Normal	124	471	46	4

Scheffe: RBC
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	18.9	34.2	0.3977
Severe, normal	6.8	28.8	0.8414
Mild, normal	−12.0	23.5	0.4526





Correlation between leukocyte count (/mm_3) at the initial examination and plasma ChE

Frequency distribution: WBC
Division variables: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
2840	4396	19	1	2	15
4396	5952	48	0	6	41
5952	7508	55	3	10	42
7508	9064	26	0	6	20
9064	10620	15	5	5	5
10620	12176	4	3	0	1
12176	13732	0	0	0	0
13732	15288	3	3	0	0
15288	16844	2	2	0	0
16844	18400	1	1	0	0
	Total	173	18	29	124

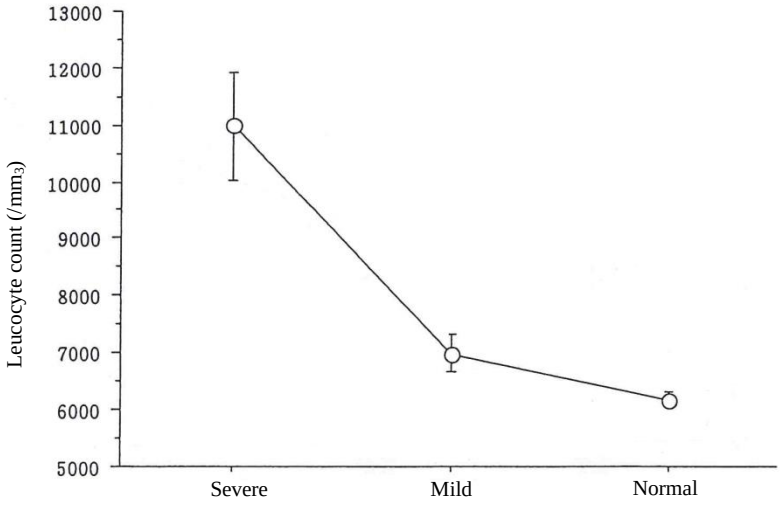
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

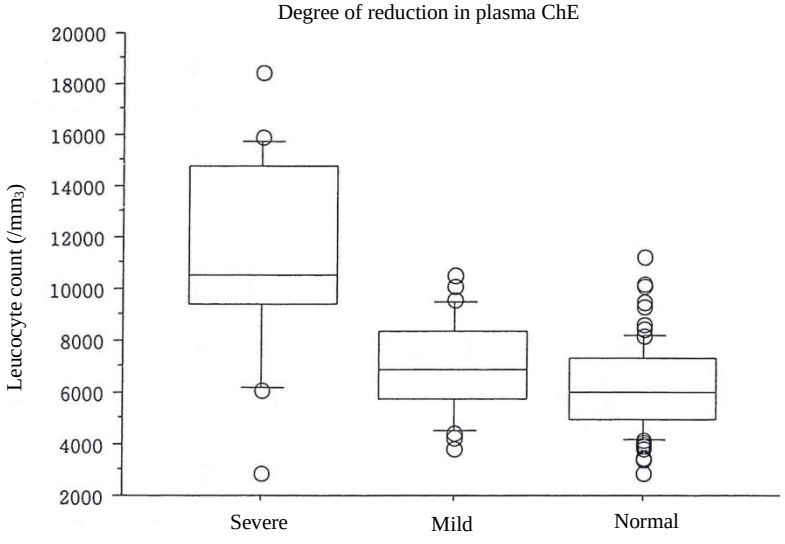
Basic statistical value: WBC
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	18	10972	4075	961
Mild	29	6986	1781	331
Normal	124	6175	1590	143

Scheffe: WBC
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Severe, mild	3986	1493	<0.0001	S
Severe, normal	4797	1255	<0.0001	S
Mild, normal	811	1027	0.1523	





Correlation between serum BUN (mg/dL) at the initial examination and plasma ChE decrease

Frequency distribution: BUN
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
5.8	8.2	10	0	6	4
8.2	10.5	29	2	4	22
10.5	12.9	30	5	5	20
12.9	15.2	48	6	2	39
15.2	17.6	40	6	8	25
17.6	20.0	16	1	2	13
20.0	22.3	9	0	3	5
22.3	24.7	4	0	0	4
24.7	27.0	3	0	1	2
27.0	29.4	2	0	1	1
	Total	191	20	32	135

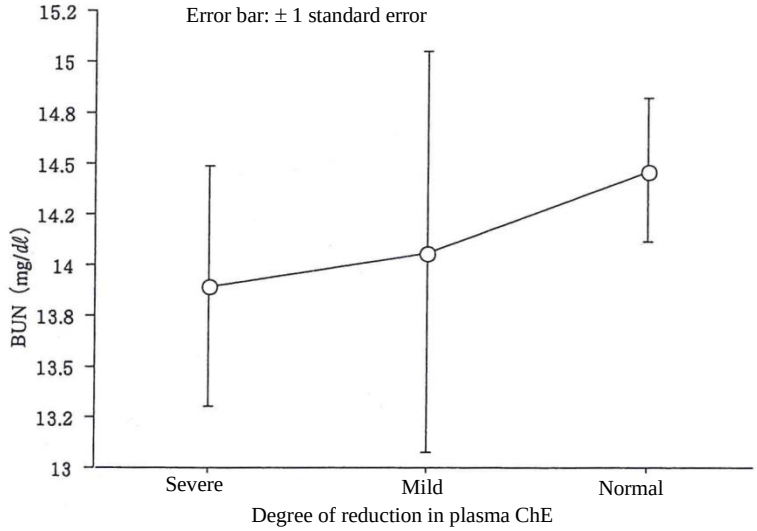
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

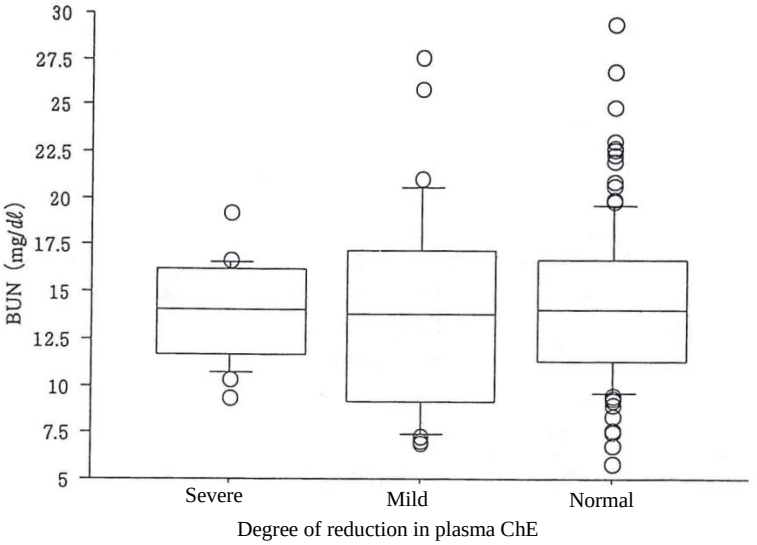
Basic statistical value: BUN
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	20	13.9	2.7	5.9E-1
Mild	32	14.1	5.6	9.8E-1
Normal	135	14.5	4.1	3.5E-1

Scheffe: BUN
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−0.161	2.989	0.9912
Severe, normal	−0.566	2.512	0.8570
Mild, normal	−0.404	2.061	0.8894





Correlation between serum creatinine (Crt) (mg/dL) at the initial examination and plasma ChE decrease

Frequency distribution: Crt
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
0.34	0.47	2	0	0	2
0.47	0.59	13	2	3	7
0.59	0.72	49	6	11	31
0.72	0.84	47	7	6	33
0.84	0.97	27	1	7	18
0.97	1.10	27	3	1	23
1.10	1.22	18	0	3	15
1.22	1.35	1	0	1	0
1.35	1.47	2	1	0	1
1.47	1.60	1	0	0	1
	Total	187	20	32	131

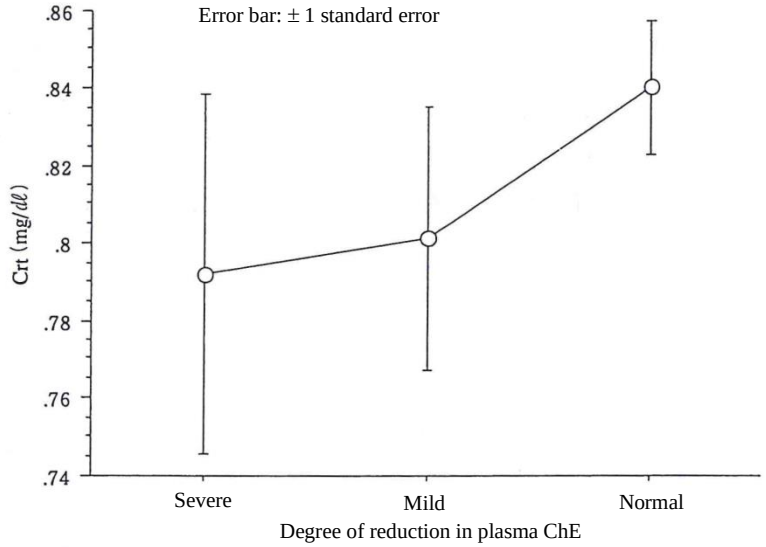
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

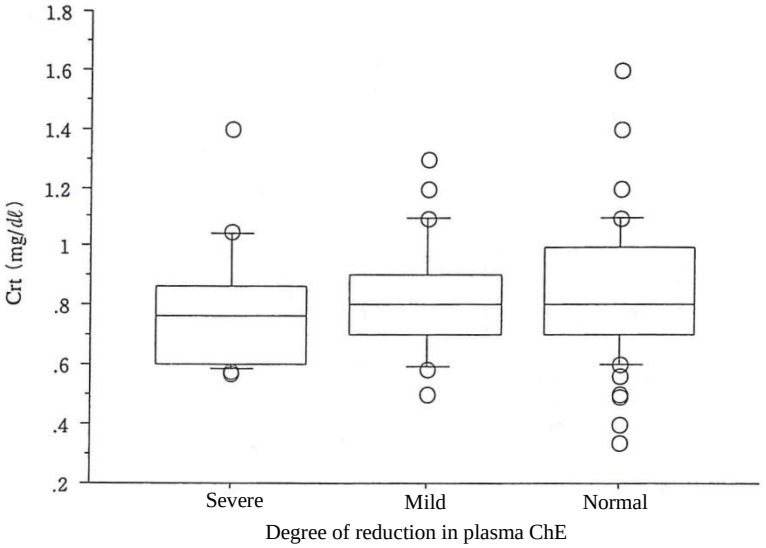
Basic statistical value: Crt
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	20	0.792	0.207	0.046
Mild	32	0.801	0.192	0.034
Normal	131	0.840	0.194	0.017

Scheffe: Crt
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−9.250E-3	0.137	0.9863
Severe, normal	−0.048	0.116	0.5910
Mild, normal	−0.039	0.095	0.6012





Correlation between serum Na (mEq/L) at the initial examination and plasma ChE decrease

Frequency distribution: Na
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
136	137	5	3	1	1
137	138	4	2	2	0
138	140	9	1	4	4
140	141	30	1	5	24
141	142	33	4	6	22
142	143	75	5	10	58
143	144	18	1	1	16
144	146	6	0	1	4
146	147	6	1	2	3
147	148	2	2	0	0
	Total	188	20	32	132

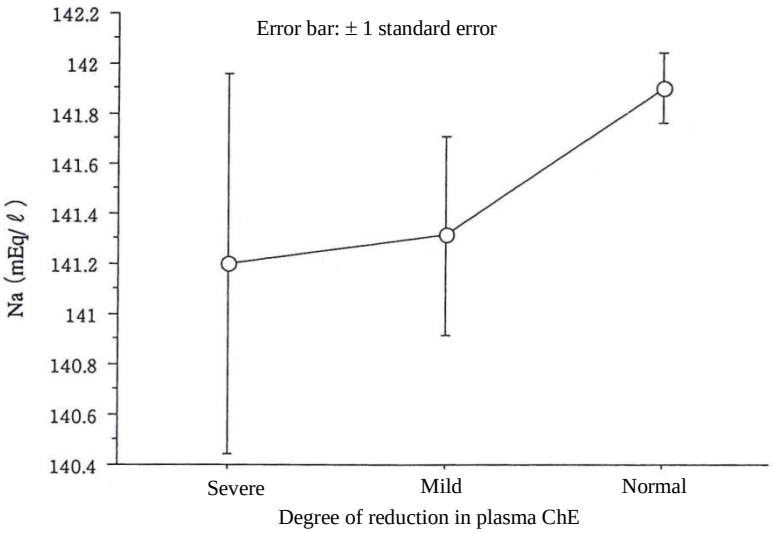
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

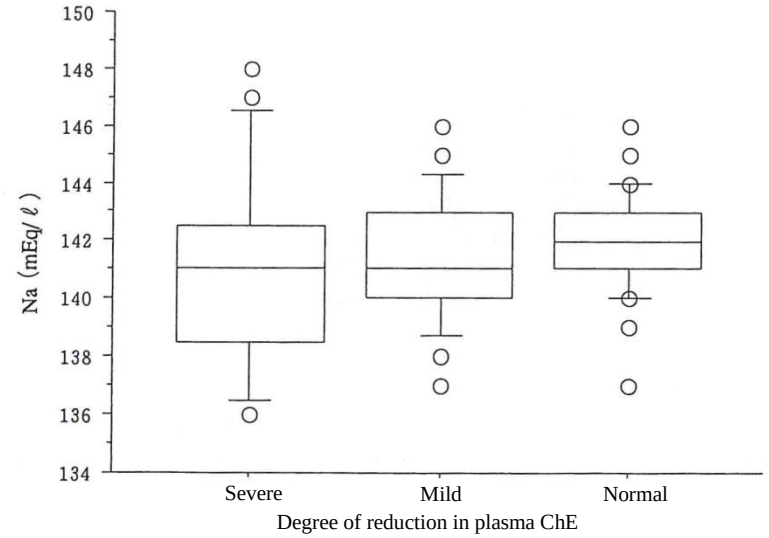
Basic statistical value: Na
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	20	141.200	3.365	0.753
Mild	32	141.312	2.235	0.395
Normal	132	141.894	1.617	0.141

Scheffe: Na
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−0.113	1.396	0.9804
Severe, normal	−0.694	1.175	0.3478
Mild, normal	−0.581	0.965	0.3332





Correlation between serum K (mEq/L) at the initial examination and plasma ChE decrease

Frequency distribution: K
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
2.7	3.0	2	2	0	0
3.0	3.3	1	1	0	0
3.3	3.6	14	7	1	5
3.6	3.9	40	5	9	26
3.9	4.2	65	4	13	47
4.2	4.5	47	0	7	38
4.5	4.8	14	0	0	14
4.8	5.1	4	0	2	2
5.1	5.4	0	0	0	0
5.4	5.7	1	1	0	0
	Total	188	20	32	132

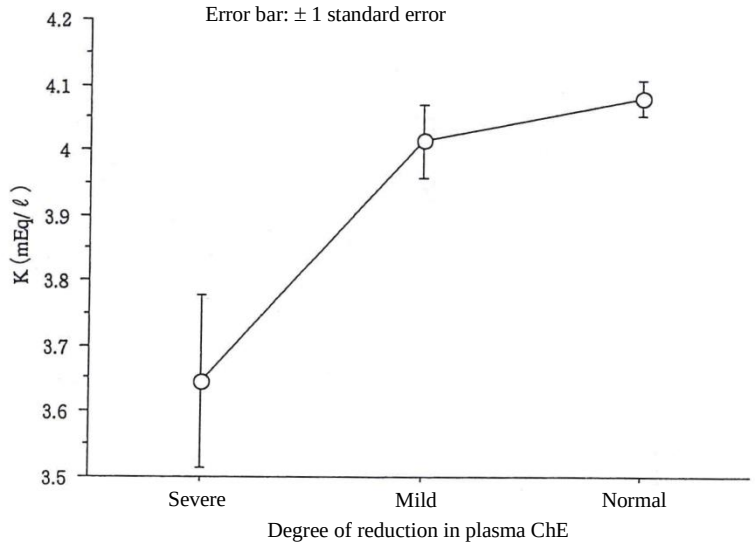
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

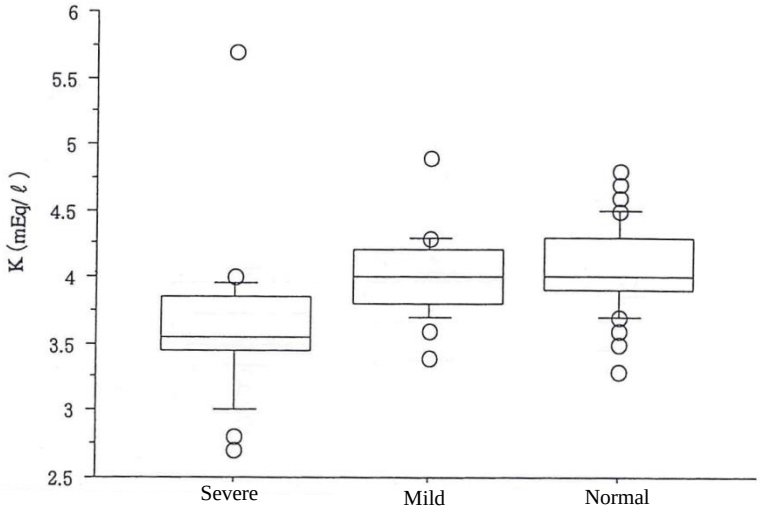
Basic statistical value: K
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	20	3.6	5.9E-1	1.3E-1
Mild	32	4.0	3.1E-1	5.5E-2
Normal	132	4.1	3.0E-1	2.6E-2

Scheffe: K
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Severe, mild	−0.368	0.242	0.0011	S
Severe, normal	−0.434	0.204	‹0.0001	S
Mild, normal	−0.066	0.167	0.6202	





Correlation between serum Cl (mEq/L) at the initial examination and plasma ChE decrease

Frequency distribution: Cl
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
96	99	1	0	1	0
99	101	9	3	2	4
101	104	31	7	6	18
104	107	44	5	7	30
107	109	77	5	13	57
109	112	23	0	2	21
112	115	1	0	0	1
115	118	1	0	1	0
118	120	0	0	0	0
120	123	1	0	0	1
	Total	188	20	32	132

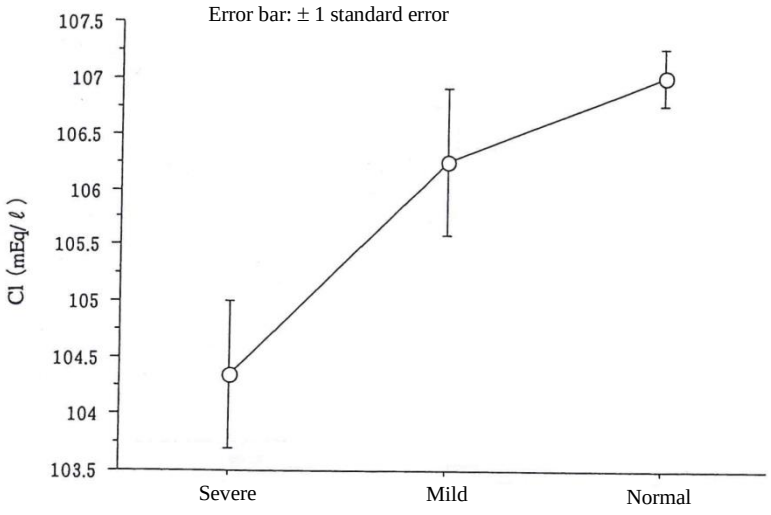
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

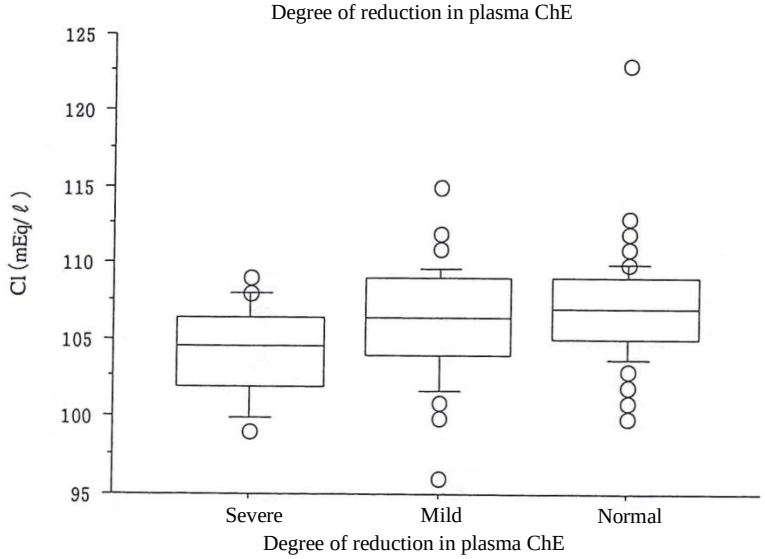
Basic statistical value: Cl
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	20	104	3	7E·1
Mild	32	106	4	7E·1
Normal	132	107	3	3E·1

Scheffe: Cl
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value	
Severe, mild	−1.9	2.2	0.0962	
Severe, normal	−2.6	1.8	0.0019	S
Mild, normal	−7.4E·1	1.5	0.4702	





Correlation between serum total Ca (mEq/L) at the initial examination and plasma ChE decrease

Frequency distribution: Ca
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
7.0	7.3	1	0	1	0
7.3	7.6	0	0	0	0
7.6	7.9	2	1	0	1
7.9	8.2	1	0	1	0
8.2	8.5	4	2	1	1
8.5	8.8	6	2	1	2
8.8	9.1	6	4	0	2
9.1	9.4	11	3	5	3
9.4	9.7	3	1	0	2
9.7	10.0	2	0	1	1
	Total	36	13	10	12

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

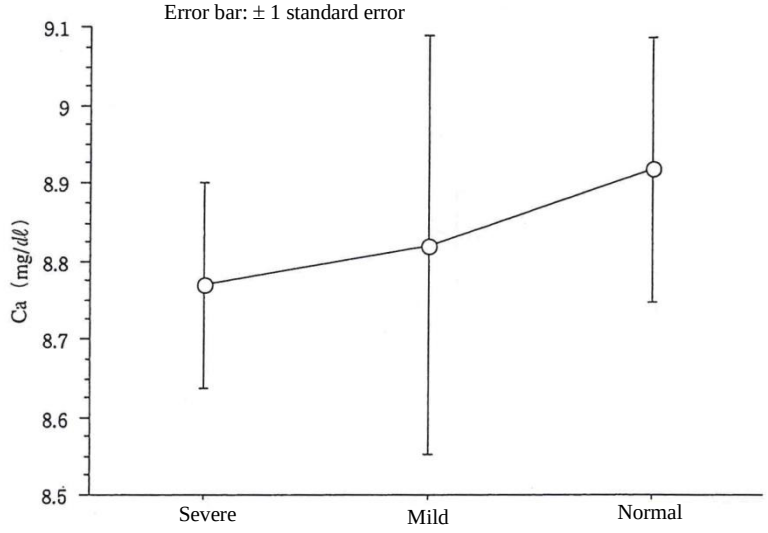
Basic statistical value: Ca
Effect: Degree of reduction in ChE

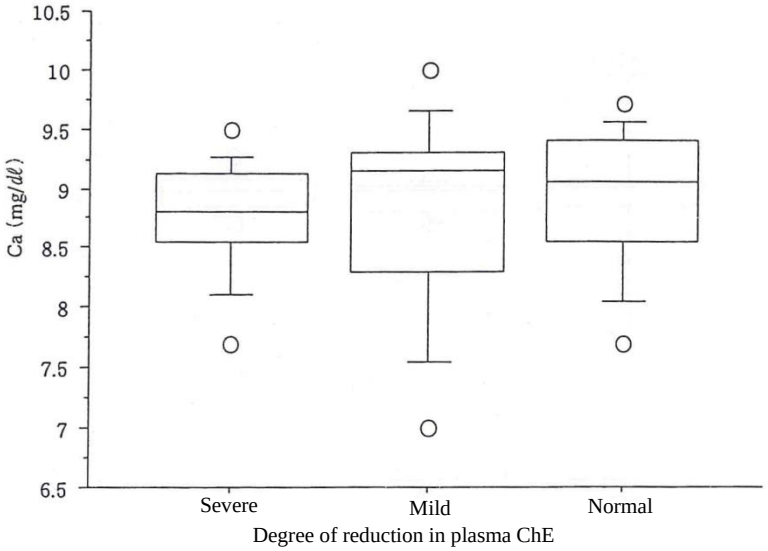
	The number of cases	Mean value	Standard deviation	Standard error
Severe	13	8.8	4.8E·1	1.3E·1
Mild	10	8.8	8.5E·1	2.7E·1
Normal	12	8.9	5.9E·1	1.7E·1

Scheffe: Ca
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−5.1E·2	6.9E·1	0.9822
Severe, normal	−1.5E·1	6.5E·1	0.8466
Mild, normal	−9.7E·2	7.0E·1	0.9391

Error bar: ± 1 standard error





Correlation between arterial blood gas pH and plasma ChE decrease

Frequency distribution: pH
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
7.105	7.156	1	1	0	0
7.156	7.207	1	1	0	0
7.207	7.259	0	0	0	0
7.259	7.310	0	0	0	0
7.310	7.361	0	0	0	0
7.361	7.412	9	2	3	4
7.412	7.463	14	6	4	4
7.463	7.515	2	0	0	2
7.515	7.566	0	0	0	0
7.566	7.617	2	2	0	0
	Total	29	12	7	10

The total result is not identical to the sum of the individual cells because of missing values of the division variables.

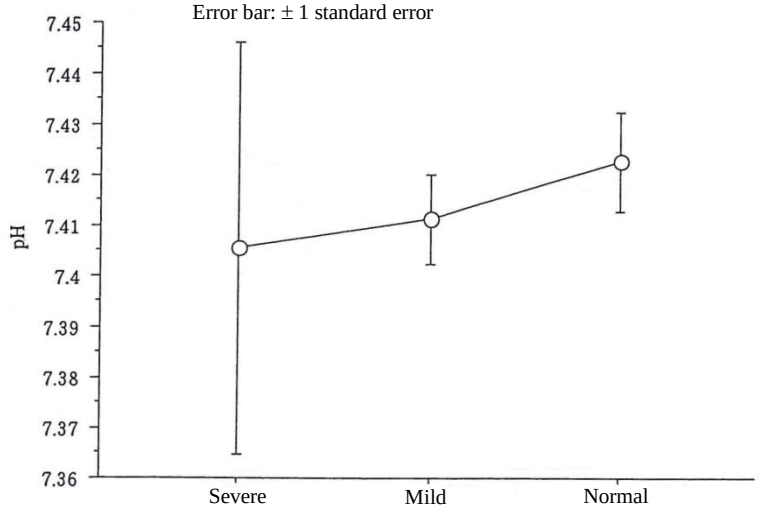
Basic statistical value: pH
Effect: Degree of reduction in ChE

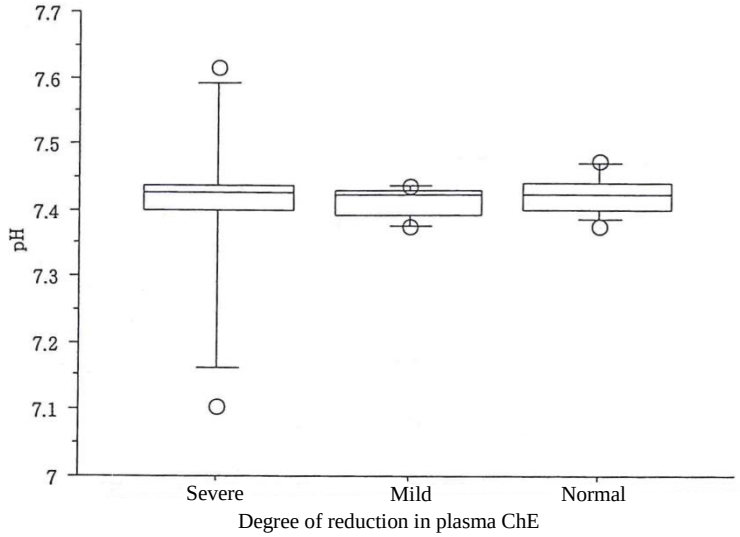
	The number of cases	Mean value	Standard deviation	Standard error
Severe	12	7.406	0.141	0.041
Mild	7	7.411	0.024	8.901E-3
Normal	10	7.422	0.031	9.675E-3

Scheffe: pH
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−5.786E-3	0.116	0.9917
Severe, normal	−0.017	0.105	0.9152
Mild, normal	−0.011	0.120	0.9713

Error bar: ± 1 standard error





Correlation between $PaCO_2$ (mmHg) and plasma ChE decrease

Frequency distribution: $PaCO_2$
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
17.7	20.3	2	2	0	0
20.3	22.9	0	0	0	0
22.9	25.5	0	0	0	0
25.5	28.1	2	1	1	0
28.1	30.7	3	1	0	2
30.7	33.3	2	1	1	0
33.3	35.9	6	2	1	3
35.9	38.5	6	3	1	2
38.5	41.1	4	1	2	1
41.1	43.7	4	1	1	2
	Total	29	12	7	10

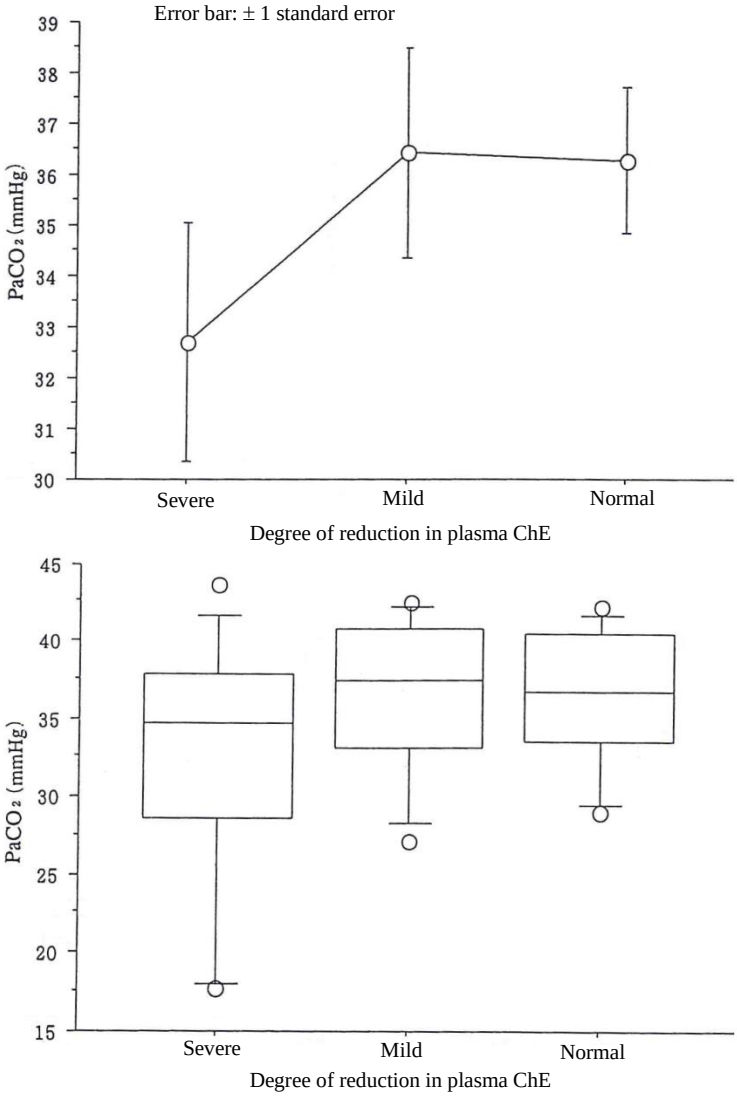
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

Basic statistical value: $PaCO_2$
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	12	32.7	8.2	2.4
Mild	7	36.4	5.5	2.1
Normal	10	36.2	4.6	1.4

Scheffe: $PaCO_2$
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−3.723	8.045	0.4956
Severe, normal	−3.558	7.243	0.4544
Mild, normal	0.164	8.336	0.9987



Correlation between arterial blood gas (PaO_2) and plasma ChE decrease

Frequency distribution: PaO_2
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
50	70	5	3	0	2
70	90	17	5	5	7
90	110	4	2	1	1
110	130	2	2	0	0
130	150	0	0	0	0
150	170	0	0	0	0
170	190	0	0	0	0
190	210	0	0	0	0
210	230	1	0	1	0
230	250	0	0	0	0
	Total	29	12	7	10

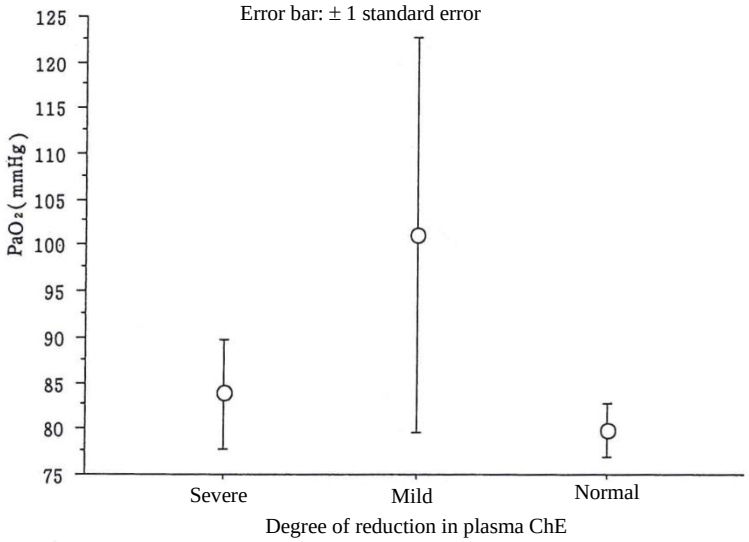
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

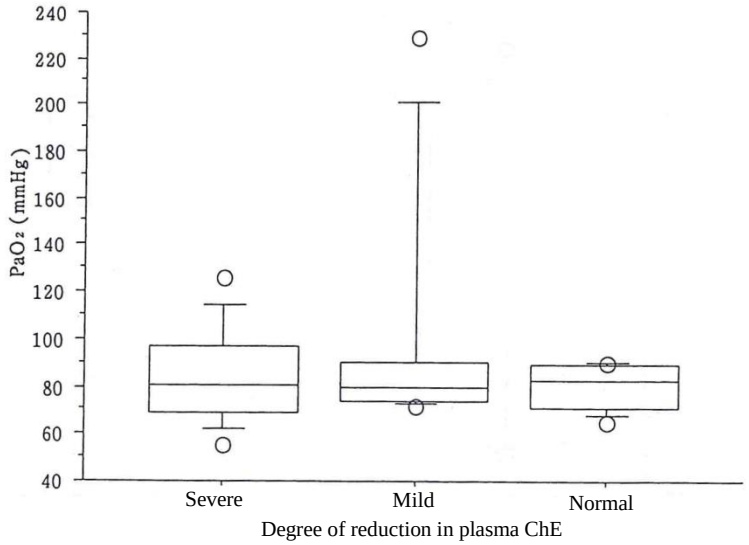
Basic statistical value: PaO_2
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	12	83.9	20.6	6.0
Mild	7	101.0	56.8	21.5
Normal	10	79.9	9.1	2.9

Scheffe: PaO_2
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−17.1	38.1	0.5151
Severe, normal	4.0	34.3	0.9555
Mild, normal	21.1	39.5	0.3947





Correlation between arterial blood gas HCO_3 and plasma ChE decrease

Frequency distribution: HCO_3
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
9.1	10.9	1	1	0	0
10.9	12.7	0	0	0	0
12.7	14.4	0	0	0	0
14.4	16.2	0	0	0	0
16.2	18.0	1	1	0	0
18.0	19.8	2	1	1	0
19.8	21.6	3	1	0	2
21.6	23.3	8	3	2	3
23.3	25.1	7	2	2	3
25.1	26.9	5	2	1	2
	Total	27	11	6	10

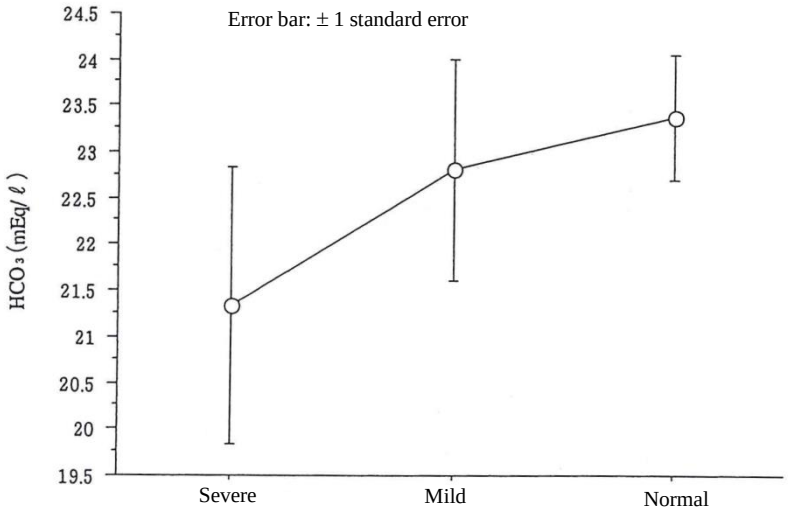
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

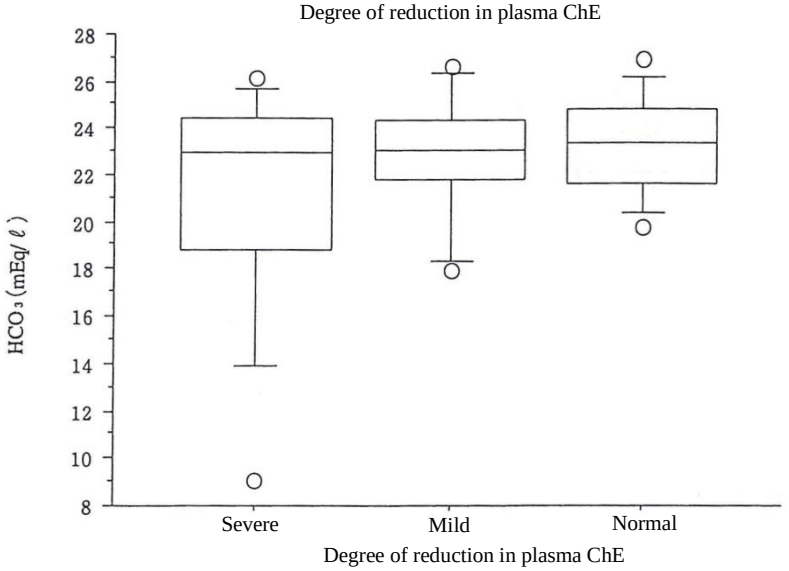
Basic statistical value: HCO_3
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	11	21.3	4.9	1.5
Mild	6	22.8	2.9	1.2
Normal	10	23.4	2.1	6.8E-1

Scheffe: HCO_3
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−1.5	4.9	0.7404
Severe, normal	−2.0	4.2	0.4641
Mild, normal	−5.7E-1	5.0	0.9565





Correlation between arterial blood gas base excess and plasma ChE decrease

Frequency distribution: BE
Division variable: Degree of reduction in ChE

Lower limit (≥)	Upper limit (<)	Total frequency	Frequency of severe	Frequency of mild	Frequency of normal
−19.7	−17.4	1	1	0	0
−17.4	−15.2	0	0	0	0
−15.2	−12.9	0	0	0	0
−12.9	−10.7	0	0	0	0
−10.7	−8.4	0	0	0	0
−8.4	−6.1	0	0	0	0
−6.1	−3.9	1	0	1	0
−3.9	−1.6	3	1	0	2
−1.6	6.4E·1	14	5	5	4
6.4E·1	2.9	6	4	0	2
	Total	25	11	6	8

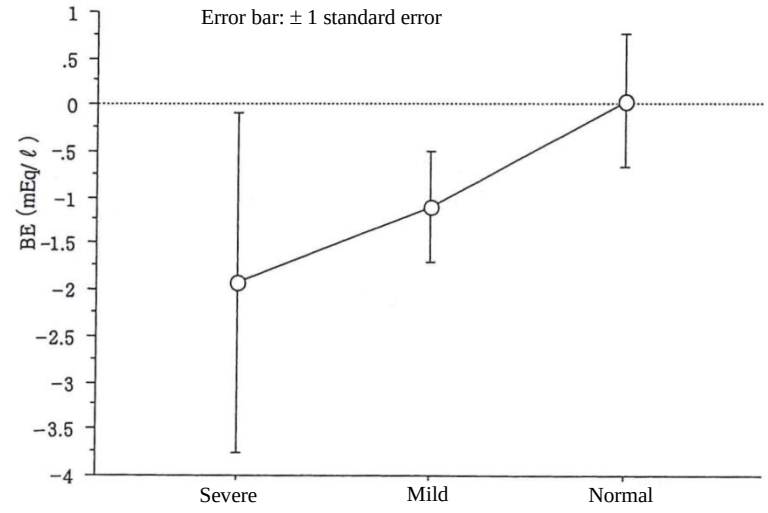
The total result is not identical to the sum of the individual cells because of missing values of the division variables.

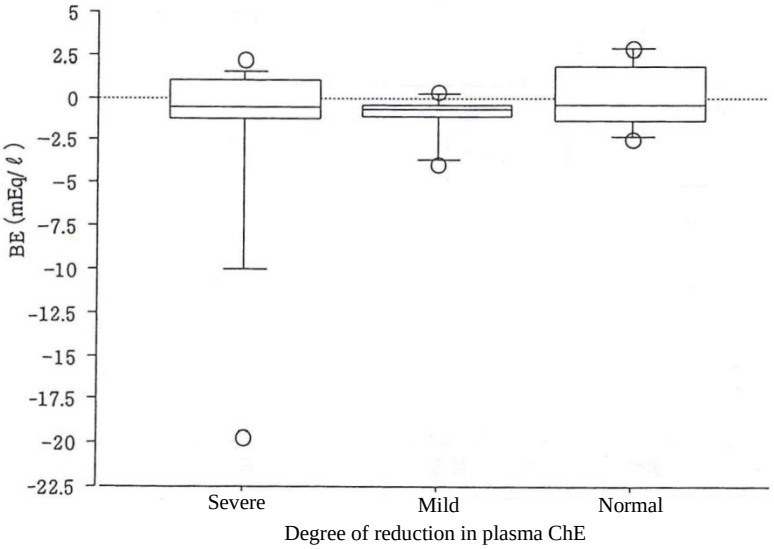
Basic statistical value: BE
Effect: Degree of reduction in ChE

	The number of cases	Mean value	Standard deviation	Standard error
Severe	11	−1.927	6.090	1.836
Mild	6	−1.100	1.453	0.593
Normal	8	0.038	2.025	0.716

Scheffe: BE
Effect: Degree of reduction in ChE
Significance level: 5%

	Difference in the mean value	Critical value	p value
Severe, mild	−0.827	5.751	0.9314
Severe, normal	−1.965	5.265	0.6254
Mild, normal	−1.138	6.120	0.8884





4. Outline of medical care for severely affected victims

To understand the symptoms and courses in the victims, we consider it necessary to investigate individual cases separately from the overall summary, and thus present an outline of disease history in representative cases.

For cases that required obtaining consent from the victims, we explained the outline of the parts written about the relevant victims and the reports to the victims individually, and then obtained their informed consent to have their cases included in the reports.

Case 1

A man in his 20s

Admission date: June 28, 1994　　Discharge date: July 15, 1994

<Background to hospitalization>

At approximately 22:30 on June 27, 1994, when the windows on the veranda side in the room were opened because the inside was very warm, the subject sensed an abnormal odor. After a while, his field of vision narrowed rapidly, and he could not see well. Although both his eyes hurt and he was coughing and experiencing breathing difficulties, he went to bed without seeking treatment.

Just after midnight on June 28, 1994, the police visited him and asked whether he had experienced physical abnormalities. He told about his symptoms and was then transported to a hospital by ambulance and hospitalized at 2:30.

<Symptoms at admission>

The findings were: Height, 166 cm; body weight, 61 kg; blood pressure, 138/90 mmHg; pulse, 64/min; chest respiration, no wheezing; body temperature, 37.2°C; hyperemia in the bilateral bulbar conjunctivae; full consciousness; clear cardiac sounds; no pulmonary adventitious sound; no cyanosis; markedly constricted pupils (0.5 mm or less); no light reflex; no salivation or sputum. None of the following was reported: nausea, vomiting, diarrhea, urinary and fecal incontinences, spasm or weakness of his extremities.

<Laboratory findings>

Blood cell counts: WBC 6300/mm^3, RBC 480 × 10^4/mm^3, Hb 14.5 g/dL, Ht 44.2%,
Plt 23.8 × 10^4/mm^3

Biochemical values: TP 6.4 g/dL, Alb 4.0 g/dL, A/G 1.7, GOT 11 IU, GPT 8 IU, ALP 168 IU,
LDH 334 IU, γGTP 15 IU, ChE 595 IU (normal: 2300–4300),
CK 78 IU/L (normal: 40–200), T.Bil 0.2 mg/dL, ZTT 3.3 U, Amy 235 IU,
T.Chol 159 mg/dL, TG 61 mg/dL, BUN 14.0 mg/dL, Crt 1.0 mg/dL,
UA 5.9 mg/dL, Fe 71 μg/dL, Na 141 mEq/L, K 3.7 mEq/L, Cl 103 mEq/L

Urine specific gravity: 1.025, pH5.0, protein (−), urobilinogen (normal +), occult blood (−), ketone body (−), normal urinary sediment

No abnormality in the chest X-ray photography.

<Progress after admission>

O_2 inhalation (2 L/min), reinfusion of electrolytes (sorbitol Hartmann 500 mL), and atropine sulfate 1A muscular infusion were conducted. O_2 inhalation was discontinued after 2.5 hours, then atropine sulfate 1A was administered. A subjective disorder of visual acuity persisted; because of pain and fatigue in the eyes, the patient could not read. The right eye in particular was affected. Apart from these findings, dry coughs occurred frequently. Physically, hyperemia in the bilateral bulbar conjunctivae and persisting markedly constricted pupils were noted. The patient was treated with a reinfusion of electrolytes 1,000 mL/day.

As for clinical examination, the ChE value was 1,107 on June 29, the second day of hospitalization, 1,484 on July 1, 1,959 on July 5, and 2,154 on July 8, increasing over time. Because the constricted pupils persisted, a professor of hygieiology recommended "*Seiketushiraku*" (stimulation of acupressure points of the automatic nerves); this was conducted twice, on July 7 and 12, but with no effects. On July 9, the patient was seen at an ophthalmologic department by our referral. It was reported that the visual acuity in both the eyes was 1.2 with congenital persistent pupillary membrane, and the constriction of the visual field could be relieved with pupillary dilatation. Subsequently, Mydrin diluted 20-fold was administered as eye drops several times a day to dilate the pupils by 2–4 mm. The patient was discharged on July 15, 1994.

<Progress after discharge>

The patient visited the outpatient section on July 19. At that time, subjective dry coughs remained. As for the visual acuity, Mydrin administered twice a day enabled him to function without difficulty. The left pupil was approximately 2 mm wide and did not open because of the residue. The patient subsequently returned to work, and made his last visit on August 27. Visual acuity was normal and no other subjective symptoms were observed. The left pupil was approximately 3 mm wide; the right pupil opened, but the residue obstructed his field of vision.

<Discussion>

Among the 147 patients with toxic gas poisoning whom we examined and treated, visual disorders and a marked reduction in ChE values were found in the relevant cases. However, it is regrettable that those cases were not understood sufficiently from a clinical standpoint, because the true ChE values had not been measured. In addition, we infer that prolonged markedly constricted pupils may be associated with a greater reduction in ChE at the initial stage after the exposure to gas.

The reduced ChE values recovered after a short period. Although only symptomatic therapy was provided, a common finding in all cases was recovery without any aftereffects.

Case 2

A man in his 40s

Admission date: June 28, 1994　　Discharge date: July 3, 1994

Medical history: Ulcerous colitis at the age of 35

<Background to hospitalization>

At 23:00 on June 27, 1994, the subject's family aroused him from sleep. He was the caretaker of a dormitory house, which was active with residents and emergency personnel. He retrieved a person with no pulse from a bathtub, and carried an unconscious, vomiting person on a stretcher with the emergency personnel. He also helped emergency personnel carry the two afflicted persons to Hospital A. While at the hospital, his vision darkened and he experienced abdominal pain, headache, eye pain, and nausea.

At around 4:00 on June 28, he was instructed to go to another hospital and, while on his way, his vision failed. At the hospital, constricted pupils were detected and he was then hospitalized at 4:30.

<Findings at admission>

Findings were: Blood pressure, 160/94 mmHg; pulse rate, 90/min; respiratory rate, 24/min; body temperature, 36.2°C.

Because the patient was conscious, he arrived at the hospital unaccompanied and was hospitalized. Pinpoint pupils and no light reflex. Hyperemia was observed in the palpebral conjunctivae. The abdomen and chest showed no abnormal physical findings, but nausea and watery diarrhea were present.

<Laboratory findings>

Blood cell counts: WBC 5100/mm^3 (St 5%, Seg 42%, Ba 1%, Eo 3%, Mono 11%, Lym 38%),
RBC 479 × 10^4/mm^3, Hb 15.0 g/dL, Ht 46.4%, Plt 26.2 × 10^4/mm^3

Biochemical values: TP 8.4 g/dL, Alb 4.6 g/dL, A/G 1.2, T.Bil 0.7 mg/dL, BUN 16 mg/dL,
Crt 1.1 mg/dL, GOT 32 IU/L, GPT 13 IU/L, γGTP 135 IU/L,
CK 122 IU/L (normal: 33–210), FBS 116 mg/dL, UA 8.8 mg/dL,
ChE 90 IU/L (normal: 100–250), T.Chol 224 mg/dL, HDL 42 mg/dL,
TG 443 mg/dL, ZTT 10.4 U, AIP 119 IU/L, LDH 305 IU/L, Na 145 mEq/L,
K 4.3 mEq/L, Cl 96 mEq/L, Ca 9.2 mg/dL, LAP 65 IU/L

Erythrocyte true cholinesterase (normal 1.2–2.0 U) 0.8 U on July 25, 1.6 U on September 30

Serum CRP 0.5 mg/dL

Urinalysis: pH 6.0, protein (−), sugar (−), urobilinogen (normal +), ketone body (−), bilirubin (−), occult blood (−), normal urinary sediment

Fecal examination on June 29: occult-blood immunization method (+)

ECG cardiac rate: 80/min, no abnormality

Chest X-ray photography: no abnormality

Head MRI on July 1: no abnormality

EEG on June 30: no abnormality

Ophthalmological findings on June 30: Visual acuity 0.2 (0.9) in the right eye and 0.1 (1.0) in the left eye. Pupils were constricted. Light reflex was dull. In addition, no other marked change was found. As for the visual field, the overall sensitivity decreased.

Barium enema x-ray of the large intestine on July 2: No findings for ulcerous colitis.

<Progress after admission>

Because symptoms requiring emergency treatment for acute poisoning did not appear, atropine sulfate 5A was administered as a drip infusion on day 1 of hospitalization. Atropine sulfate 2A and Solu-Cortef 100 mg were administered on day 2, and atropine sulfate 1A on days 3–5. The patient was discharged on day 7.

Ophthalmologic symptoms

The diameter of the constricted pupils was 2 mm at 17:00 on day 1 of hospitalization, and then increased gradually. As for conjunctival hyperemia, although thiasin eye drops were administered, the symptom persisted for one week after discharge from the hospital. Subjective symptoms, including eye pain, blurred vision, easy fatigue, etc. continued until four months after discharge.

Respiratory symptoms

Although coughs and a runny nose were present up to day 2 of hospitalization, these symptoms did not require treatment.

Digestive symptoms

Nausea and three-time watery diarrhea were present on day 1 and subsequently, soft feces once or twice a day and a dull abdominal pain persisted. However, the patient ate his meals, and examinations on day 5 showed no evidence of ulcerous colitis. As a result, he did not wish to receive oral drugs. He was then followed up.

<Progress after discharge>

Once he was discharged from the hospital, the patient became busy because of intense media coverage, such as TV, and his work. Although he returned to work, he could not write or conduct inspection work because of his visual disorder, eye pain, and difficulty concentrating. Mental and physical stresses had accumulated to cause mucous and bloody stool 5–6 times a day and severe abdominal pain. Abdominal echo and gastric camera exams, which were conducted on July 16, revealed no abnormality. Because the symptoms were severe, he was hospitalized on July 21. On July 26, colonofiberscopy was performed. Ulcerous colitis was diagnosed through endoscopic findings and histopathologic findings. On August 18, colonofiberscopy was performed again. The absence of ulcerous colitis was confirmed, supported by histopathologic findings. On August 29, the symptoms were relieved and he was discharged.

<Cholinesterase>

	Jun. 28	Jun. 30	Jul. 11	Jul. 25	Sep. 29
Plasma cholinesterase (normal: 100–250)	90	102	142	144	
Erythrocyte true cholinesterase (normal: 1.2–2.0 U)				0.8	1.6

<Discussion>

To perform rescue work, the subject had entered the narrow bathroom where one victim died and the room where another victim had become seriously ill, as well as into other rooms contaminated by gas. These activities may have aggravated his medical condition, making it more severe than those of his family and associates who were hospitalized at the same time.

Ulcerous colitis was a recurrence of anamnestic disease. Although an association with the toxic gas was unknown, physical and mental stresses induced by the gas attack were presumed to be a major cause for the recurrence.

Although he is on treatment at present (December 5), diarrhea occurs when he becomes tired. In addition, he has persisting ophthalmologic symptoms such as non-focusing vision, a sensation of pressure, and bleary eyes.

Case 3

A woman in her 20s

Admission date: June 28, 1994 Discharge date: July 8, 1994

No notable medical history or family history

<Background to hospitalization>

At around 18:00 on June 27, 1994, the subject returned home and opened the windows. At around 21:00, while the windows remained open, she studied facing the windows. At 21:30, she talked with a friend on the telephone and was sensed that her voice was trembling. At around 22:30, unexpectedly, she experienced whistling breath and inspiratory dyspnea. Later, she felt that her head was heavy. Then, suddenly, her visual field darkened and blurred as if an electric light was turned down, and her nose started running. She slept for approximately one hour from about 23:10. Next, she found out about the gas attack and went outside by herself to request assistance. She was transported by ambulance to a hospital and admitted at 1:30 on June 28.

<Physical findings at admission>

Findings were: Height, 155 cm; body weight, 49 kg; BP, 104–56 mmHg; HR, 60/min (reg); BT, 36.9°C. Heart: no murmur. Lungs: normal resonance, normal vesicular sound, no rales. Abdomen: flat & soft, no tenderness. Liver: not palpable. Diarrhea (-), vomiting (-), incontinence (-),

consciousness GCS3–5–6. Extraocular movements: full range, but saccadic. Nystagmus was negative, pupils were 1 mm/1 mm, round/round, and light reflex was unknown because of miosis. No other abnormality was observed in the cranial nerves. Normal deep reflex, Babinski ±/±, Chaddock ±/+, reduced muscular strength in the extremities (−). Normal sensation.

<Laboratory findings at admission>

Blood cell counts: Normal ranges

Biochemical findings: T.P 6.6 g/dL, ZTT 9.6 KU, TTT 1.7 KU, T.Bil 0.9 mg/dL, ALP 174 U/L, LAP25 U/L, GOT 14 U/L, GPT 8U/L, γGTP 10 U/L, LDH 152 U/L, Amy 62 U/L, CK 60 U/L (normal: 30–165), ChE 75 U/L (normal: 109–249), T.Chol 122 mg/dL, TG 28 mg/dL, Glu 80 mg/dL, BUN 7 mg/dL, Crt 0.5 mg/dL, UA 3.4 mg/dL, Na 141 mEq/L, K 3.9 mEq/L, Cl 104 mEq/L, Ca 8.6 mg/dL, Fe 120 μg/dL, CRP 0.00 mg/dL

blood gas (inspiron 10 L/min, O_2 50%): pH 7.423, PCO_2 37.5 mmHg, PO_2 128.9 mmHg, SAT 99.7%, HCO_3 24.3 mM/L, BE 0.3 mM/L

<Progress after admission>

Immediately after the patient was hospitalized in the ICU on June 28, 1994, the vessel was secured (Zorita T3, 60 mL/hr) and O_2 (inspiron 10 L/min, FiO_2 98%) was administered; she was then transferred to a room for general patients. She was conscious, and followed up with inspiron (10 L/min, FiO_2 50%). At 10:00, although the sensation of a heavy head remained, other subjective symptoms were relieved, and the darkness in her visual field disappeared. Although O_2 was not aspirated during MRI, findings of the blood gas were favorable with PCO_2 36.0 mmHg, PO_2 90.1 mmHg, BE -1.8 mM/L, and SAT 96.8%. To prevent cranial nerve disorder caused by the unknown gas, the patient was delivered oxygen 2 L/min through nasal cannula until the next morning. However, pupil diameter was 1 mm/1 mm and the patient's light reflex was not clear owing to constricted pupils, which persisted. Pain in the bilateral ocular posterior region appeared on the afternoon of June 28. When a little light entered her eyes, the patient had a strong reaction and hyperemia was present in the bulbar conjunctivae. Because the symptoms were marked, the patient was examined by an ophthalmologist, who prescribed eye drops of a cornea-protecting agent and antibiotics.

On June 29, examinations of pulmonary functions were conducted, and increased residual air volume and a reduction in %DLco to 74.5 were detected. Although the patient felt nauseated after the examinations, it was relieved after resting. When she walked to a rest room, she felt nauseous. The patient's blood pressure was measured in the supine position, and was found to be reduced to 70 mmHg. When body position was changed from a supine to a standing position, a reduction in blood pressure was not detected. The patient noted that she had sometimes exhibited similar symptoms since the age of around 10. Although she received detailed examinations at the time, the etiology was

unknown. She was followed up for the symptom, which had then disappeared. From the same day, the patient started to eat and had no difficulty in swallowing. The pupils did not change markedly, and the pain in her eyes was still strong, although it was relieved slightly. Because opening her eyes was difficult, she received home visits by the ophthalmologist. The cause of the pain was presumed to be ciliary because erosion was absent in the cornea and the condition had been treated with atropine eye drops. Subsequently, a mild photophobic sensation appeared and the pain in the bilateral ocular posterior regions was relieved. The ChE value was 92 (normal range: 109–249). On July 1, the pupil diameters were 6 mm/6 mm and the eye pain was relieved to a degree that the patient felt pain only when light entered the right eye. The ChE value was 90. On July 2, the eye pain disappeared. On July 4, the patient visited the outpatient section of the ophthalmologic department, and no problems were observed. The pupil diameters were 5–6 mm. The ChE value was 87. On July 5, the pupil diameters were 5 mm/5 mm and the light reflex was sound in both eyes. The ChE value was 81. On July 6, examinations of pulmonary functions showed an increase in the %VC and %DLco compared with previous examinations, indicating an improvement. The electromyograms showed a reduction tendency in the peripheral nervous conduction velocity on the distal side, indicating that a future appearance of neuropathy could not be excluded. The ChE value was 94. On July 7, the patient's brain waves were measured, and no abnormality was detected. On July 8, no other physical abnormality was found, and the patient was then discharged as ambulatory. The ChE value was 87.

<Transition of ChE values during the hospitalization (normal range 109–249)>

	Jun. 28	Jun. 29	Jun.30	Jul. 1	Jul. 4	Jul. 5	Jul. 6	Jul. 8
ChE	75	81	92	90	87	81	94	87

Case 4

A man in his 30s

Admission date: June 28, 1994 Discharge date: July 1, 1994

Medical history: Not notable

<Background to hospitalization>

At around 23:30 on June 28, 1994, because of noisy outdoors, he opened a window. Next, his vision became dark, and he felt nausea and experienced repeated vomiting. He bathed and showered. Because the nausea persisted until the next day, after he visited a hospital, he was referred to another hospital, where he was admitted at 10:30 on June 28.

<Symptoms at admission>

General physical findings: Height, 167 cm; body weight, 59 kg; BP, 135/75 mmHg; HR, 77/min; respiratory rate, 20/min; body temperature, 36.7°C; anemia (−); jaundice (−); hyperemic conjunctiva; constricted pupils (0.5 mm); disappearance of the light reflex; no ocular deviation. The

cervical region: No palpable lymph nodes. Chest region: Clear pulmonary sounds; clear cardiac sounds. The abdominal region: Soft, flat, tenderness (−), no palpable liver and spleen. The extremities: No cold sensation and no cyanosis.

<Laboratory findings>

ESR: 3 mm/hr

Blood cell counts: RBC 444 × 10^4/mm^3, Hb 15.8 g/dL, Ht 41.7%, Plt 27.9 × 10^4/mm^3,
WBC 9530/mm^3 (Neut 84.3%, Lymp 10.7%, Mono 3.4%, Eos 0.5%, Baso 0.3%)

Coagulation: PT 11.4 sec, APTT 38.3 SEC, TT 130%

Biochemical findings: TP 7.4 g/dL, Alb 4.3 g/dL, BUN 15 mg/dL, Crt 0.9 g/dL, T.Chol 167 mg/dL, TG 40 mg/dL, T.Bil 0.85 mg/dL, ALP 108 IU/L, LDH 156 IU, GOT 22 IU, GPT 6 IU/L, ChE 2.3 IU/mL (normal: 6.0–13.5), Amy 46 IU/L, BS 111 mg/dL, CK 405 IU/L (normal: 35–23), CKMB 3, Na 143 mEq/L, K 4.0 mEq/L, Cl 105 mEq/L, CRP 0.2 mg/dL

Erythrocyte ChE (July 4, 1994): 0.1 U (normal: 1.2–2.0)

ECG: Normal range without arrhythmia, rate 61/min

Arterial blood gas analyses: pH 7.425, PO_2 64.9 mmHg, PCO_2 40.7 mHg, HCO_3 26.2 mM/L, BE 2.2 mM/L

Respiratory functions: %FVC 103.2%, $FEV_{1\%}$ 104.9

<Progress after admission>

Drip infusion was secured and 120 mL/hr reinfusion and atropine sulfate 1A × 5 (June 28) were administered intravenously. Because the PaO_2 value was low, O_2 inhalation was also given. Although the blurry vision, pain, and hyperemia in the eyes still persisted, the visual field expanded gradually. On July 1, although the constricted pupils persisted, the patient was discharged. At the time, the systemic fatigue sensation persisted. On July 4, at the outpatient section, the systemic deep reflex decreased and the muscular strength of the lower thigh decreased. The ChE value was 6.9 and the CK value was 481. On July 20, at the outpatient section, the systemic deep reflex was slightly improved. The ChE value was 9.8 and the CK value was 146. The systemic fatigue improved gradually during August and was almost gone in September.

Case 5

A man in his 40s

Admission date: June 27, 1994 Discharge date: July 30, 1994

Medical history: Not notable

<Background to admission>

When the subject was relaxing in his room after 22:30 on June 27, 1994, a family member claimed to feel sick, and he thus telephoned for an ambulance. During that time, the subject felt sick,

had double vision, and vomited. He was transported by ambulance to a hospital and admitted at 23:40.

<Symptoms at admission>

General findings: BP, 132/74 mmHg; HR, 96/min; respiratory rate, 20/min; systemic constricted fiber fascicle; body temperature, 36.1℃; anemia (−); jaundice (−); hyperemic conjunctiva; vomit (+). The cervical region: Palpable lymph nodes and thyroid (−). The chest region: Heart: S1, S2 clear, no murmur, S3 (−), S4 (−), pain in the left chest region. Lung: Normal vesicular sound, no rales. Palpable axillary lymph nodes (−). The abdominal region: Soft, flat, tenderness (−), abdominal pain (+), palpable liver and spleen (−). The lower extremities: Cold sensation (+). The skin: Cyanosis (−).

Neurologic findings: Right handedness. Although the patient was conscious, he showed an excitatory tendency. The bilateral pupils were constricted markedly (1 mm or less). Light reflex −/−; no ocular deviation. Systemic numbness sensation. No diarrhea and incontinence.

<Laboratory findings>

ESR: 3 mm/hr

Blood cell counts: WBC 9700/mm^3, RBC 490 × 10^4/mm^3, Hb 13.8 g/dL, Ht 40.0%,
Platelet 31.5 × 10^4/mm^3

Biochemical findings: TP 7.2 g/dL, BUN 19.3 mg/dL, Crt 1.05 mg/dL, UA 8.4 mg/dL,
Glu 170 mg/dL, T.Chol 237 mg/dL, TG 62 mg/dL, HDL-C 47 mg/dL,
T.Bil 0.6 mg/dL, LDH 407 U/L, GOT 20 IU/L, GPT 21 IU/L,
ChE 24 IU/L (normal: 100–240), ALP 151 IU/L, γGTP 24 IU/L, Amy 67 IU/L,
CK 150 IU/L (normal: 0–180), Na 136 mEq/L, K 2.7 mEq/L, Cl 100 mEq/L,
Ca 8.4 mg/dL, P 2.6 mg/dL, CRP 0.10 mg/dL

Blood gases: O_2 1 L/min through cannula, pH 7.617, PCO_2 17.7 mmHg, PO_2 103.9 mmHg,
HCO_3 18.0 M/L, SBE 1.1 mM/L, SaO_2 98.6%

ECG: Sinus rhythm

No abnormal chest X-ray photography findings

Examinations of pulmonary functions: %VC 85.2%, $FEV_{1\%}$ 86.0%

EEG: As for basic activities, although approximately 10 Hz of α waves and sharp waves were observed at three sites, the focus was absent.

<Progress after admission>

At admission or later, the findings were constricted pupils, headache, nausea/vomit, left chest pain, abdominal pain, systemic fasciculation, a systemic numbness sensation, an excitatory tendency, full consciousness enabling the patient to talk. Reinfusion, oxygen inhalation, and hydrocortisone administration were conducted. On June 28, at 8:30, headache, nausea/vomit, systemic numbness, left chest pain, and fasciculation in the tongue were present. Because the pupils were constricted,

atropine sulfate was administered every 2 hr as the symptom was evaluated. Reinfusion of 2500 mL/day was conducted, and forced urination was conducted with Lasix. At 20:40, pyrexia in the 38°C range was present. The pyrexia persisted until July 1 and then decreased to 37°C. At 4:45 on June 29, a short spasm occurred at the right upper extremities. The constricted pupils persisted until July 2, and were then relieved gradually. From July 3, the light reflex was present. Although fasciculation was observed systemically at admission, it occurred only in the tongue the next morning, and disappeared on June 29. The patient started to eat on July 3 and experienced diarrhea at the same time. Subsequently, because the headache, sleeplessness, diarrhea, and pyrexia had not been relieved, the patient required hospitalization until July 30. After discharge, he was followed up at the outpatient section for approximately five months. Symptoms were not exacerbated and new complications did not appear.

Case 6

A male university student

Admission date: June 28, 1994 Discharge date: July 14, 1994

Medical history and family history: Not notable

<Background to admission>

On June 27, 1994, the subject had a common cold with a slight fever of 37°C and was sleeping with the windows open. At around 23:00, he went outside to the veranda to collect his washed clothes and saw white smoke rising. He felt sick and he had flickering vision. He thought that the cold had become worse, and went back to sleep after telephoning a friend. At around 1:00 on June 28, a rescue team visited him in the apartment and found him lying unconscious. They transported him in an ambulance to our hospital. He was admitted at 1:25.

<Symptoms at admission>

General physical findings: Height, 165 cm; body weight, 55 kg; BP, 158/80 mmHg; HR, 120 bpm; respiratory rate, 15/min. The breathing was forced and accompanied by groans. Systemic fasciculation was seen, and a white foamy liquid was expelled from the mouth. Body temperature, 37.5°C; anemia (−); jaundice (−); hyperemic conjunctiva; a large quantity of secreted liquid in the mouth. The cervical region: Palpable lymph nodes and thyroid (−). The chest region: Heart: S1, S2 clear, no murmur, S3 (−), S4 (−), lung: LLB 6 ics, normal vesicular sound, no rales. Palpable axillary lymph nodes (−). The abdominal region: Soft, flat, tenderness (−), palpable liver and spleen (−), palpable inguinal lymph nodes (−). The extremities: Cold sensation (+). The skin: Cyanosis (−). Favorable bilateral pulses of dorsal pedis arteries.

Neurologic findings: Right handedness. Although the eyes were open, the patient presented with nystagmus and did not respond when called. Meningeal irritation sign (−). Eyeground: No abnormality. Pupils: Bilateral marked constriction (0.5 mm), light reflex −/−, no ocular deviation,

pharyngeal reflex −/−, no vomit/diarrhea/incontinence.

<Laboratory findings>

ESR: 2 mm/hr

Blood cell counts: WBC 27000/mm^3 (band 1%, seg 62%, mono 12%, eos 0%, lymph 25%),
RBC 547 × 10^4/mm^3, Hbl 7.1 g/dL, Ht 47.5%, Plt 33.2 × 10^4/mm^3

Coagulation: PT 13.4 sec, APTT 26.6 sec, FIB 201 mg/dL

Biochemical findings: TP 6.6 g/dL, Alb 4.4 g/dL, BUN 14 mg/dL, Crt 0.8 mg/dL, UA 3.9 mg/dL, Glu 248 mg/dL, T.Chol 122 mg/dL, TG 15 mg/dL, T.Bil 1.0 mg/dL, D.Bil 0.3 mg/dL, ZTT 4.7 KU, TTT 1.0 KU, LDH 285 U/L, GOT 27 IU/L, GPT 17 IU/L, ChE 21 IU/L (normal: 109–249), ALP 255 IU/L, γGTP 10 U/L, Amy 172 U/L, CK 233 IU/L (normal: 43–272), Na 140 mEq/L, K 3.2 mEq/L, Cl 101 mEq/L, Ca 9.3 mg/dL, IP 3.6 mg/dL

Serum: CRP 0.44 mg/dL, RA test (−), RAHA <40, antinuclear antibody (−), immune complex 6.8 μg/mL, C3 68 mg/dL, C4 23.3 mg/dL, CH50 33.1 U/mL

Erythrocyte ChE: 0.1 IU or less (normal: 1.2–2.0)

Urinalysis: Yellow, clouded (−), pH 7.5, gravity 1.020, protein (−), sugar (3+), ketone body (1+), occult blood (−). Sediment: no abnormality.

Blood gases: Inspiron 5 L, 50%: pH 7.395, PCO_2 36.3 mmHg, PO_2 86.7 mmHg, HCO_3 22.0 mM/L, SBE -2.3 mM/L, SaO_2 96.4%

Spinal fluid: Pressure, 165/140 mmHg, transparent, cell count 1/mm^3 (mono 100%), TP 20 mg/dL, IgG 1.8 mg/L, Glu 83 mg/dL, Na 153 mEq/L, K 3.0 mEq/L, Cl 113 mEq/L

ECG: Sinus bradycardia, frequent monofocal PVC, normal R-R interval (at 11:00 on June 28)

Holter ECG: Frequent PVC (multifocal)

Chest X-ray photopraphy: CTR 34%, no abnormal finding

Examinations of pulmonary functions: %FVC 62.3%, $FEV_{1\%}$ 67.5%

Cardiac echo: Slightly reduced LV contraction

Head CT: No abnormality

Head MRI: No abnormality

EEG: The basic activity was approximately 9 Hz and 30–50 μV of α waves and fast waves with approximately 20 Hz and 80–100 μV of high amplitude frequently occurred dominantly in the frontal cortex. Three Hertz of spike and wave complexes and sporadic spikes were detected dominantly in the left frontal cortex.

Needle electromyograms (day 5 of hospitalization): Measured at the right and upper and lower extremities. Although the number tended to be low overall, no abnormality was detected.

Peripheral nerve conduction velocity (day 5): Although it was within the normal range, taking age into consideration, a reduction tendency was found in the lower extremity MCV and the upper and

lower extremities SCV distal positions.

Harvey-Masland test: Waxing was found even with 10 Hz or higher. It was evaluated as normal.

Ophthalmologic search: The visual acuity was 1.5 in both eyes. No abnormality was detected in the eyeground and optic nerves. It was considered an adjustment disorder induced by the constricted pupils and cycloplegia.

Schellong test: Orthostatic hypotension (−)

<Progress after admission>

Endotracheal intubation and venous infusion of diazepam 10 mg were conducted immediately. After intubation, blood gas findings were FiO_2 0.5, pH 7.432, PO_2 90.7, PCO_2 27.6. At 1:50, a respiratory apparatus was applied and forced respiration was started. From 2:20 onwards, the patient nodded his head when called. Because his spontaneous respiration became stable at 2:50, the respiratory apparatus was removed. At 3:30, the patient could communicate by writing such his address and name on a sheet. At 3:50, the tube was removed. From 5:00, the patient could engage in simple conversation.

At 10:00, blood pressure was 130/80 mmHg and pulse was 90/min. The patient was drowsy (E3V4M6). Full and smooth ocular movement, nystagmus (−), normal facial sense, masseteric muscular strength 5/5, orbicularis oculi muscle 5/5, orbicularis oris muscle 5/5, normal taste sensation, normal auditory power, buzzing in the ears (−), dizziness (−), Weber test: midline, Rinne: +/+. Favorable lifting of the soft palate, sternocleidomastoid muscle strength 5/5, trapezius muscle strength 5/5, lingual atrophy (−), normal tongue protrusion, tongue deviation (−), marked fasciculation in the tongue and orbicularis oris muscle, articulation disorder (+), nasal speech, deglutition disorder (+) with choking over both food and water. The extremities/body trunk: Muscle atrophy (−), fasciculation (+) in the triceps brachii muscle. Muscle tone: Flaccid in the extremities. Muscular strength: Normal. Deep reflex: Complete disappearance. Coordinated motion: Full range of diadochokinesis. Finger/nose test, pastern/knee test: Dysmetria (−), decomposition (−). Standing and walking: Impossible. Senses: No abnormality in heat, pain, touch, and vibration senses. Vesicorectal disorder (−).

Subsequently, although the consciousness disorder was relieved gradually, it persisted for 7 days (the drowsy state persisted for 4 days and prolonged sleep time and attentiveness disorder persisted until day 7). No problem was found in highly ranked functions such as attentiveness, counting, and memory. Atropine was administered until day 3 because bradycardia was severe and the drug could not be used then.

The pupils constricted for 5 days and then opened gradually. On day 2 of hospitalization, although the patient responded to atropine eye drops, the effect disappeared 24 hr later. On day 5, the pupil abnormality disappeared completely.

The bradycardia disappeared on day 5, but subsequently, non-escape rhythm multifocal PVC

occurred frequently and decreased gradually. The cardiac echography taken around the same time showed a reduction in the constriction, although it was within normal range.

Although the deep reflex was absent for 3 days, it recovered and became normal on day 5.

At admission, fasciculation was observed over the entirely body, but 6 hr later it was observed only in the tongue, facial muscles, and triceps brachii muscle (it was the most marked in the tongue). On day 2, fasciculation was present only in the tongue and disappeared on day 14. The pharyngeal reflex was normalized on day 5 and oral intake became possible.

On day 5, because a numbness sensation occurred around the mouth, at the distal positions of the extremities, methycobal and Alinamin F were administered and the numbness disappeared 3 days later. Subsequently, no peripheral nervous disorder appeared.

Epileptic EEG abnormalities observed at the initial stage were relieved gradually. However, they were not confirmed to be normalized completely.

<Discussion>

We recognized nicotine receptor stimulation symptoms such as fasciculation, acute tachyarrhythmia, hypertension, hyperglycemia, urinary sugar, reduced neutral fat; muscarine receptor stimulation symptoms such as constricted pupils, increased secretion in the airway, bradycardia, and hypotension; and central nervous symptoms such as decreased level of consciousness, systemic spasm, articulation disorder, and deglutition disorder. Although the severities of these clinical symptoms are said to correlate well with serum and erythrocyte cholinesterase activity, in this case, the plasma ChE values was 21 and erythrocyte true ChE values decreased markedly to 0.1 or less, indicating a severe condition. There are two obvious differences between sarin poisoning and organophosphorous pesticide poisoning: (1) Sarin’s toxicity is so strong that exposure to even small amounts can become lethal because spontaneous recovery of acetylcholine is completely absent and ageing is extremely rapid, and (2) sarin is volatile and aspirated from the skin, eyes, and mucous easily. Thus, even in cases in which the cholinesterase value does not decrease much and the systemic symptoms are mild, very strong local symptoms such as constricted pupils are detected. The finding of prolonged constricted pupils is considered evidence of exposure to sarin. In this case, because a causative chemical was unknown at the initial stage of the disease and diazepam and atropine administered for systemic management enabled symptom relief, other special treatments were not conducted.

5. Analysis of ocular symptoms

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At midnight on June 27, 1994, an acute gas poisoning attack that appeared to have been caused by an organic phosphorus compound occurred, resulting in seven deaths and 200 persons or more with severe or mild symptoms. In this document, we report the results of our investigation into the major ocular symptoms reported in 49 cases of the victims who were seen at the Department of Ophthalmology, Shinshu University Hospital, eye clinics in Matsumoto City, and ophthalmologic departments of nearby medical institutions.

1. Methods

We were provided the clinical investigation sheets by the Hospital/Clinic Liaison Conference for “toxic gas poisoning attack” and medical care records in 49 cases from medical institutions, including the Department of Ophthalmology, Shinshu University Hospital, Mimura Eye Clinic, Nakamura Eye Clinic, Minsodo Nonaka Eye Clinic, Hatakeyama Eye Clinic, Hirabayashi Eye Clinic, Koide Eye Clinic, and the Department of Ophthalmology, Japanese Red Cross Society Toyoshina Hospital; we then summarized the information provided.

2. Results

Regarding the number of persons seen at individual medical institutions, the referral patients were mostly seen in the Department of Ophthalmology, Shinshu University Hospital, and the outpatients were mainly seen at the eye clinics in Matsumoto City (Table 1).

Regarding the first medical examination, on June 28, 10 persons with relatively mild ocular symptoms as a major symptom visited the outpatient section of the Department of Ophthalmology, Shinshu University Hospital, the eye clinics in Matsumoto City, and the ophthalmologic departments of nearby medical institutions. On June 30, 8 persons visited these clinics. After that, few people have visited the outpatient sections or clinics. During the period between July 1 and July 13,

relatively severe patients who were hospitalized at hospitals in the city or visited there after the attack were referred to the outpatient sections. On July 20, one person who visited a hospital in the city as an outpatient immediately after the attack visited the outpatient section or clinic. After that date, no person received the first medical examination. The total number of outpatients was 32 and the number of referral patients was 17. A total of 49 persons received ophthalmologic medical care (Table 2).

With regard to visiting other medical institutions to receive medical care, 28 persons received only ophthalmologic care, five persons visited outpatient sections or clinics for internal medicine complaints as well as ophthalmologic care, and 16 persons received ophthalmologic care after being hospitalized at internal medicine departments of other hospitals (Table 3).

The number of visits to the ophthalmologic department was once for 28 persons, twice for 11, three times for six, four times for three, and five times for one. Most subjects received medical care once or twice (Table 4).

Regarding age and sex of the persons visiting the hospitals or clinics, the number of the males aged 10–69 was large. It was reported that although the gas exposure was presumed to be uniform, the symptoms seen in children and elderly persons were relatively mild (Table 5).

With regard to subjective ocular symptoms, persons who visited hospitals or clinics immediately after the attack mainly complained about darkened vision, eye hyperemia, itchy eyes, and a narrowed visual field. Some patients reported that the hyperemia became stronger 12 hr later rather than immediately after the attack. Some of the more-severe patients who were hospitalized at the department of internal medicine reported ciliary pain, such as ocular pain, when seeing a strong light or near objects, lack of focus, reduced adjustment power such as unclear near sight, and eye fatigue. In addition, eye floaters were reported by four patients, and some patients said that they could not see well upward; this symptom appeared similar to the upward gaze disorder seen in chronic organophosphate poisoning (Table 6).

Regarding systemic symptoms apart for ocular symptoms, patients who visited only the ophthalmologic department or clinic reported a runny nose and throat pain. The patients who visited departments of internal medicine at other hospitals or clinics or were hospitalized for a short time experienced nausea, headache, numbness in the feet and hands, pyrexia, and sweating. The severe patients who were hospitalized for a long period displayed lowering/loss of consciousness, coma, difficulty in breathing, and spasms (Table 7).

Regarding clinical findings, most of the patients who visited the outpatient sections immediately after the attack had markedly constricted pupils with diameters of 1.0–2.0 mm.

Regarding the pupil diameter on different visit days, most of the patients who received an initial examination by day 3 after the attack had marked constriction with a diameter of 1.0–2.0 mm. The following week, referral patients from other medical institutions in the city displayed pupil diameters

of 3.0 mm or more. In the patients with relative severe systemic symptoms who had been hospitalized, the diameter was 3.0–3.5 mm. On day 4, pupil diameter expanded to 2.5 and 3.0 mm in the patients who had visited hospitals or clinics on the day following the attack and whose pupil diameters had been 1.0 and 1.5 mm (Table 8).

With regard to the total number of patients seen and pupil diameter, the diameter increased gradually over time. On June 28, pupil diameter was 1.0–1.5 mm in most patients. The following day, pupil diameter was 2.0 mm in most patients. On day 3, pupil diameter ranged between 1.5 and 3.0 mm, a wide dispersion. The following week, pupil diameter expanded to 3.0 mm in the patients who had experienced markedly constricted pupils (Table 9).

Conjunctival hyperemia was observed in 21 patients. The symptom was mostly found by day 3, and disappeared the following week (Table 10).

Regarding visual acuity, an acuity of 0.7 or less was found in four eyes. Poor visual acuity was seen in patients with other concomitant ocular diseases, such as cataracts. Most patients had visual acuity of 1.0 or higher (Table 11).

Regarding the visual field, dynamic quantitative measurement of the visual field (Goldmann perimetry) was conducted in 16 patients. The results were afferent constriction of the visual field in two patients and mild constriction of the visual field in five; these were measured within 4 days after the attack. In the patients who had considerable constriction of the visual field on June 28, the measurement conducted the next day revealed that the pupil diameter did not change markedly but constriction of the visual field was mitigated considerably (Table 12).

Fig. 1 shows data of a man aged 24 who displayed afferent constriction of the visual field on June 28. By the next day, the afferent constriction had been mitigated considerably. However, the pupil diameter did not change and remained at 1.5 mm. We presumed that the constriction of the visual field may have occurred owing to some retinal disorder.

In addition, when static quantitative measurement of the visual field by automatic perimeter was conducted in 16 patients, three patients were diagnosed with afferent constriction of the visual field and reduced retinal sensitivity and four patients diagnosed with mild constriction. On day 3 or later, most cases had a normal visual field (Table 13).

Fig. 2 shows the visual fields in a man aged 50 who was almost normal and another man aged 46 who had constriction. In the man aged 46, the center of the visual field became pale in the contrasting density, around which became dark, indicating afferent constriction of the visual field and reduction in the retinal sensitivity. In the man aged 50, the overall visual field was clear and the sensitivity was almost normal.

Regarding changes in the refractive power, no pattern was found because some cases presented as far-sighted and other cases presented as near-sighted at the initial examination (Table 14).

With regard to intraocular pressure, in most patients, the pressure was lower at the initial

examination than at re-examination. It was presumed that because outflow resistance of the aqueous fluid may decrease due to markedly constricted pupils, the intraocular pressure may have decreased (Table 15).

Regarding flicker value, a slight reduction was present in some cases; a great reduction was absent (Table 16).

For markedly constricted pupils, when Mydrin P eye drops and adrenaline eye drops were administered as mydriatic agents, favorable pupillary dilatation was obtained with Mydrin P, whereas it did not occur with adrenaline. Although one person had poor pupillary dilatation by Mydrin P, the reason was presumed to be because the patient had received the examination at 6:00 on June 28, only a short time after the exposure. The patient responded to atropine and intermediate pupillary dilatation was obtained. In the victims who reported ciliary pain, atropine and Mydrin P eye drops relieved the ciliary pain markedly (Table 17).

Regarding other clinical findings, there were two persons with punctuate keratoconjunctival erosion; the details were unknown because the eyeground was constricted. Partial optic atrophy was also detected in both cases. In the other cases, no abnormality was found in the optic papilla and retinal posterior fundus, which could be observed visually.

Regarding chromatic vision, a panel D-15 test was conducted in one person, and the result was normal.

Regarding treatments, there were 30 persons who did not receive treatment but were followed up only, 13 patients who received the eye drops, and six patients who received both oral drugs and eye drops. Breakdown of the eye drops were steroids in 15 persons, corneal protective agents in six, mydriatic agents in four, antibiotics in three, antiphlogistics in one, and contractile agents of the conjunctival blood vessels in one. Oral drugs were vitamin B12 and exogenous enzymes in six persons (Table 18).

Ocular symptoms and systemic symptoms were summarized in different severities. In the mild cases of the patients who visited only ophthalmologic departments or sections, an ocular symptom was darkened vision and systemic symptoms were a runny nose and sore throat; clinical findings were constricted pupils and hyperemia. In the patients with severe symptoms, constriction of the visual field was noticed, and afferent constriction was detected by measurement of the visual field. In the patients who had systemic symptoms such as headache, nausea, sweating, numbness in the feet and hands, and who had visited internal medicine departments or sections, frequent complaints were ciliary pain and an oppressive feeling at near vision. In the severe patients had symptoms such as lowering/loss of consciousness, coma, difficulty in breathing, and spasms, and who were hospitalized in departments of internal medicine, many patients experienced strong ciliary pain and persistent constricted pupils.

Even in victims of the gas poisoning whose cholinesterase values hardly decreased and whose

systemic symptoms were mild, local symptoms in the anterior eye part such as constricted pupils and conjunctival hyperemia were found as initial symptoms. It was presumed that the organic phosphorus compound may have been absorbed easily in the cornea and tunica conjunctiva. Moreover, ocular symptoms such as constriction of the visual field and ciliary pain appeared in tandem with exacerbation of the systemic symptoms.

In this review, we summarized the clinical investigation sheets by the Hospital/Clinic Liaison Conference for “toxic gas poisoning attack” and the medical care records in 49 persons which were provided by the medical institutions. According to the questionnaires, in addition to the 49 persons, more than 10 other persons reported visiting ophthalmologic departments or sections. Thus, further follow-up investigations may be necessary.

3. Summary

In summarizing the ocular symptoms reported by patients, many of the patients who visited only ophthalmologic department or section complained about darkened visions, and presented with constricted pupils and hyperemia. When the symptoms increased, constriction of the visual field was noticed subjectively, and afferent constriction of the visual field was detected by clinical measurement. In the intermediate or severe patients who visited internal medicine departments or were hospitalized, the constricted pupils persisted over a relatively long time, accompanied by ciliary pain and an oppressive feeling at near sight.

VI. Causative substance analysis results

Matsumoto Healthcare Center
Environment Pollution Section, Living Environment Department, Nagano Prefecture

1. Document announced on June 30

2. Document announced on July 3, and its supplement

Document publicly announced on June 30

Examination results of samples collected after the poisoning attack in Matsumoto City

The examination results after the poisoning attack in Matsumoto City on June 27, 1994, are as follows:

Description

1. Purpose of the examinations

To understand the extent of contamination by examining parameters such as water quality around the spot of the attack. We investigated standard environmental parameters based on the Basic Environment Act.

2. Collected samples

(1) Water from pond 1 near the spot of the attack (as shown in the map attached separately).
(2) Water from pond 2 near the spot of the attack (as shown in the map attached separately).
(3) Underground water that is raw water for pond 2 near the spot of the attack (as shown in the map attached separately).
(4) Indoor air from a house near the spot of the attack (as shown in the map attached separately).
(5) Air from the garden of a house near the spot of the attack (as shown in the map attached separately).

3. Facilities where the examinations were implemented

Nagano Research Institute for Health and Pollution
Matsumoto Healthcare Center

4. Examined items and results

As shown in the separate sheet

Results of the measurement of water quality

Items	Measured value			Standard value	Measurement facility	Remark
	Pond 1	Pond 2	Underground water (raw water of pond 2)			
Date of collection	June 28, 1994	June 28, 1994	June 28, 1994			
Time of collection	9:25 11:00	11:25	11:45		MHC NRIHP	
Water temperature	15.6°C 16.5°C	16.2°C	14.6°C		MHC NRIHP	
pH	6.9 6.71	6.90	6.88	5.8 – 8.6 [1)]	MHC NRIHP	
Transparency	>30 >30	>30	>30		MHC NRIHP	
Electric conductivity	306 μS/cm	315μS/cm	290 μS/cm		NRIHP	
Residual chlorine	<0.1 mg/l <0.1 mg/l	<0.1 mg/l			MHC NRIHP	
Chlorine ion	15 mg/l	15 mg/l	15 mg/l	200 mg/l or less [1)]	NRIHP	
Sulfate ion	26 mg/l	28 mg/l	25 mg/l		NRIHP	
Nitrate-nitrogen	5.4 mg/l	5.4 mg/l	6.5 mg/l	10 mg/l or less [1)]	NRIHP	
Phosphate-phosphorous	0.093 mg/l	0.11 mg/l	0.077 mg/l		NRIHP	
Zinc	<0.05 mg/l	<0.05 mg/l	<0.05 mg/l	1.0 mg/l or less [1)]	NRIHP	
Aluminum	<0.1 mg/l 0.057 mg/l	0.020 mg/l	0.001 mg/l	0.4 mg/l or less [2)]	MHC NRIHP	
Cyanide ion	<0.1 mg/l	<0.1 mg/l	<0.1 mg/l	N.D. [3)]	NRIHP	
Whole cyanogens	N.D. *			N.D. [3)]	MHC	

Methylene chloride	N.D.			0.02 mg/l or less [3)]	MHC	Solvent
Carbon tetrachloride	N.D.			0.002 mg/l or less [3)]	MHC	Solvent, bug repellent
1,2Dichloroethane	N.D.			0.004 mg/l or less [3)]	MHC	Raw material of resin, solvent
1,1-Dichloroethylene	N.D.			0.02 mg/l or less [3)]	MHC	Raw material of resin
cis-1,2-Dichloroethylene	N.D.			0.04 mg/l or less [3)]	MHC	Solvent
1,1,1-Trichloroethane	N.D.			1 mg/l or less [3)]	MHC	Dry cleaning, solvent

MHC: Matsumoto Healthcare Center

NRIHP: Nagano Research Institute for Health and Pollution

*N.D.: Not detected

1) Standard of water quality based on the Water Supply Act

2) Standard of comfortable water quality based the Water Supply Act

3) Environmental standard

4) Indicator values of necessary monitored items

5) Target values for maintenance of water quality

6) Old environmental standards (total value of EPN, parathion, methyl parathion, and methyl demeton)

Results of the measurement of water quality

Items	Measured value			Standard value	Measurement facility	Remark
	Pond 1	Pond 2	Underground water (raw water of Pond 2)			
1,1,2-Trichloroethane	N.D.			0.006 mg/l or less [3)]	MHC	Solvent, raw material
Trichloroethylene	N.D.			0.03 mg/l or less [3)]	MHC	Solvent, cleanser
Tetrachloroethylene	N.D.			0.01 mg/l or less [3)]	MHC	Dry cleaning, cleanser
1,3-Dichloropropene	N.D.			0.002 mg/l or less [3)]	MHC	Soil fumigant, pesticide
Benzol	N.D.			0.01 mg/l or less [3)]	MHC	Solvent
Simazine	N.D.			0.003 mg/l or less [3)]	MHC	Herbicide
Thiobencarb	N.D.			0.02 mg/l or less [3)]	MHC	Herbicide
Chloroform	N.D.			0.06 mg/l or less [4)]	MHC	Raw material, disinfectant, solvent
trans-1,2-Dichloroethylene	N.D.			0.04 mg/l or less [4)]	MHC	Solvent

1,2-Dichloropropane	N.D.			0.06 mg/l or less [4)]	MHC	Solvent, raw material
p-Dichlorobenzene	N.D.			0.3 mg/l or less [4)]	MHC	Pesticide, deodorizer
Isoxathion	N.D.	N.D.	N.D.	0.008 mg/l or less [4)]	MHC, NRIHP	Pesticide
Diazinon	N.D.	N.D.	N.D.	0.005 mg/l or less [4)]	MHC, NRIHP	Pesticide
Fenitrothion (MEP)	N.D.	N.D.	N.D.	0.003 mg/l or less [4)]	MHC, NRIHP	Pesticide
Isoprothiolane	N.D.			0.04 mg/l or less [4)]	MHC	Disinfectant
Chlorothalonil (TPN)	N.D.			0.04 mg/l or less [4)]	MHC	Disinfectant
Propyzamide	N.D.			0.008 mg/l or less [4)]	MHC	Herbicide
EPN	N.D.	N.D.	N.D.	0.006 mg/l or less [4)]	MHC, NRIHP	Pesticide
Dichlorvos (DDVP)	N.D.	N.D.	N.D.	0.01 mg/l or less [4)]	MHC, NRIHP	Pesticide
Fenobucarb (BPMC)	N.D.			0.02 mg/l or less [4)]	MHC	Pesticide
Iprobenfos (IBP)	N.D.	N.D.	N.D.	0.008 mg/l or less [4)]	MHC, NRIHP	Disinfectant

Chloronitrofen (CNP)	N.D.			0.005 mg/l or less [4)]	MHC	Herbicide
Toluene	N.D.			0.6 mg/l or less [4)]	MHC	Dye, pigment
Xylene	N.D.			0.4 mg/l or less [4)]	MHC	Dye, pigment
Isofenphos	N.D.	N.D.	N.D.	0.001 mg/l or less [5)]	MHC, NRIHP	Pesticide
Chlorpyrifos	N.D.	N.D.	N.D.	0.004 mg/l or less [5)]	MHC, NRIHP	Pesticide
Trichlorfon (DEP)	N.D.			0.03 mg/l or less [5)]	MHC	Pesticide

MHC: Matsumoto Healthcare Center

NRIHP: Nagano Research Institute for Health and Pollution

*N.D.: Not detected

1) Standard of water quality based on the Water Supply Act

2) Standard of comfortable water quality based the Water Supply Act

3) Environmental standard

4) Indicator values of necessary monitored items

5) Target values for maintenance of water quality

6) Old environmental standards (total value of EPN, parathion, methyl parathion, and methyl demeton)

Results of the measurement of water quality

Items	Measured value			Standard value	Measurement facility	Remark
	Pond 1	Pond 2	Underground water (raw water of pond 2)			
Pyridaphenthion	N.D.	N.D.	N.D.	0.002 mg/l or less [5)]	MHC, NRIHP	Pesticide
D-D (1,3-Dichloropropene)	N.D.			0.002 mg/l less [5)]	MHC	Pesticide
Parathion	N.D.	N.D.	N.D.	0.1 mg/l or less[6)]	MHC, NRIHP	Pesticide
Methyl parathion	N.D.			0.1 mg/l or less [6)]	MHC	Pesticide
Malathion	N.D.				MHC	Pesticide
Methyl demeton	N.D.	N.D.	N.D.	0.1 mg/l or less[6)]	MHC, NRIHP	Pesticide
Iprodione	N.D.			0.3 mg/l or less[5)]	MHC	Disinfectant
Etridiazole	N.D.			0.004 mg/l or less [5)]	MHC	Disinfectant
Captan	N.D.			0.3 mg/l or less [5)]	MHC	Disinfectant
Quintozene (PCNB)	N.D.			0.01 mg/l les [5)]	MHC	Disinfectant
Chloroneb	N.D.			0.05 mg/l less [5)]	MHC	Disinfectant
Tolclofos-methyl	N.D.	N.D.	N.D.	0.08 mg/l less [5)]	MHC, NRIHP	Disinfectant
Flutolanil	N.D.			0.2 mg/l less [5)]	MHC	Disinfectant
Pencycuron	N.D.			0.04 mg/l less [5)]	MHC	Disinfectant
Mepronil	N.D.			0.1 mg/l or less [5)]	MHC	Disinfectant

Simetryn	N.D.			0.06 mg/l or less [5)]	MHC	Herbicide
Terbucarb (MBPMC)	N.D.			0.02 mg/l or less [5)]	MHC	Herbicide
Napropamide	N.D.			0.03 mg/l or less	MHC	Herbicide
Butachlor	N.D.			0.002 mg/l or less[5)]	MHC	Herbicide
Butamifos	N.D.			0.004 mg/l or less[5)]	MHC	Herbicide
Bensulide (SAP)	N.D.			0.1 mg/l or less [5)]	MHC	Herbicide
Benfluralin	N.D.			0.08 mg/l or less [5)]	MHC	Herbicide
Pendimethalin	N.D.			0.05 mg/l or less [5)]	MHC	Herbicide
Methyldymron	N.D.			0.03 mg/l or less [5)]	MHC	Herbicide
Molinate	N.D.			0.005 mg/l or less [5)]	MHC	Herbicide

MHC: Matsumoto Healthcare Center

NRIHP: Nagano Research Institute for Health and Pollution

*ND: Not detected

1) Standard of water quality based on the Water Supply Act

2) Standard of comfortable water quality based on the Water Supply Act

3) Environmental standard

4) Indicator values of necessary monitored items

5) Target values for maintenance of water quality

6) Old environmental standards (total value of EPN, parathion, methyl parathion, methyl demeton)

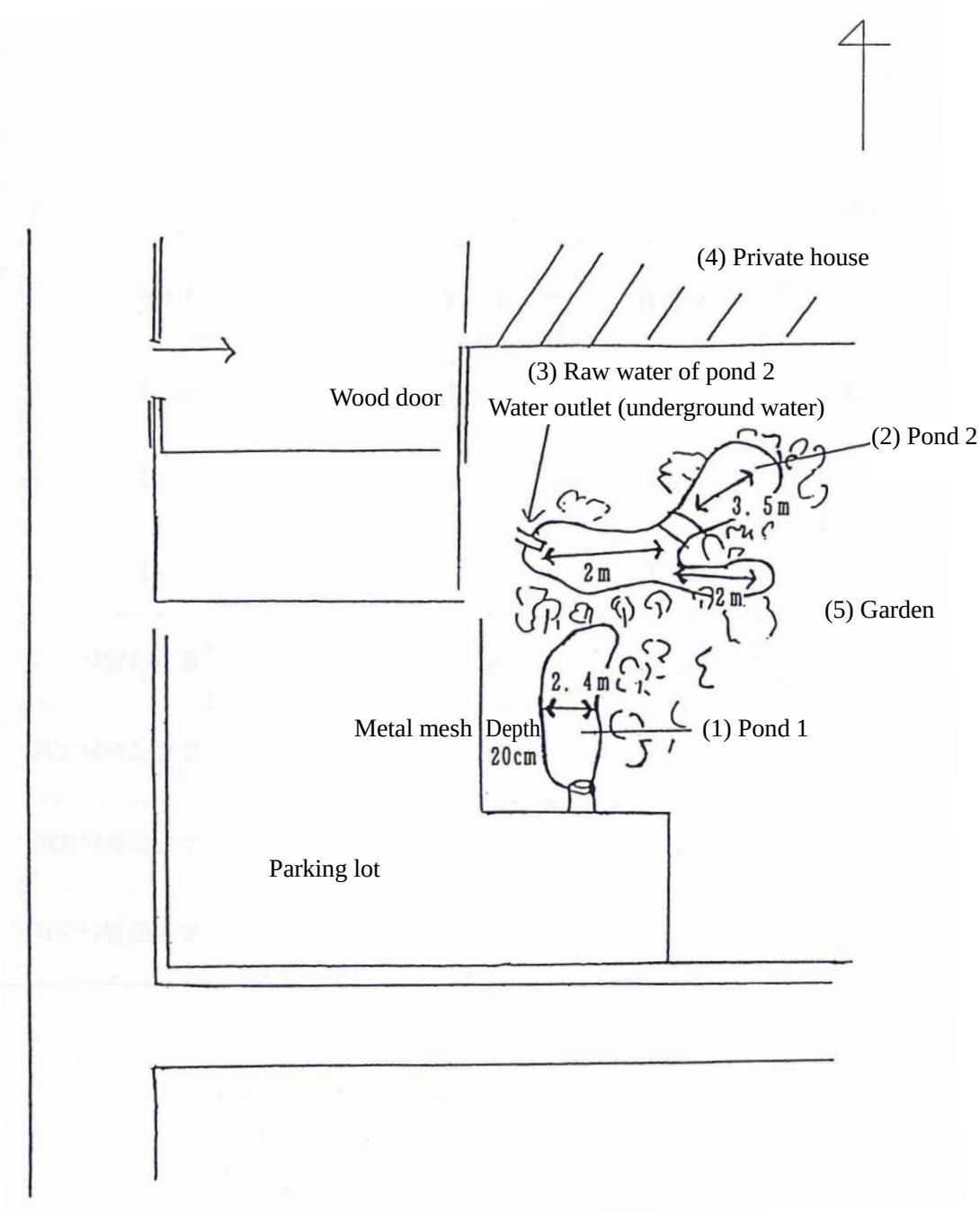
Results of the measurement of the air

Items	Measured value		Standard value	Measurement facility	Remarks
	Indoor	Garden			
Ammonia	N.D.	N.D.		NRIHP	Specific substances based on the Article 17-1 of the Air Pollution Control Act
Methanol	N.D.	N.D.		NRIHP	
Hydrogen sulfide	N.D.	N.D.		NRIHP	
Sulfur dioxide	N.D.	N.D.		NRIHP	
Carbon bisulfide	N.D.	N.D.		NRIHP	
Carbon dioxide	N.D.	N.D.		NRIHP	
Benzol	N.D.	N.D.		NRIHP	
Pyridine	N.D.	N.D.		NRIHP	
Methyl mercaptan	N.D.	N.D.		NRIHP	
Trichloroethylene	N.D.	N.D.	250 μg/m^3 1)	NRIHP	
Tetrachloroethylene	N.D.	N.D.	250 μg/m^3 1)	NRIHP	

NRIHP: Nagano Research Institute for Health and Pollution

1) Air-environmental indicator (provisional value)

Sketch map of sample collection points



Document announced on July 3

Detection of a substance that was presumed to be the causative substance of the poisoning attack in Matsumoto City

The substance that was presumed to be the causative substance of the poisoning attack in Matsumoto City on June 27 was detected as follows:

Description

1. Cause of examinations

On June 30, in relation to the poisoning attack, examination results such as the environmental standards were made public. Subsequently, an investigation into the causative substance of the attack had been initiated.

2. Samples that were examined (collected on June 28)

(1) Water from a pond near the spot of the attack (shown in the map attached separately).

(2) Air from a house near the spot of the attack (shown in the map attached separately).

3. Facility implementing the examinations

Nagano Research Institute for Health and Pollution

4. Examination results

A substance that was presumed to be sarin was detected.

Supplement

The water collected from the pond was extracted by solvent and analyzed by a gas chromatograph mass spectrometer. From the following findings, the substance was presumed to be sarin.

1. The mass spectrum obtained from the peak of the chromatogram was compared with those from a library. The result showed it to be identical to sarin.

2. Measurement by chemical ionization method demonstrated that the molecular weight of the substance at the peak was identical to that of sarin.

3. Retention index of the peak was compared with the retention index of sarin, the reference value. The indices were identical.

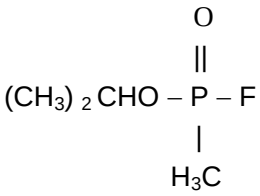
Public announcement by the Environment Pollution Section, Living and Environment Department, Nagano Prefecture

Sarin

1. Name and structure

Sarin $C_4H_{10}FO_2P$

Methylphosphonofluoridic acid l-methylethyl ester



2. Nature

Molecular weight	140.09
Gravity	1.10
Fusing point	-57°C
Boiling point	147°C/one air pressure

Although the substance is liquid at ordinary temperatures, it evaporates easily.

3. Toxicity

This substance has a parasympathomimetic effect (fatigue, headache, dizziness, vomiting, diarrhea, excessive sweating, constructed pupils, clouded consciousness, and systemic spasms) caused by cholinesterase inhibition similar to organophosphate agents.

In addition, this substance is characterized by the low natural recovery capacity of cholinesterase.

Lethal amount for humans: 0.01 mg/kg

Reference: The Merck Index
Iwanami physics and chemistry dictionary the 4th version (Iwanami Shoten)
Hiroshi Naito. Poisoning dictionary (Nankodo)

Annex 2

Health Crisis Management System in Matsumoto City

A study on health and medical actions and crisis management system after sarin exposure

Health and Hygiene in Matsumoto City
Separate volume
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Matsumoto City Council of Community-Based Integrated Care
Matsumoto City

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Ophthalmology, Shinshu University School of Medicine)

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Chapter 4: Documents

Matsumoto sarin attack reviewed in the research papers

* partially translated.

Significance of activities by Matsumoto City Council of Community-Based Integrated Care during and after the sarin attack

Nobuo Yanagisawa
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Former Chair of the Expert Committee on Medical Cares Against Toxic Gas Poisoning Attack

More than 50 years have passed since sarin was developed as a chemical weapon. The chemical is so dangerous that it has not been used in actual wars, although there is some evidence of it being used as a weapon during the Iran-Iraq War. The toxicity of sarin, an organic phosphorus chemical, to humans has barely been determined. Its action was clarified for the first time in the Matsumoto sarin attack.

The attack caused substantial damage, including loss of seven lives and many victims who are experiencing mild aftereffects even today. We have learnt much about medical aspects and the regional emergency medical system from this experience.

1. Medical knowledge regarding sarin toxicity

Sarin inhibits acetylcholinesterase as an acetylcholine-degrading enzyme by binding the enzyme, resulting in excess acetylcholine within the nervous system. Acetylcholine is an important substance for normalizing various nervous responses, including muscle movement, respiration, digestion, and consciousness. Since sarin disturbs these nervous actions, it is called a nerve agent.

The symptoms of sarin poisoning observed during the Matsumoto and Tokyo subway sarin attacks were the same as those noted during organophosphorus pesticide poisoning in the 1950s. However, because sarin, as a chemical weapon, is designed to be a fatal toxin, it caused immediate deaths through respiratory paralysis and loss of consciousness, as well as caused severe poisoning, resulting in coma and a convulsive state. Characteristically, the effects of sarin exposure could be recovered with appropriate treatments rapidly and without aftereffects even in the most severely affected patients.

2. Disaster countermeasures and the Matsumoto City Council of Community-Based Integrated Care

The Matsumoto City Council of Community-Based Integrated Care was a relatively inactive coordination body comprising the Matsumoto City government, as well as the Matsumoto Healthcare Center, Matsumoto City Medical Association, Matsumoto City Dental Association, Matsumoto Pharmaceutical Association, and the Shinshu University Hospital. Its previous activities were not particularly vigorous, and the council appeared to be just a liaison organ.

In Japan, emergency action strategies have been absent for a long period because of various factors including topographic conditions, ethnic homogeneity, a uniformly high standard of living, long-persisting peace, and a pervading social idea of individualism accompanied by mutual nonintervention during ordinary life. During the three recent crises, the Matsumoto sarin attack, the Great Hanshin-Awaji Earthquake, and the Tokyo subway sarin attack, the Japanese emergency action system has been tested, with many lessons being learned. The response to the Matsumoto sarin attack can be said to have demonstrated noteworthy results, in that the local government and medical staffs gave a proper response at various important time points to minimize acute victim injuries, alleviate resident health anxiety, and minimize mental aftereffects. On the other hand, civil rights violations did occur, which cast a great shadow over the response. This attack served as a major lesson to reflect on the social immaturity observed across the nation, as well as the responsibility of the police and media.

3. Response to the Matsumoto sarin attack

a. Emergency activities

The first noteworthy aspect of emergency activities at the epicenter of the sarin gas attack was the effective doctor-car activities. Doctor-cars acted promptly, with physicians in the vehicles conducting appropriate triage, thus minimizing human suffering caused by the poisoning attack. Triage, which is an emergency activity performed during large-scale disasters, is work where physicians promptly evaluate the necessity of life-saving medical treatment in individual victims and determine treatment and transfer procedures. In the Matsumoto sarin attack, except for one victim who presented a cessation of heartbeat and breathing on hospital arrival and therefore suffered brain damage due to oxygen insufficiency, all other victims recovered without aftereffects. The most severely affected victim, presenting with repeated systemic convulsions and deep coma, regained consciousness several hours later because of appropriate treatment despite any precedent in conventional toxicological knowledge. This experience was applied to the Tokyo subway sarin attack, which occurred 6 months later.

Medical institutions in Matsumoto City were so busy conducting emergency activities during the night of June 27 that mutual contact was impossible. However, post hoc investigation revealed that although the causative substance was unknown at the time, all hospitals independently suspected organophosphate poisoning and treated the victims appropriately. During the first 24 hours after the attack, a large doses of atropine sulfate was administrated, again without precedent in conventional medical knowledge. Thus, academically precious knowledge was obtained and the high quality and skill of medical institutions in Matsumoto City was demonstrated.

On June 30, three days after the attack, it was decided to establish a consultative system among the related medical institutions. Generally speaking, medical institutions tend strongly to conduct

their own medical activities. Thus, at the beginning, there was uncertainty regarding the liaison organ involvement and function after the acute phase post-attack. However, the organ was positioned as the Hospital/Clinic Liaison Conference under the Council of Community-Based Integrated Care, and their work led to achievements documented in poisoning survey reports and contributed to the generation of follow-up health survey and medical consultation project basic documentation, both of which were then conducted continuously. These achievements were in sharp contrast with the medical activities related to the Tokyo subway sarin attack, which at present (5 years after the attack) has only generated a few reports, from individual medical institutions.

b. Response by the local government

When I considered the health damage affected all over the region from my viewpoint as a physician, the most important things were to eliminate any anxiety held by residents regarding their future health and to detect any disorder which may be overlooked in ordinary medical activities and treat them. To implement this in detail, it was necessary to conduct medical checkups in residents during the initial stages of any disaster, subsequent regular examinations of any victims in whom aftereffects are suspected, and any necessary medical care. When this is properly implemented, it may be possible to eliminate resident anxiety regarding future health and limit post-traumatic stress disorders (PTSDs). For this object, financial support as well as a close link between the government and medical institutions are necessary.

Given this, the actions of Matsumoto City were extremely appropriate from the initial stages. On June 28, the day after the attack, residents with anxiety concerning the disaster were recommended to receive medical checks at any medical institution at the government's expense. This was the action of an autonomous body designed to maintain resident health outside the system, and continued in the form of repeated questionnaires, health consultations, explanatory meetings, and informational activities for the residents, which increased resident security and the reliability of the government. Medical examinations in some victims with aftereffects identified during the medical checkups were conducted regularly at the Shinshu University Hospital who provided various accommodations.

As the result, PTSD incidence was limited to only a few victims. In addition, mild cardiac or nervous abnormalities identified in several victims during the acute stage did not disturb their quality of life, although they are still carefully followed up at present.

4. Epidemiological survey

Because the toxic gas attack occurred at midnight in the residential area, it was extremely important to conduct epidemiological surveys regarding the affected situation, symptoms, progress, and distribution of the toxin. In the aftermath of the Matsumoto sarin attack, Dr. Tamie Nakajima

(Nasu), a lecturer at the Department of Public Health, Shinshu University School of Medicine, with others, had conducted many surveys in cooperation with Matsumoto City and the Matsumoto Healthcare Center. The results were reported in English-language international medical journals. Taking the situation on the ground, the house structures, and the weather conditions into consideration, the survey reports regarding the secondary damages of the rescue team on the day of the attack provided precious information about a proper rescue system for sarin poisoning.

5. Contribution to the Tokyo subway sarin attack and others

At the Tokyo subway sarin attack in March 1995, the prompt supply of information from Shinshu University and others greatly helped medical institutions in Tokyo who treated the victims. This was greatly appreciated by many of the involved medical institutions and was highly regarded internationally.

The basis of this provided information was the report on surveys of the toxic gas poisoning in Matsumoto City. This report covered various activities such as medical care and local administration, and toxicology-related information in the Matsumoto sarin attack. It started to be prepared in the autumn of last year and was completed in March. The high quality of this report, which differed from ordinary reports regarding this type of case, was because the medical and epidemiological reports concerning the poisoning, as well as reports regarding the activities of various organs and institutions, were provided by all the involved medical and research institutions and then summarized. This work was conducted by the Expert Committee on Medical Cares Against Toxic Gas Poisoning Attack, which was part of the Matsumoto City Council of Community-Based Integrated Care. This report was a product of the competence of the organizational response to this attack.

This poisoning survey report was then translated into English by an American government agency. In addition, the report concerning the medical activities during the Matsumoto sarin attack was presented at the international conference on biological and chemical terrorism held in a suburb of Washington DC in July 1995, and at the end of the lecture, it was highly regarded with a standing ovation.

The risk that biological and chemical weapons will be used outside of warfare is still present, and internationally, the matter has been discussed mainly at the United Nations. In Japan, the matter is positioned as a subject that must be handled through welfare scientific research by the Ministry of Health and Welfare.

The abhorrent sarin poisoning attack in Matsumoto City deprived seven precious lives and caused aftereffects in some victims. However, the records concerning medical and administrative activities conducted during and after the attack provides precious information regarding how relevant local organs and institutions must response and operate during a crisis, given that a national emergency response system is currently not established in Japan.

Progress of health surveys and medical checkups for the victims of toxic gas poisoning

Questionnaires			Medical checkups	
Times	Date	Contents	Date	Contents
1st, 3 weeks later	July 15–18, 1994	1. Subjects: 2,052 persons (1,002 households) 2. Respondents: 1,743 persons (84.9%) 3. Symptoms Presence of subjective symptoms just after the attack: 468 persons Presence of subjective symptoms three weeks later: 129 persons	July 23–24, 1994	1. Subjects (persons desiring): 150 persons 2. Persons visiting hospitals: 155 persons 3. Examination results No abnormality: 96 persons Mild abnormality: 59 persons
2nd, 3 months later	October 20 – November 15, 1994	1. Subjects: 266 2. Respondents: 160 (60.2%) 3. Symptoms Persons noticing subjective symptoms: 55	September 29–30, 1994	1. Subjects: 45 2. Persons visiting hospitals: 13 (28.9%) 3. Examination results No abnormality: 13
3rd, 1 year later	June 23–30, 1995	1. Subjects: 2,052 2. Respondents: 1,237 (60.3%) 3. Symptoms Persons noticing subjective symptoms: 58	July 17–19, 1995	1. Subjects: 148 2. Persons visiting hospitals: 73 (49.3%) 3. Examination results No abnormality: 52 Mild abnormality: 21
4th, 1 year and 8 months later	February 9–17, 1996	1. Subjects: 108 2. Respondents: 75 (69.4%) 3. Symptoms Persons noticing subjective symptoms: 40	February 29 – March 1, 1996	1. Subjects: 121 2. Persons visiting hospitals: 29 (24.0%) 3. Examination results No abnormality: 15 Mild abnormality: 14

5th, 2 years and 8 months later	January 28 – February 7, 1997	1. Subjects: 2,000 2. Respondents: 836 (41.8%) 3. Symptoms Persons noticing subjective symptoms: 46	March 13–14, 1997	1. Subjects: 87 2. Persons visiting hospitals: 31 (35.6%) 3. Examination results No abnormality: 25 Mild abnormality: 6
6th, 3 years and 8 months later	February 17 – March 2, 1998	1. Subjects: 66 2. Respondents: 33 (50.0%) 3. Symptoms Persons with subjective symptoms: 23	March 19, 1998	1. Subjects: 15 2. Persons visiting hospitals: 10 (66.7%) 3. Examination results No abnormality: 6 Mild abnormality: 1 Presence of abnormality: 3
7th, 4 years and 8 months later	February 12 – March 1, 1999	1. Subjects: 387 2. Respondents: 175 (45.2%) 3. Symptoms Persons with subjective symptoms: 23	March 11–12, 1999	1. Subjects: 17 2. Persons visiting hospitals: 15 3. Examination results No abnormality: 8 Mild abnormality: 1 Presence of abnormality: 6 Consulting with the department of psychosomatic medicine
8th, 5 years and 1 month			August 25, 1999	1. Subjects: 10 2. Persons visiting hospitals: 2 3. Examination results No abnormality: 1 Presence of abnormality: 1

Health survey results (3rd–7th) – long-term effects of sarin poisoning –

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1. Introduction

The Health Survey Committee reported the effect of sarin exposure on the health during the acute stage of the Matsumoto sarin attack victims [1-3]. As there had been no previous report on the long-term effects of sarin on the human body, we conducted questionnaires and medical checkups regularly at the acute stage or later and investigated the effect on the health of the victims [4]. In this paper, we report the results of the medical checkups 1 year or later after the attack (the 3rd–7th health surveys).

2. Results of medical checkups for the victims of toxic gas poisoning in Matsumoto City (the 3rd–7th)

The 3rd-7th medical checkups were conducted at the Shinshu University Hospital, at 1 year and 8 months, 2 years and 8 months, 3 years and 8 months, and 4 years and 8 months after the attack. For internal medical and neurological checkups, Dr. Morita at the Third Department of Internal Medicine, conducted the 3rd medical checkup and I and others did the 4th-7th medical checkups. Ophthalmologic checkups were conducted by Dr. Nohara at the Department of Ophthalmology, Maruko Central Hospital. The medical checkups included history taking, internal medical, neurological, and ophthalmologic examinations, and when necessary, blood tests, electrocardiography, Holter electrocardiography, electroencephalography, nerve conduction velocity, plain radiography (Xp), CT, and MRI.

Details of the medical checkups are shown below. In this paper, severe cases are defined as having serum ChE values less than 25% of the normal lower limit at the acute stage and consciousness disorders. Intermediate cases are defined as having serum ChE values of 25% or more and less than 100% of the normal lower limit at the acute stage. Mild cases are defined as having the normal range of serum ChE at the acute stage or absence of the measurement, as well as only local symptoms, such as ocular or mucosal symptoms.

1) The 3rd (1 year after the attack) medical checkup

Implementation: July 17–19, 1995

Subjects: 154

Total number of people receiving the checkup: 72 (consultation rate: 46.8%)

People who had constricted pupils or a reduced ChE value at the acute stage.

People who desired to receive the medical checkup.

Results

Evaluation A: No abnormality associated with the poisoning attack (49 people)

Evaluation B: Although checkup and examination results were abnormal, the association with the poisoning is low (18 people)

Evaluation C: Presence of abnormality, which is suspected to be associated with the poisoning (5 people)

Breakdown of Evaluation C:

Electroencephalogram abnormality:	3 people
Peripheral nerve disorder (numbness in the hands and feet):	1 person
Ventricular extrasystole (arrhythmia):	1 person
Slight fever:	1 person
Afferent contraction of the visual field:	1 person
Posttraumatic stress disorder (PTSD):	1 person

Discussion

All of the people who received medical checkups returned to their daily lives and had no severe aftereffects. However, abnormal findings which are suspected to be associated with sarin were detected in five victims, including four severe patients who received this medical checkup. Among the symptoms found, electroencephalogram abnormalities were the most frequent, although no one had a convulsion seizure. As for peripheral nerve disorder (for details refer to Case 2 in "4. Severe cases") and ventricular extrasystole (for details refer to Case 1 in "4. Severe cases"), the frequencies of symptoms were low, but they were accompanied by subjective symptoms, such as numbness in the hands and feet as well as palpitations. Thus, those cases were considered to require careful follow-up observations. Another victim, who had intermediate symptoms at the acute stage, had afferent constriction of the visual field.

2) The 4th (1 year and 8 months after the attack) medical checkup

Implementation: February 29–March 1, 1996

Subjects: 121

Total number of people receiving the checkup: 29 (consultation rate: 24.0%)

People who were considered as Evaluation B or C at medical checkups in July 1995.

People who were subjects for but did not receive the medical checkups in July 1995.

People who required detailed examinations after the questionnaires in February 1996, including people who desired to receive the medical checkup.

Results

Evaluation A: No abnormality associated with the poisoning attack (15 people)

Evaluation B: Although checkup and examination results were abnormal, the association with the poisoning is low (9 people)

Evaluation C: Presence of abnormality, which is suspected to be associated with the poisoning (5 people)

Breakdown of Evaluation C:

Electroencephalogram abnormality:	3 people
Peripheral nerve disorder (numbness in the hands and feet):	1 person
Ventricular extrasystole (arrhythmia):	1 person
Hypoxia:	1 person
Slight fever:	1 person
Posttraumatic stress disorder (PTSD):	1 person

Discussion

Similar to the situation of the 3rd medical checkup, all people who received this checkup returned to their daily lives and had no severe aftereffects. There were no subjective symptoms or abnormal findings, which appeared 1 year or later after sarin exposure. In all five victims who were considered as Evaluation C, they were severe cases at the acute stage (In this medical checkup, there were five severe patients at the acute stage with abnormal findings). The symptoms, such as electroencephalogram abnormalities, peripheral nerve disorder, ventricular extrasystole, and slight fever, did not markedly change in comparison with those observed at the 3rd medical checkup. Hypoxia persisted from the acute stage. Although the subjective symptom was absent at the time of the medical checkup, the arterial O_2 pressure was lower than the normal range (for details refer to Case 3 in “4. Severe cases”).

3) The 5th (2 years and 8 months after the attack) medical checkup

Implementation: March 13–14, 1997

Subjects: 87

Total number of people receiving the checkup: 31 (consultation rate: 35.6%)

People with any abnormalities that appeared to be associated with sarin in the previous medical checkups.

People who were considered to require detailed examinations from the questionnaires in February 1997, including people who desired the medical checkup.

Results

Evaluation A: No abnormality associated with the poisoning attack (25 people)

Evaluation B: Although checkup and examination results were abnormal, the association with the poisoning is low (3 people)

Evaluation C: Presence of abnormality, which is suspected to be associated with the poisoning (3 people)

Breakdown of Evaluation C

Electroencephalogram abnormality:	2 people
Peripheral nerve disorder (numbness in the hands and feet):	1 person
Posttraumatic stress disorder (PTSD):	2 people

Discussion

Similar to the previous medical checkups, all people received this checkup returned to their daily lives and had no severe aftereffects. There were no new subjective symptoms or abnormal findings. Among the three people who were considered as Evaluation C in this checkup, two patients were severe cases at the acute stage. Abnormalities, such as peripheral nerve disorders and electroencephalogram abnormalities, were also found in the previous checkup, and the symptoms and examination findings did not change. Another person who were considered as Evaluation C was not a severe case at the acute stage, but the patient still felt nauseous when seeing foods that were eaten at the time of the attack, which indicated PTSD. On the other hand, electroencephalograms were normalized in severe victims at the acute stage that showed abnormalities in the 3rd medical checkup (1 year after the attack) (for details refer to Case 4 in "4. Severe cases").

4) The 6th (3 years and 8 months after the attack) medical checkup

Implementation: March 19, 1998

Subjects: 15

Total number of people receiving the checkup: 10 (consultation rate: 66.7%)

People with any abnormalities that appeared to be associated with sarin in the previous medical checkups.

People who were considered to require detailed examinations from the questionnaires in February 1998, including people who desired the medical checkup.

Results

Evaluation A: No abnormality associated with the poisoning attack (6 people)

Evaluation B: Although checkup and examination results were abnormal, the association with the poisoning is low (1 person)

Evaluation C: Presence of abnormality, which is suspected to be associated with the poisoning (3 people)

Breakdown of Evaluation C

Electroencephalogram abnormality:	1 person
Peripheral nerve disorder (numbness in the hands and feet):	1 person
Posttraumatic stress disorder (PTSD):	3 people
Reduced retinal sensitivity:	1 person

Discussion

Similar to the previous medical checkups, there were no severe aftereffects, new subjective symptoms or abnormal findings. Among the three people who were considered as Evaluation C in this checkup, one person who had a severe case at the acute stage showed a peripheral nerve disorder, electroencephalogram abnormalities, reduced retinal sensitivity, and PTSD, which were similar to those in the previous checkups. The other two people who were considered as Evaluation C were not severe cases at the acute stage, had mild PTSD. In this medical checkup, Dr. Yokoyama of the Department of Public Health / Health Policy at the University of Tokyo conducted detailed psychoneurotic examinations with encephalography and autonomous nervous function tests, as well as history taking. In people in whom PTSD was clinically suspected, the results did not contradict diagnoses of PTSD.

5) The 7th (4 years and 8 months after the attack) medical checkups

Implementation: March 11–12, 1999

Subjects: 17

Total number of people receiving the checkup: 15 (consultation rate: 88.2%)

People with any abnormalities that appeared to be associated with sarin in previous medical checkups.

People who desired the medical checkup in the questionnaires in February 1999.

Results

Evaluation A: No abnormality associated with the poisoning attack (8 people)

Evaluation B: Although checkup and examination results were abnormal, the association with the poisoning is low (1 person)

Evaluation C: Presence of abnormality, which is suspected to be associated with the poisoning

(6 people)

Breakdown of Evaluation C

Peripheral nerve disorder (numbness in the hands and feet):	1 person
Ventricular extrasystole (arrhythmia) and myocardial disorder:	1 person
Slight fever:	1 person
Posttraumatic stress disorder (PTSD):	4 people

Discussion

The three victims with severe conditions at the acute stage had abnormal findings that appeared to be aftereffects of sarin poisoning, such as peripheral nerve disorder, ventricular extrasystole, mildly reduced cardiac function, and slight fever. Reduced cardiac function was newly observed in patients with persisting ventricular extrasystole in whom cardiac echography was performed. On the other hand, degrees of nervous conduction velocity and slight fever in the patients with the peripheral nerve disorder were alleviated in comparison to the previous year. Electroencephalogram abnormality that were present in the previous checkups disappeared in one person, and no one had this abnormality in this checkup. Three people who were considered as Evaluation C, except for severe victims at the acute stage, had mild PTSD. Questionnaires and medical checkups revealed that 29 people had PTSD, and we conducted counseling for people desiring it.

3. Summary of the 3rd–7th medical checkups

Table 1 shows a summary of the results of the 3rd–7th medical checkups. The number of people who received checkups was 72 people at 1 year, 29 people at 1 year and 8 months, 31 people at 2 years and 8 months, 10 people at 3 years and 8 months, and 15 people at 4 years and 8 months after the attack. Among those, the number of people in whom abnormal findings suspected to be associated with sarin was five people at 1 year, five people at 1 year and 8 months, three people at 2 years and 8 months, three people at 3 years and 8 months, and six people at 4 years and 8 months after the attack. In addition, as these included the victims who received the medical checkups multiple times, when overlapping was subtracted the total number of the residents who received these medical checkups was 107. Among those, there were 12 people with abnormal findings suspected to be associated with sarin exposure (Table 1).

Table 1. Results of the medical checkups

Medical checkup	Subjects	People receiving the checkup (consultation rate)	People with abnormality (Evaluation C)
The 3rd (1 year)	154	72 (46.8%)	5
The 4th (1 year and 8 months)	121	29 (24.0%)	5
The 5th (2 years and 8 months)	87	31 (35.6%)	3
The 6th (3 years and 8 months)	15	10 (66.7%)	3
The 7th (4 years and 8 months)	17	15 (88.2%)	6
Total *		107	12

* Calculated by subtracting the overlapping number of people who received the medical checkups multiple times

Breakdown of abnormal findings were electroencephalogram abnormalities in four people, a peripheral nerve disorder in one, ventricular extrasystole in one, a myocardial disorder in one, hypoxia in one, persisting slight fever in one, afferent constriction of the visual field in one, reduced retinal sensitivity in one, and PTSD in six (Table 2).

Table 2. Breakdown of abnormal findings in medical checkups

Abnormal findings	Number of people
Electroencephalogram abnormality	4
Peripheral nerve disorder	1
Ventricular extrasystole	1
Myocardial disorder	1
Hypoxemia	1
Slight fever	1
Afferent constriction of the visual field	1
Reduced retinal sensitivity	1
Posttraumatic stress disorder	6
Total number of people with abnormal findings*	12

* Calculated by subtracting the overlapping number of people with multiple abnormal findings

Table 3. Relationship between severity of the acute stage and abnormal findings at the chronic stage

Severity*	People received medical checkups	People with abnormalities	Forms of abnormalities (number of people)
Mild	74	4	Posttraumatic stress disorder (4)
Intermediate	27	2	Afferent constriction of the visual field (1), Posttraumatic stress disorder (1)
Severe	6	6	Electroencephalogram abnormality (4), Peripheral nerve disorder (1), Ventricular extrasystole (1), Myocardial disorder (1), Hypoxemia (1), Slight fever (1), Reduced retinal sensitivity (1), Posttraumatic stress disorder (1)
Total	107	12	

* Mild: ChE ≥ 100% or not measured, Intermediate: 100% > ChE ≥ 25%, Severe: 25% > ChE

Next, the relationship between the severity of the acute stage and abnormal findings at the chronic stage will be considered. There were 74 mild cases, among which four cases had PTSD, but no other abnormal physical findings. In 27 intermediate cases, there was one case of afferent constriction of the visual field and one case of PTSD. In all the six severe cases, apparent objective physical abnormalities were found (Table 3). From those findings, it is apparent that abnormal physical findings (aftereffects) correlated with the exposed dose at the acute stage. However, the forms of abnormal findings were not even, which indicated influences of individual differences or hypoxemia conditions. On the other hand, PTSD did not always correlate with the severity at the acute stage, which indicated that it was influenced by personality and the living environment of the individual victims.

Specific severe cases showing abnormal physical findings are presented below.

4. Severe cases

In the Matsumoto sarin attack, seven severe cases showed serum ChE value less than 25% of the normal lower limit and consciousness disorders at the acute stage. Here, the six victims who received the medical checkup are present. The other one victim had hypoxemia at the acute stage and has been hospitalized at a medical facility to date. Thus, the victim could not receive the medical checkup.

1) Case 1

The patient had a severe consciousness disorder and convulsions at the acute stage and was given an artificial respiration apparatus. The ChE value at the acute stage was 19% of the normal lower limit. The patient was hospitalized at the Third Department of Internal Medicine of the Shinshu University Hospital for 18 days. After being discharged from the hospital, subjective symptoms such as slight fever and fatigue persisted for about three months after the attack. Palpitation was often noticed. At the time of discharge, ventricular extrasystole and epileptic electroencephalogram abnormality were detected (Fig. 1A).

At the medical checkup 1 year after the attack, ventricular extrasystole occurred frequently, and epileptic electroencephalogram abnormality was present, which was similar to the acute stage (Fig. 1B). At the checkup 3 years later, the electroencephalogram had normalized, but ventricular extrasystole was still present. At the checkup 4 years and 8 months after the attack, ventricular extrasystole still frequently occurred. At that time, cardiac sonography revealed a mild reduction in the movement of the left ventricular wall, indicating a myocardial disorder. This patient had not shown abnormalities, such as electrocardiography, at school medical checkups. Thus, those findings were inferred to be caused by sarin poisoning.

2) Case 2

At the acute stage, a mild consciousness disorder was found, and the ChE value was 12% of the normal lower limit. From 7 months after the attack, numbness appeared at the distal sites of the extremities.

The patient received the medical checkup every time, and distal dominant reduction in all of the sensations and abnormal sensations in the extremities. Examinations revealed epileptic electroencephalogram abnormality and reductions in sensory nerve conduction velocity of the lower extremity as well as reduced retinal sensitivity. Although treatment with vitamin B12 was attempted for numbness in the extremities, the symptoms did not change. The nerve conduction velocity was almost constant up to 3 years and 8 months after the attack and then tended to improve after 4 years and 8 months after the attack (Table 4). Electroencephalogram abnormality was absent in the examination conducted 4 years and 8 months after the attack. Furthermore, when recalled that time, the patient was in poor physical condition and could not continue the work they had done before the attack, which was inferred that the patient also had PTSD.

3) Case 3

A severe consciousness disorder was observed at the acute stage, and the ChE value was 9% of the normal lower limit, the lowest among the people receiving the medical checkup. The patient was given an artificial respiration apparatus and had persistent hypoxemia even after removal of the

respiration apparatus.

The patient received the medical checkup 1 year and 8 months after the attack and had no subjective symptoms, although hypoxemia was still present (Table 5). No notable abnormality was detected in the chest Xp, CT, or respiratory functional examinations. Because this patient moved to another place after the attack, the subsequent progress is unknown.

4) Case 4

At the acute stage, a mild consciousness disorder was present, and the ChE value was 21% of the normal lower limit. After the acute stage, no subjective symptoms were present. Although epileptic electroencephalogram abnormality was detected 1 year after the attack, the electroencephalogram was normalized in the re-examination 2 years and 8 months after the attack.

5) Case 5

At the acute stage, an intermediate consciousness disorder was present, and the ChE value was 16% of the normal lower limit.

This patient had no subjective symptoms after the acute stage; epileptic electroencephalogram abnormality was detected in medical checkups conducted 1 year and 8 months and 2 years and 8 months after the attack. Because the patient proceeded to a university, the patient did not receive subsequent medical checkups and it is not known if the electroencephalogram normalized.

6) Case 6

At the acute stage, a mild consciousness disorder was present, and the ChE value was 24% of the normal lower limit. After the acute stage, pyrexia persisted and subsequently, although it tended to improve, a slight fever of 37℃ appeared at night even 4 years and 8 months after the attack. Although a hypothalamic abnormality was suspected, no abnormality was detected in the head MRI or endocrine examinations.

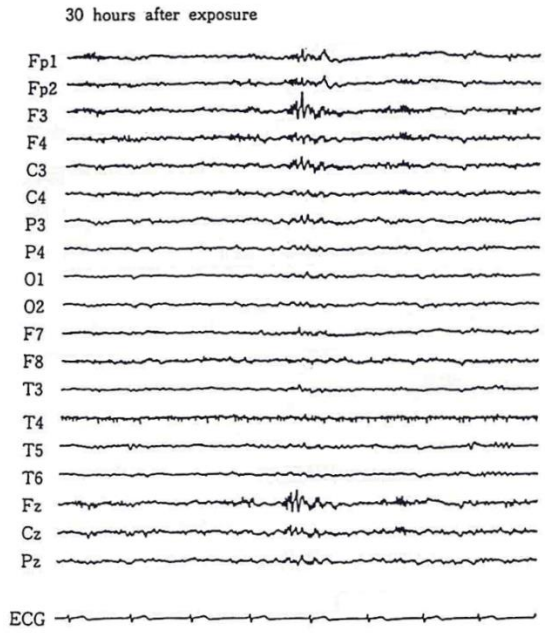

Fig. 1A.
Electroencephalogram 30 hours after exposure in Case 1. Frontoparietal dominant fast waves with high amplitudes occurred frequently, and left procephalic dominant polyspike and wave complexes were detected (cited from reference 3).

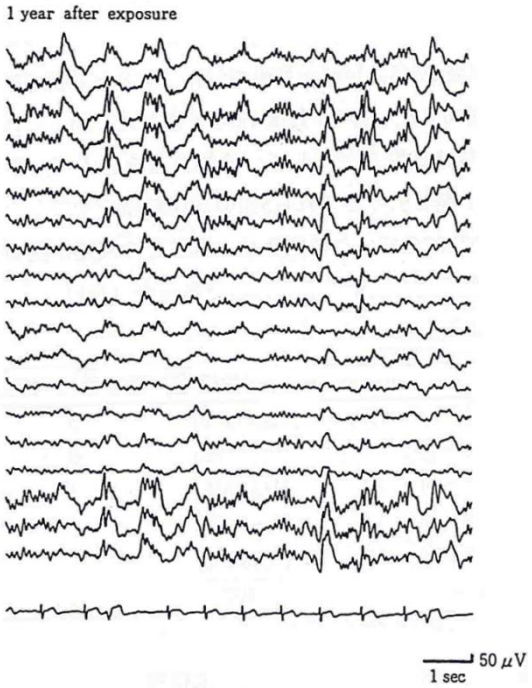

Fig. 1B.
Electroencephalogram 1 year after the attack in Case 1. Sporadic sharp waves and d waves occurred frequently, and electrocardiography revealed frequent ventricular extrasystole (cited from reference 3).

5. Discussion about individual aftereffects

1) Central nervous system

One year or later after the attack, four victims among the severe six victims had epileptic electroencephalogram abnormalities frequently occurring, which was the most frequent abnormal finding in the medical checkups after the acute stage. Subsequently, however, the condition was normalized in some cases 2 years and 8 months or later after the attack. At the time of the medical checkup 4 years and 8 months after the attack, the electroencephalogram was normalized in three of the four patients (the other person could not be followed up after the medical checkup 2 years and 8 months after the attack). In the references, the long-term influence of sarin on the electroencephalogram in animals was reported [(5)]. The presumed mechanism involves direct toxicity to GABA receptors and an influence of the hypoxemia condition at the acute stage.

Although pyrexia was presented in many cases at the acute stage, slight fever persisted in one severe case after the acute stage. There is a report on hypothalamic disorders caused by sarin in animals [(6)] and central nervous pyrexia was suspected.

2) Peripheral nervous system

In the peripheral nervous system, numbness in the hands and feet appeared temporally at the acute stage in about 40% of the inpatients. The numbness was alleviated in all the cases. Besides those, in one severe case, numbness in distal extremities (polyneuropathy) appeared from 7 months after the attack. As an aftereffect of phosphororganic poisoning, organophosphate-induced delayed polyneuropathy (OPIDN) is well known as a peripheral nervous disorder. Recently, anatomy cases of the victims of the subway sarin attack who died 15 months after the attack were reported [(7)] and because of the marked peripheral nervous disorder, it was inferred that the polyneuropathy, in this case, might be due to OPIDN caused by sarin.

3) Cardiovascular system

In the cardiovascular system, polymorphic ventricular extrasystole was present in one severe case immediately after the attack and did not improve even at the time of the medical checkup 4 years and 8 months after the attack. In this case, cardiac ultrasonography revealed a reduction in the force of heart contractions. In the references, ventricular arrhythmia and myocardial disorders caused by organophosphorus pesticides are reported [(8)]. Mechanistically organic phosphorus is suggested to have a direct influence on myocardial cells, such as disorder of K channel, inhibition of Na/K-ATPase, or necrosis of cardiac muscles. In addition, myocardial disorders by hypoxemia have been presumed. Multiple factors were presumed to be involved in this case.

4) Respiration system

In the respiration system, in one severe case, hypoxemia persisted from immediately after the attack up to 1 year and 8 months after the attack. In phosphororganic poisoning, prolonged respiratory muscle disorder is well known as the intermediate syndrome [(9)]. The intermediate syndrome is reported to occur in about 7% of the phosphororganic poisoning cases, and the cause is inferred to be a postsynaptic block of the neuromuscular junction. In this case, because analysis of the images showed no apparent abnormality, a respiratory muscle disorder by the intermediate syndrome was suspected. Compared to intermediate syndrome by general organophosphorus agent, the progress is longer, which may be due to the stronger toxicity of sarin.

5) Optical system

In the optical system, one severe case had mildly reduced retinal sensitivity and one intermediate case had prolonged afferent constriction of the visual field [(10)]. Although mechanisms of these conditions are presumed to be a direct toxicity of sarin on the retina, because the reduced ChE value did not always appear in severe victims, the dose of the exposure on the local ocular site might influence it. For the details, refer to the results of the ophthalmologic medical checkups.

6) Mental system

Among the people receiving these medical checkups, PTSD was diagnosed in six people. The correlation between PTSD and the severity of sarin poisoning was not found to be sufficient, and the individual personality and living environment were inferred to a have a large influence. PTSD was investigated in many of the victims by the questionnaires in February 1999. For the details, refer to the results of the questionnaires.

Table 4. Variation in the sensory nerve conduction velocity (SCV) in Case 2

Time of the implementation	1 year after the attack	1 year and 8 months after the attack	2 years and 8 months after the attack	3 years and 8 months after the attack	4 years and 8 months after the attack
SCV of the tibial nerve (ankle – toe)*	33 m/sec	30 m/sec	26 m/sec	29 m/sec	39 m/sec

*Normal: 35 m/sec or more

Table 5. Variation in arterial oxygen saturation (SaO_2) in Case 3

Time of the implementation	immediately after the attack	1 month after the attack	2 months after the attack	3 months after the attack	1 year and 5 months after the attack	1 year and 8 months after the attack
SaO_2	57.0%	60.0%	62.0%	64.8%	73.9%	71.5%

6. Summary

With cooperation from Mr. Yajima of the Citizens' Health Division of the Matsumoto City government, we could understand the health conditions in many of the victims through the medical checkups reported here. All of the people who received the medical checkups returned to their normal social lives, and there was no person with critical aftereffects. However, in the severe victims, having ChE value less than 25% of the normal lower limit at the acute stage, abnormal findings, including electroencephalogram abnormality, peripheral nervous disorder, ventricular extrasystole, myocardial disorder, hypoxemia, and pyrexia, persisted for a long period. Thus, subsequently, these victims are required to be followed up individually. In addition, there are some victims with mental aftereffects, whom we mentally support.

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Ophthalmologic medical checkups after sarin exposure

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Ophthalmologic findings at the acute stage after sarin exposure include markedly constricted pupils as well as constriction of the visual field, hyperemia, adjustment disorders, and a reduced electroretinographic response. However, because there were many unknown aspects about the long-term prognosis, the medical checkups of the aftereffects were conducted mainly for symptoms at the acute stage.

A major characteristic symptom after sarin exposure is the constricted pupils. The diameter of the pupils at the time of exposure was measured by various physicians using a scale under urgent and busy conditions. The diameter of the constricted pupils was reported to range from 0.5–2.0 mm in 0.5 mm intervals. The results are a rough indication, which could not be considered accurate and objective data. In subsequent measurements, the diameter of the pupils had gradually normalized over one week. However, to measure the diameter precisely to detect residual aftereffects, an objective measurement using accurate hardware is required. Thus, we conducted the measurement under a constant condition using an electronic pupillometer to investigate its aftereffect. This enabled the measurement of reaction to light, such as the constriction rate and velocity, and the diameter of the pupil, and an analysis of the remaining abnormality of the autonomic nervous system. Thus, for medical checkups of the aftereffects, we measured the diameter of the pupils using an electronic pupillometer as its focus.

As many people experienced eye fatigue and an adjustment disorder, measurements of the adjustment ability (width for focus slide) using an infrared optometer and an examination of the adjustment (ocular focus adjustment ability) were conducted as objective measurements. Moreover, an examination of the visual field was conducted to measure residual constriction and electroretinogram was measured. A general measurement of the visual acuity and an ophthalmoscopic examination were also conducted.

Ophthalmologic findings 1 year after the attack

During July 17–19, 1995, 1 year after the attack, medical checkups were conducted at the Shinshu University Hospital. The checkups were conducted in people who had cholinesterase (ChE) value less than 100% of the normal lower limit, had a pupil diameter of 2.0 mm or less at the time of the exposure, or those who were otherwise required or desired it. The ophthalmologic examinations were conducted on 72 people. First, the diameter of the pupils was measured using an electronic

pupillometer in all the persons. Then, when necessary, ophthalmologic examinations, such as on the visual field were conducted.

1. The measurement of diameter of the pupils and reaction to light using an electronic pupillometer

Using an infrared electronic pupillometer C2514 (Hamamatsu Photonics), the diameter of the pupils was measured in 72 people (144 eyes). After a dark adaption lasting six minutes, the measurement was conducted in a dark room for the right eye and then the left.

Fig. 1 shows a distribution of the diameter of the pupils at different ages from the medical checkup. The mean diameter was 6.0 ± 0.9 mm (mean ± standard deviation) (range: 2.9–8.1 mm). The diameter of the pupils of 70 people (141 eyes) was 4.0 mm or higher. The diameter tended to decrease with age and no difference was found in the control. Fig. 2 shows ChE values at the time of exposure and the distribution of the diameter of the pupils from the medical checkup. The minimum diameter of the pupil was 2.9 mm in a severe victim with 12% ChE of the normal lower limit at the time of exposure.

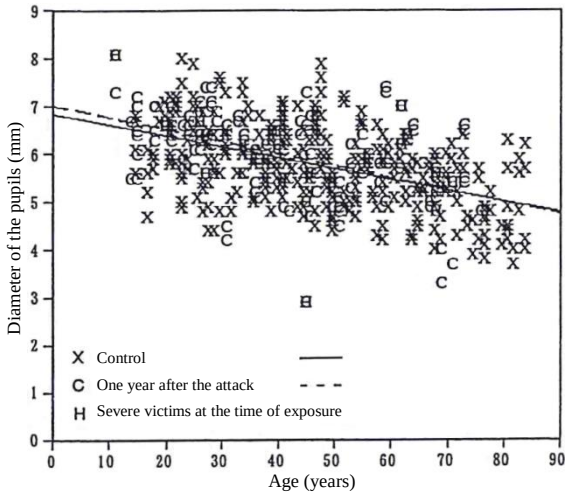


Fig. 1 Diameter of the pupils at different ages from medical checkups 1 year after the attack (Severe victims were defined as those having ChE less than 30% at the time of exposure.)

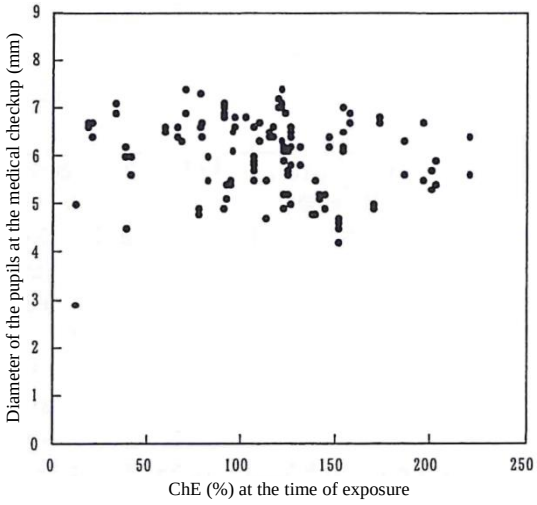


Fig. 2 ChE values at the time of exposure and the diameter of the pupils from the medical checkup

Fig. 3 shows the diameter of the pupils from the medical checkup in different diameters at the time of exposure. The diameters of the pupils ranging 0.5–2.0 mm at the time of exposure showed no difference in diameter at the medical checkups. Table 1 shows the results of the analyses of reaction to light measured using an electronic pupillometer in different diameters (0.5–2.0 mm) and ChE values (0–29%, 30–99%, 100%–) at the time of exposure. Although it was not a simple comparison, as the mean age was different at each examination and data was different according to the age of the victim, no differences were found in the severity of the exposure. For the control of the measured values using an electronic pupillometer, the measurement was conducted in staffs of the Maruko Central Hospital (Marukomachi, Chiisagatagun), and people receiving comprehensive medical examinations who had no ocular diseases and consented to the measurement (Table 2).

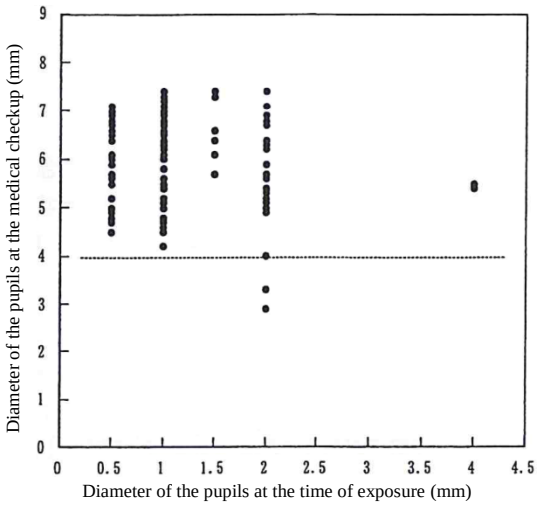


Fig. 3 Diameter of the pupils at the time of exposure and the medical checkup 1 year after the attack

Table 1. Reaction to light measured using an electronic pupillometer in different diameters of the pupils and ChE values at the time of exposure

Items	Control	Total	Diameter of the pupils at the time of exposure (mm)					ChE value at the time of exposure (%)			
			0.5	1	1.5	2 (4)	Unknown	0–29%	30–99%	100%	Unknown
Number of people (number of eyes)	177 (354)	72 (144)	13 (26)	33 (66)	3 (6)	15 (30)	8 (16)	3 (6)	19 (38)	39 (78)	11 (22)
Age (years)	47.7 ± 18.3	41.0 ± 17.4	44.6 ± 17.4	36.9 ± 16.5	35.0 ± 18.7	45.5 ± 14.6	45.9 ± 22.2	30.3 ± 11.7	40.2 ± 15.9	39.8 ± 16.6	49.5 ± 21.3
Diameter of the pupils at the time of exposure (mm)		1.2 ± 0.6						1.3 ± 0.9	1.0 ± 0.8	1.2 ± 0.5	1.4 ± 0.4
ChE values (%) at the time of exposure		112 ± 46	84 ± 40	116 ± 39	120 ± 5	136 ± 49	21 ± 0				
D1 (mm) (Diameter in the initial condition)	5.7 ± 0.9	6.0 ± 0.9	5.9 ± 0.8	6.1 ± 0.7	6.6 ± 0.7	5.6 ± 1.0	6.2 ± 1.0	5.7 ± 1.5	6.1 ± 0.7	5.9 ± 0.8	6.0 ± 1.2
D2 (mm) (The minimum diameter after light stimulation)	3.8 ± 0.8	4.2 ± 0.8	4.2 ± 0.7	4.3 ± 0.7	4.5 ± 0.6	3.9 ± 0.9	4.4 ± 0.8	3.8 ± 0.8	4.3 ± 0.7	4.2 ± 0.8	4.4 ± 0.9
CR (Constriction rate of the pupil (D1-D2/D1))	0.33 ± 0.07	0.29 ± 0.07	0.28 ± 0.07	0.29 ± 0.06	0.32 ± 0.03	0.28 ± 0.07	0.27 ± 0.08	0.32 ± 0.08	0.29 ± 0.06	0.28 ± 0.07	0.26 ± 0.07
A1 (mm^2) (Area of the pupil in the initial condition)	26.5 ± 7.9	29.0 ± 8.0	28.1 ± 7.8	30.1 ± 6.9	38.4 ± 6.9	24.9 ± 8.6	31.0 ± 9.4	27.6 ± 11.8	30.5 ± 7.7	28.2 ± 6.9	29.6 ± 10.8
t1 (ms) (Time between light stimulation and constriction of the pupil)	257 ± 25	256 ± 36	255 ± 48	254 ± 34	275 ± 35	259 ± 31	258 ± 29	230 ± 50	249 ± 36	261 ± 36	258 ± 26
t2 (ms) (Time until the diameter of the pupil changed by half)	293 ± 58	297 ± 66	277 ± 56	299 ± 61	344 ± 39	289 ± 53	300 ± 56	306 ± 95	303 ± 60	294 ± 55	281 ± 55
t3 (ms) (Time when the pupil reached the minimum size)	1061 ± 166	1040 ± 174	961 ± 198	1057 ± 169	1136 ± 53	1035 ± 164	1049 ± 162	1105 ± 174	1043 ± 187	1033 ± 170	1021 ± 162
t5 (ms) (Time between the minimum and 63% dilatation)	1494 ± 402	1683 ± 500	1610 ± 548	1720 ± 470	1883 ± 543	1572 ± 479	1772 ± 559	1377 ± 405	1752 ± 525	1677 ± 479	1663 ± 544
vo (mm/s) (The maximum constriction velocity)	4.3 ± 0.9	4.0 ± 0.7	4.1 ± 0.9	4.0 ± 0.6	4.1 ± 0.4	3.6 ± 0.7	3.9 ± 0.8	4.2 ± 1.0	4.1 ± 0.8	3.9 ± 0.6	3.9 ± 0.8
vd (mm/s) (The maximum dilatation velocity)	1.9 ± 0.5	1.8 ± 0.4	1.8 ± 0.4	1.8 ± 0.4	2.0 ± 0.2	1.7 ± 0.4	1.9 ± 0.6	2.1 ± 0.3	1.9 ± 0.4	1.8 ± 0.3	1.8 ± 0.5
ac (mm/s^2) (The maximum acceleration velocity of constriction)	58 ± 15	57 ± 16	60 ± 19	57 ± 14	53 ± 9	51 ± 14	61 ± 21	57 ± 17	59 ± 15	55 ± 15	59 ± 20
ChE value (μ/L) at the medical checkup		171 ± 36	185 ± 45	167 ± 32	150 ± 16	171 ± 38	172 ± 36	147 ± 24	156 ± 39	181 ± 34	170 ± 30

Table 2. Controls at different ages for reactions to light using an electronic pupillometer

	Age							
Examination using an electronic pupillometer	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89
D1 (mm) (Diameter in the initial condition)	6.0 ± 0.6	6.2 ± 0.8	6.1 ± 0.7	6.0 ± 0.7	5.5 ± 0.8	5.3 ± 0.7	5.1 ± 0.7	4.9 ± 0.8
D2 (mm) (The minimum diameter after light stimulation)	4.1 ± 0.8	4.1 ± 0.8	4.0 ± 0.7	3.9 ± 0.8	3.7 ± 0.7	3.6 ± 0.7	3.4 ± 0.7	3.3 ± 0.8
CR (Constriction rate of the pupil (D1-D2/D1))	0.32 ± 0.08	0.34 ± 0.08	0.34 ± 0.07	0.35 ± 0.07	0.31 ± 0.06	0.32 ± 0.07	0.32 ± 0.06	0.31 ± 0.08
A1 (mm^2) (Area of the pupil in initial conditions)	28.9 ± 6.2	31.4 ± 8.2	29.5 ± 6.6	29.2 ± 7.0	24.2 ± 6.8	22.6 ± 5.3	20.9 ± 5.6	19.3 ± 6.7
t1 (ms) (Time between light stimulation and constriction of pupils)	263.1 ± 27.1	255.3 ± 33.2	254.0 ± 24.2	251.8 ± 23.8	259.6 ± 21.0	260.4 ± 21.4	259.1 ± 27.0	276.0 ± 27.9
t2 (ms) (Time until the diameter of the pupil changed by half)	319.0 ± 84.9	311.0 ± 59.6	318.1 ± 52.1	295.6 ± 51.7	288.4 ± 60.6	261.4 ± 45.1	278.2 ± 44.2	246.8 ± 48.8
t3 (ms) (Time when the pupil reached the minimum size)	1094.0 ± 178.7	1094.3 ± 139.3	1106.6 ± 137.4	1093.5 ± 147.1	1063.1 ± 152.3	989.2 ± 189.8	1015.1 ± 154.6	956.2 ± 218.0
t5 (ms) (Time between the minimum and 63% dilatation)	1427.3 ± 331.5	1536.9 ± 486.9	1478.1 ± 392.1	1484.0 ± 303.5	1571.4 ± 444.3	1476.7 ± 410.0	1419.3 ± 302.8	1526.0 ± 536.8
vc (mm/s) (The maximum constriction velocity)	4.2 ± 0.8	4.6 ± 1.0	4.3 ± 0.9	4.7 ± 0.9	3.9 ± 0.7	4.2 ± 0.8	3.9 ± 0.8	3.8 ± 0.7
vd (mm/s) (The maximum dilatation velocity)	2.0 ± 0.4	2.1 ± 0.6	2.1 ± 0.6	2.1 ± 0.5	1.8 ± 0.4	1.8 ± 0.4	1.7 ± 0.3	1.7 ± 0.5
ac (mm/s^2) (The maximum acceleration velocity of constriction)	61.1 ± 11.8	62.2 ± 17.1	58.4 ± 15.8	62.6 ± 15.1	55.6 ± 14.6	55.0 ± 13.1	51.6 ± 10.6	51.6 ± 10.5

2. Visual acuity

A visual acuity measurement was conducted in 30 people (60 eyes). Reduction in the visual acuity was found in the one eye with a measurement of 0.08 due to cataracts and macular degeneration as well as in two eyes with 0.8 and one eye with 0.9 due to cataracts. The visual acuity in the other 56 eyes was 1.0 or higher, which indicated no influence from the sarin exposure.

3. Visual field

In 14 people who received ophthalmologic examinations at the time of exposure, measurements were conducted using a program 24-2 threshold test of Humphrey Field Analyzer. The afferent constriction of the visual field remained in one person who had a marked constriction at the time of exposure (Fig. 4) and a mild reduction in the mean sensitivity was found in four people.

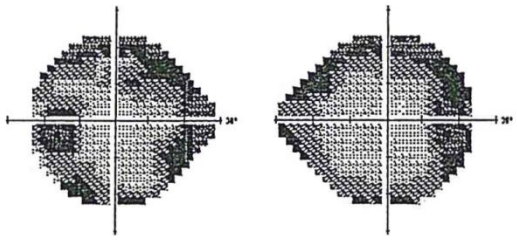


Fig. 4 Residual afferent constriction of the visual field found at the medical checkup 1 year after the attack

4. Findings

In 24 people who desired ophthalmologic examinations, the anterior eyes and eye grounds were examined. Diffuse epithelial keratitis was detected in one person, mild conjunctival congestion in one person, posterior synechia in one person, and cataracts in two people. In the eye ground, macular degeneration was found in one person and no abnormalities were found in the other people, which indicated no influence from the sarin exposure.

5. Electroretinogram

The measurement was conducted in eight people who had ChE values less than 100% at the time of exposure. The results were normal in seven people and a mild reduction in the electroretinographic response occurred in one person who had 12% ChE of the normal lower limit at the time of exposure (Fig. 5).

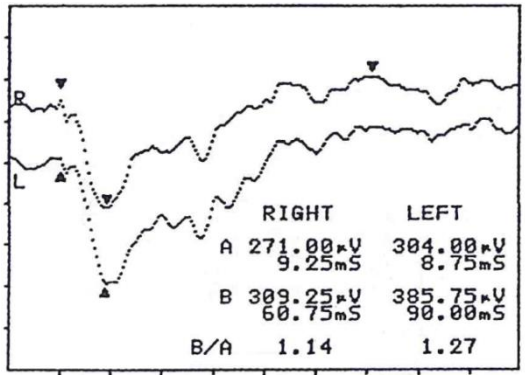


Fig. 5 Reduced electroretinographic response in the medical checkup 1 year after the attack

6. Subjective symptoms

Twenty-four people who desired to receive ophthalmologic examinations were asked about the presence or absence of subjective symptoms. The answers were “not notable” in 11 people, eye fatigue in six, reduced visual acuity of the naked eyes / unsuitable eyeglasses in six, and the eyes not coming into focus, or dazzling, irritated eyes in one or two victims.

Summary

The diameter of the pupils and reaction to light using an electronic pupillometer were overall normal, and in general, the sarin exposure did not have an influence. In addition, no difference was

found according to the severity of sarin exposure. However, a 45-year-old woman who had 12% ChE of the normal lower limit at the time of exposure had constricted pupils, a mild reduction in the electroretinographic response, and a reduced mean sensitivity in the visual field. A 47-year-old man who had a marked afferent constriction of the visual field at the time of exposure still had the constriction. Those two people were considered as Evaluation C, having abnormalities suspected to be associated with the poisoning. In some people, it was considered that there was an influence from the sarin on the diameter of their pupils or that the influence on the retina and optical nerves remained unchanged.

Ophthalmologic findings in the medical checkups 1 year and 6 months (1 year and 8 months) after the attack

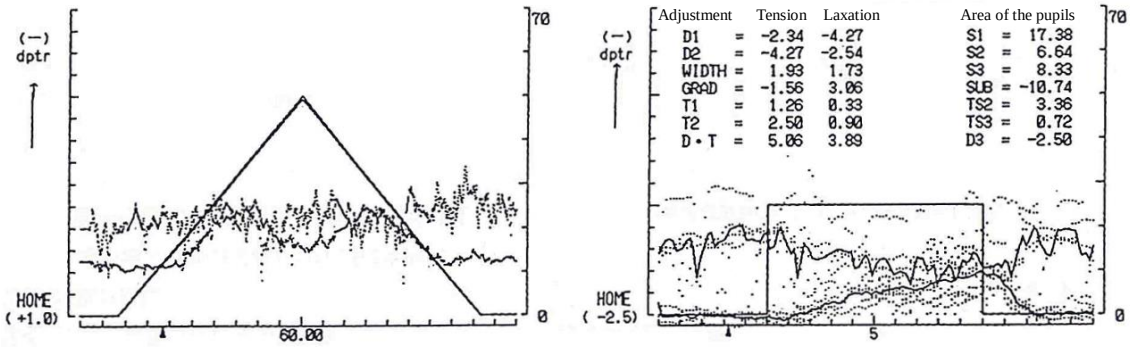
During February 29–March 1, 1996, the medical checkups 1 year and 6 months after the attack were conducted at the Shinshu University Hospital. Although the diameter of the pupils and reaction to light were measured previously using an electronic pupillometer, several of the people receiving this checkup had eye fatigue and an adjustment disorder. Therefore, an infrared optometer (Nidek) was used to measure the objective adjustment ability in 26 people.

1. Measurement of the objective adjustment ability and the diameter of the pupils using an infrared optometer and an electronic pupillometer

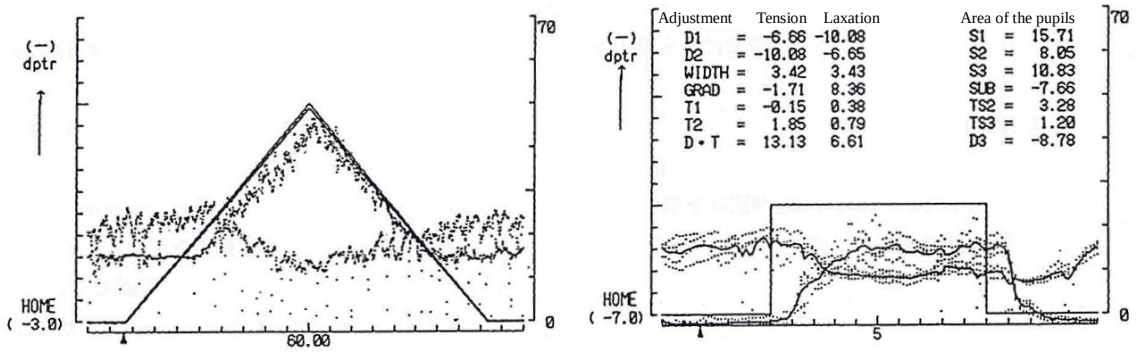
Measurement of the diameter of the pupils

This time, the objective adjustment ability and the diameter of the pupils were measured using an infrared optometer AA-2000 (Nidek). All 26 victims received the measurement. In particular, a constant velocity control measurement was conducted to examine what degree the right eye could focus on indices that moved gradually from a distal to proximal site, and then from a proximal to distal site. A step control measurement was conducted to examine what degree and how fast the left eye could focus on indices that moved to a distal or proximal site in five second intervals. In people who had enough time, both the constant velocity control and step control measurements were conducted. The diameter of the pupils, as well as the objective adjustment ability, was also measured. Of ten young people in their teens to 20s, two people showed slightly reduced adjustment abilities in one eye in the constant velocity control measurement, whereas another eye was not affected. The results in the other eight people were normal. In the step control measurement, two people in their late 20s showed a slight reduction in starting the reaction, whereas it was normal in the others. In the other 16 victims, who were 40 years old or older, the objective adjustment ability almost disappeared. The reduced results were considered to be due to age and there was no difference caused by the presence or absence of subjective symptoms and the degree of the sarin exposure. Fig. 6 shows representative cases in which some people had no subjective symptoms but exhibited a reduced

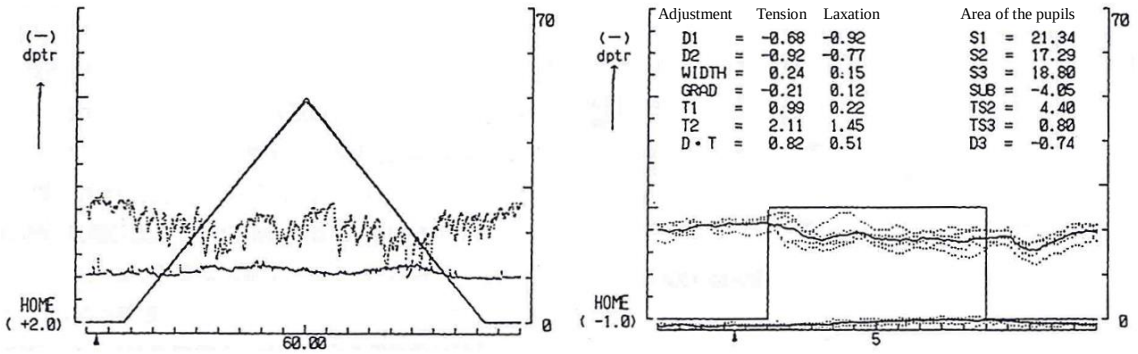
adjustment ability while others who had subjective symptoms had a normal adjustment ability. In the constant velocity control measurement, the difference between the adjusted tracking point and the maximum adjusted point was defined as the objective adjustment ability. As shown in Fig.7, the value decreased with age, and no difference was present when compared with the control. For the control to the measured values by infrared optometer, staff at the Maruko Central Hospital and their family and people who received comprehensive medical examinations were measured. They had no ocular diseases other than ametropia.



Person in his/her 20s with 33% ChE at the time of exposure
No marked subjective symptoms



Person in his/her 20s with 66% ChE at the time of exposure
Eye fatigue, progressed nearsightedness / astigmatic vision,
new eyeglasses were obtained



Person in his/her 40s with 12% ChE at the time of exposure
Eye fatigue, nausea when looking at small objects

Fig. 6 Constant velocity control measurement and step control measurement using an infrared optometer in the medical checkup 1 year and 6 months after the attack

This time, the diameter of the pupils was measured using an electronic pupillometer attached to an infrared optometer. As shown in Fig. 8, it was 5.4 ± 0.8 mm (3.2–6.9 mm). Compared to the control its reduction was absent.

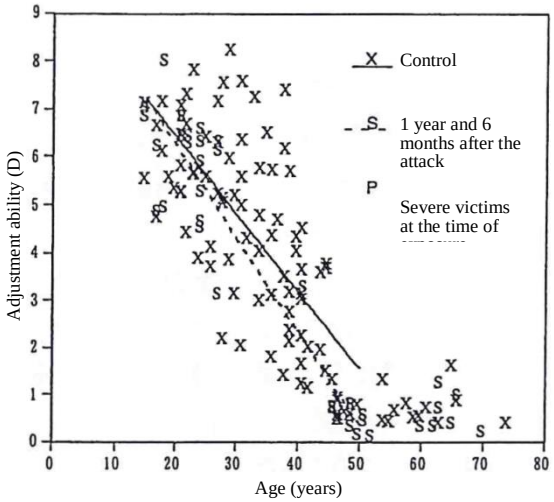


Fig. 7 Objective adjustment ability in the medical checkup 1 year and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

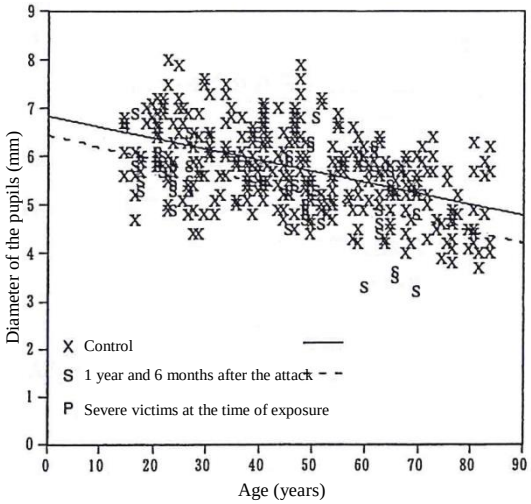


Fig. 8 Diameter of the pupils at different ages from the medical checkup 1 year and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

2. Visual acuity

A visual acuity measurement was conducted in 26 people (52 eyes) receiving the medical checkup. Reduction in the visual acuity was found in each one eye with a measurement of 0.3 due to macular degeneration, and cataracts and keratitis as well as in one eye with 0.9 due to cataracts and keratitis. The visual acuity in the other 49 eyes was 1.0 or higher, which indicated no influence from the sarin exposure.

3. Visual field

In six people who received ophthalmologic examinations at the time of exposure, measurements were conducted using a Humphrey Field Analyzer. Two people showed reduced mean sensitivity. Both also had a reduced sensitivity in the medical checkup 1 year after the attack, among whom one person had 12% ChE of the normal lower limit at the time of exposure.

4. Findings

In examinations of the anterior eye and eye ground, one person had keratitis and two people had cataracts. In the eye ground, one person exhibited retinal breaks after treatment and another had macular degeneration after retinal bleeding. No abnormalities were found in the other people. No influence from the sarin exposure was present.

5. Subjective symptoms

There were ten people without symptoms, 13 people who had eye fatigue, eight people with reduced visual acuity of the naked eyes, and one or two people with runny eye or an uncomfortable sensation in the eyes. Subjective symptoms appeared in 40% of victims in their teens and 20s and 75% of people in their 40s–50s.

Summary

Many people exhibited eye fatigue and reduced adjustment ability. Although many people in their 40s–50s or older had such symptoms, their objective adjustment ability disappeared, and the measured values and subjective symptoms did not always correspond in the measurement using an infrared optometer. Thus, it was considered difficult to detect subjective symptoms using objective findings. As for the diameter of the pupils, there was no one with constricted pupils, and some people had mildly reduced retinal sensitivity. Some young people exhibited a reduced adjustment ability, but those symptoms were not considered to be associated with sarin poisoning. In these ophthalmologic examinations, no one was considered as Evaluation C, having abnormalities suspected to be associated with the poisoning.

Ophthalmologic findings in the medical checkup 2 years and 6 months (2 years and 8 months) after the attack

During March 13–14, 1997, the medical checkup 2 years and 6 months after the attack was conducted at the Shinshu University Hospital. In the medical checkup 1 year after the attack, the diameter of the pupils was measured using an electronic pupillometer. In the medical checkup 1 year and 6 months after the attack, as many victims exhibited eye fatigue and adjustment disorders, an infrared optometer was used to measure the objective adjustment ability. As only 28 people received the checkup this time, the diameter of the pupils was measured using an electronic pupillometer, and examinations were further conducted using an infrared optometer.

1. Measurement of diameter of the pupils using an electronic pupillometer

Similar to the medical checkup 1 year after the attack, the diameter of the pupils was measured in 28 people (56 eyes) using an electronic pupillometer C2514 (Hamamatsu Photonics). After a dark adaptation lasting six minutes, the measurement was conducted in a dark room for the right eye and then the left. Fig. 9 shows the diameter of the pupils at different ages. The mean diameter was 6.0 ± 0.9 mm (2.9–8.1 mm). The diameter of the pupils of 26 people (52 eyes) was 4.0 mm or higher. In severe victims with 12% ChE of the normal lower limit at the time of exposure, who had a minimum diameter of 2.9 mm at the medical checkup 1 year after the attack, the diameter was 4.0 mm. The

minimum diameter of people in their 80s was 2.0 mm, indicating senile constricted pupils. Overall, no marked reduction was observed.

2. Objective adjustment ability using an infrared optometer

Similar to the medical checkup 1 year and 6 months after the attack, an infrared optometer AA-2000 (Nidek) was used. As a rule, ten people who were less than 50 years old and in whom the objective adjustment ability remained underwent the examination. The constant velocity control measurement was conducted in the right eye and the step control measurement in the left eye. In the constant velocity control measurement, the adjustment ability decreased in two of the seven people in their teens and 20s, and it was normal in the other five people. In the step control measurement, the reaction was slightly poor in one person and normal in the others. Person in whom both values decreased had a reduced adjustment ability and 81% ChE at the time of exposure. In this measurement, the person did not particularly have ocular subjective symptom. The remaining three people were in their 40s, and had a considerable reduction in the objective adjustment ability because of aging. Therefore, reduced adjustment abilities were detected in both the constant velocity control and step control measurements. Fig. 10 shows the distribution of the adjustment abilities in different ages. It decreases with age and no difference was found compared with the control.

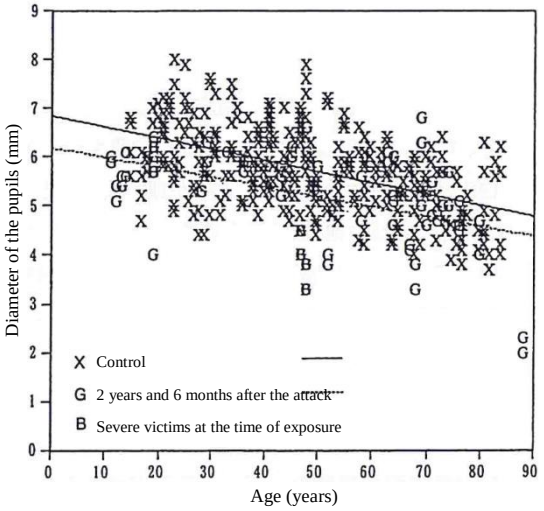


Fig. 9 Diameter of the pupils at different ages from the medical checkup 2 years and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

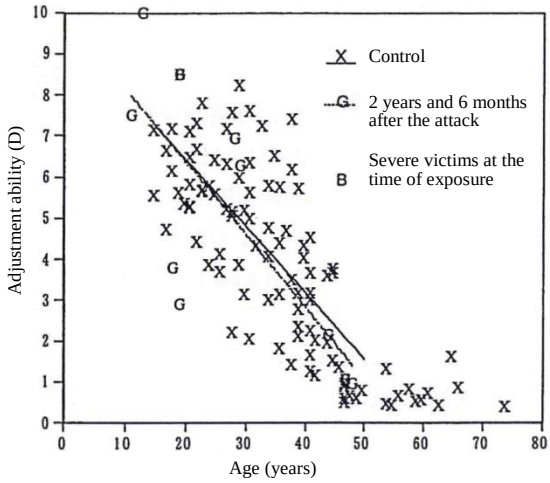


Fig. 10 Objective adjustment ability in the medical checkup 2 years and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

3. Visual acuity

A visual acuity measurement was conducted in 28 people (56 eyes) receiving the medical

checkup. The measurements were less than 0.01 (hand motion), 0.4 and 0.6 in one eye each, 0.7 and 0.8 in two eyes each, and 0.9 in four eyes with cataracts; 0.8 and 0.9 in one eye each after surgery for cataracts; and 0.9 in four eyes with nearsightedness and astigmatisms. The visual acuity in the other eyes was 1.0 or higher. As 14 people of the subjects were aged 60 or older, reduced visual acuities due to cataracts were notable.

4. Visual field

In six people (ten eyes) with low ChE values at the time of exposure or subjective symptoms, the visual field was measured using a Humphrey Field Analyzer. Five people (five eyes) showed slightly reduced mean sensitivity. In the people with a slight reduction in both eyes, the ChE values at the time of exposure was 12% of the normal lower limit. A glaucomatous defect in the visual field was detected in one person.

5. Findings

In examinations of the anterior eye and eye ground, because of a relatively large number of older victims, seven people (13 eyes) had cataracts and two people (three eyes) inserted intraocular lenses after surgery for cataracts. In the eye ground, one person (one eye) exhibited retinal breaks after treatment, and one person (one eye) with glaucomatous defect in the visual field had glaucomatous cupping of the optic disc. No abnormalities were found in the other people. No influence from the sarin exposure was present.

6. Subjective symptoms

Because many people with strong subjective symptoms received the examinations, there were four people without symptoms, 13 people who had eye fatigue, six people with unclear vision, four people with reduced visual acuity, and one or two people with narrowed visual field, runny eye, or an uncomfortable sensation in the eyes. In one person with strong subjective symptoms, the findings included, “the eyes do not open three to four hours after getting out of bed”, “eye fatigue”, “the surrounding is seen as sliding like a roller coaster”, and “objects are seen as if an anesthetic has been administered”.

Summary

In this medical checkup, because of the relatively large number of the elderly, senile diseases, such as cataracts, were notable. As for subjective symptoms, one of the major symptoms was eye fatigue, particularly of the people in their 50s or older. As eye aging progresses over time, it is unknown if the symptom was associated with sarin exposure. Except for the elderly, most of the diameter of the pupils were normal at 4.0 mm or more. A slight reduction in the retinal sensitivity

was found in some people and a reduction in the adjustment ability was found in some young people. Those symptoms were considered to have a low association with sarin poisoning. In these ophthalmologic examinations, no one was considered as Evaluation C, having abnormalities suspected to be associated with the poisoning.

Ophthalmologic findings in the medical checkup 3 years and 6 months (3 years and 8 months) after the attack

On March 19, 1998, the medical checkup 3 years and 6 months after the attack was conducted at the Shinshu University Hospital. In the medical checkups 1 year and 2 years and 6 months after the attack, the diameter of the pupils was measured using an electronic pupillometer. In the medical checkups 1 year and 6 months and 2 years and 6 months after the attack, as many victims exhibited eye fatigue and adjustment disorders, an infrared optometer was used to measure the objective adjustment ability. This time, ophthalmologic examinations were conducted in ten people using an infrared optometer and an electronic pupillometer.

1. Measurement of the diameter of the pupils using an electronic pupillometer

Similar to previous checkups, the diameter of the pupils was measured in 10 people (20 eyes) using an Iriscorder C2514 (Hamamatsu Photonics). After a dark adaptation lasting six minutes, the measurement was conducted in a dark room for the right eye and then the left. As shown in Fig. 11, the mean diameter was 5.4 ± 0.8 mm (3.3–6.4 mm). The diameter of the pupils of 26 people (52 eyes) was 4 mm or higher. In severe victims with 12% ChE of the normal lower limit at the time of exposure, who had a minimum diameter of 2.9 mm at the medical checkup 1 year after the attack, the diameter was 3.3 mm. Overall, no reduction was observed in comparison to the control.

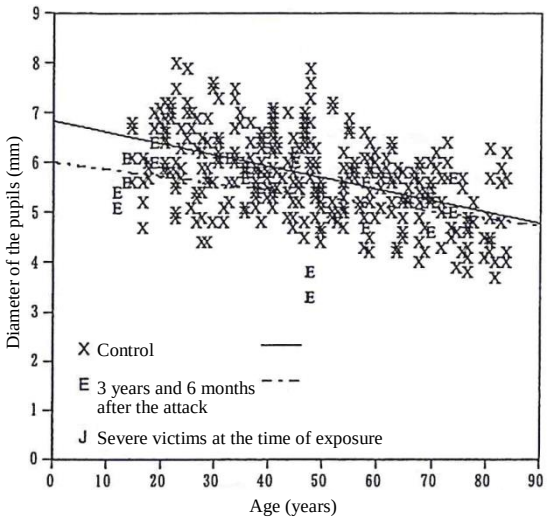


Fig. 11 Diameter of the pupils at different ages from the medical checkup 3 years and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

2. Objective adjustment ability using an infrared optometer

Similar to previous checkups, an infrared optometer AA-2000 (Nidek) was used. As a rule, six people who were less than 50 years old and in whom the objective adjustment ability remained underwent the measurement. The constant velocity control measurement was conducted in the right

eye and the step control measurement in the left eye. As shown in Fig. 12, the adjustment ability was normal in four people in their teens to 20s. In two people in their 40s, reduced adjustment ability due to age was detected in both the constant velocity control and step control measurements.

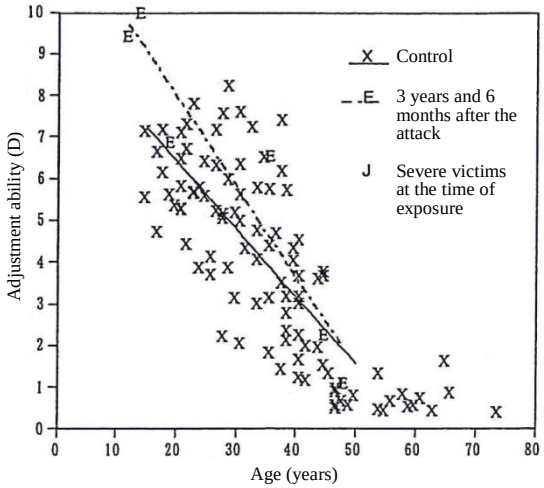


Fig. 12 Objective adjustment ability in the medical checkup 3 years and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

3. Visual acuity

A visual acuity measurement was conducted in 20 people (40 eyes) receiving the medical checkup. The measurements were 1.0 or higher in 8 people (16 eyes), 1.0 or less in one person with strong astigmatism and another person after surgery for cataracts.

4. Visual field

In five people (ten eyes) with low ChE value at the time of exposure or subjective symptoms, the visual field was measured using a Humphrey Field Analyzer. Three people (five eyes), including a person with 12% ChE at the time of exposure, showed mild reduction in the sensitivity.

5. Electroretinogram

The measurement was conducted mainly in people who had ChE values less than 100% at the time of exposure. A mild reduction in the electroretinographic response occurred in one person who had 12% ChE of the normal lower limit at the time of exposure (Fig. 13).

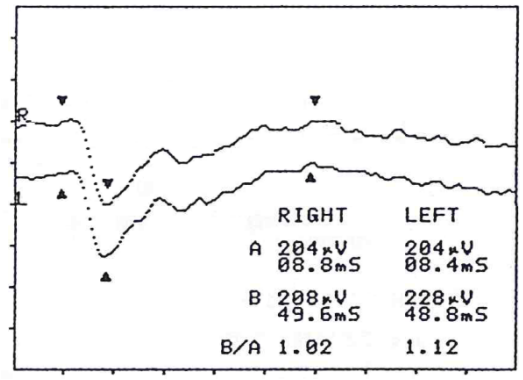


Fig. 13 Reduced electroretinographic response in the medical checkup 3 years and 6 months after the attack

6. Findings

One person (two eyes) inserted intraocular lenses after surgery for cataracts. One person (one eye) exhibited the constriction of the visual field in which glaucoma was suspected. No influence from the sarin exposure was found.

Summary

Although eye fatigue was a major symptom, it was considered difficult to detect data as an objective finding such as the measurement of the adjustment ability. The diameter of the pupils and visual acuity were almost normal. The Evaluation C was made in people with 12% ChE at the time of exposure who had mild reduction in the retinal sensitivity, reduction in the electroretinographic response, and small diameter of the pupils.

Ophthalmologic findings in the medical checkup 4 years and 6 months (4 years and 8 months) after the attack

During March 11–12, 1999, the medical checkup 4 years and 6 months after the attack was conducted at the Shinshu University Hospital. This time, ophthalmologic examinations were conducted in 14 people using an electronic pupillometer and an infrared optometer.

1. Measurement of the diameter of the pupils using an electronic pupillometer

Similar to previous checkups, the diameter of the pupils was measured in 14 people (28 eyes) using an Iriscorder C2514 (Hamamatsu Photonics). After a dark adaptation lasting six minutes, the measurement was conducted in a dark room for the right eye and then the left. As shown in Fig. 14, the mean diameter was 5.8 ± 1.5 mm (2.8–8.1 mm). In victims with 12% ChE at the time of exposure, who had the constricted pupil previously, the diameter was 5.5 mm in the right eye and 5.6 mm in the left eye. In victims in their 30s–50s, the diameter was higher in comparison to the control and slightly smaller in the elderly.

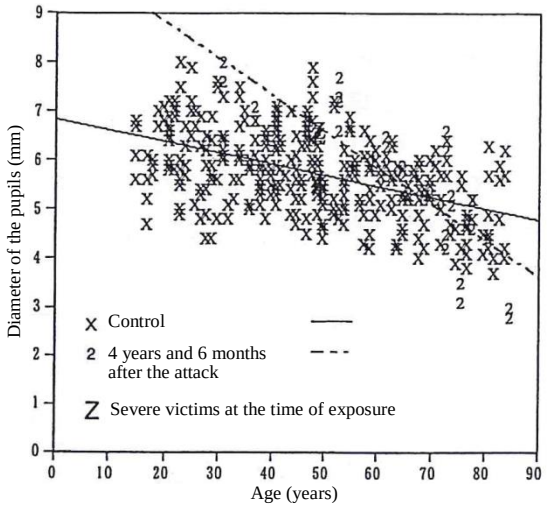


Fig. 14 Diameter of the pupils at different ages from the medical checkup 4 years and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims.)

2. Objective adjustment ability using an infrared optometer

Similar to previous checkups, an infrared optometer AA-2000 (Nidek) was used. As a rule, four people who were less than 50 years old and in whom the objective adjustment ability remained underwent the measurement. The constant velocity control measurement was conducted in the right eye and the step control measurement in the left eye. As shown in Fig. 15, the adjustment ability reduced mildly in one person in their 30s and reduced due to the age in two people in their 40s, although it did not reduce in comparison with the control.

3. Visual acuity

A visual acuity measurement was conducted in 14 people (28 eyes) receiving the medical checkup. The measurements were 1.0 or higher in 22 eyes, and 1.0 or less in four eyes with cataracts or after surgery for cataracts (mild reduction) and in two eyes with macular degeneration (marked reduction).

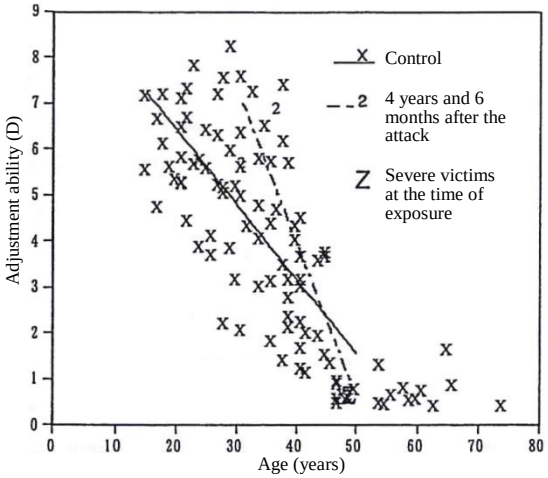


Fig. 15 Objective adjustment ability in the medical checkup 4 years and 6 months after the attack (People with ChE less than 30% at the time of exposure were defined as severe victims).

4. Visual field

In two people (four eyes) with low ChE value at the time of exposure or subjective symptoms, the visual field was measured using an automated perimeter. No marked abnormalities were detected.

5. Electroretinogram

The measurement was conducted in two people (four eyes) who had ChE value less than 100% at the time of exposure. A mild reduction in the electroretinographic response occurred in one person who had 12% ChE of the normal lower limit at the time of exposure (Fig. 16).

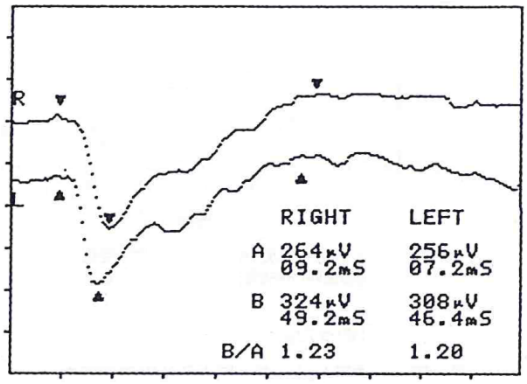


Fig. 16 Reduced electroretinographic response in the medical checkup 4 years and 6 months after the attack

6. Findings

One person (two eyes) inserted intraocular lenses after surgery for cataracts. One person (one eye) exhibited the constriction of the visual field in which glaucoma was suspected. No influence from sarin was found.

Summary

As many people received the checkups were the elderly, there were many cases of cataracts and after surgery. Except for the elderly, the diameter of the pupils and visual acuity were normal, and the visual field was also normal. In one person with 12% ChE of the normal lower limit at the time

of exposure, a mild reduction in the electroretinographic response remained and the case was considered as Evaluation C, having abnormalities suspected to be associated with the poisoning.

Summary of ophthalmologic findings from the previous medical checkups for the toxic gas aftereffects

1. The diameter of the pupils (measurement using an electronic pupillometer)

Fig. 17 shows the diameter of the pupils at different ages from each medical checkup. Although its dispersion is high in the medical checkup 4 years and 6 months after the attack, overall, no difference was observed. Overall, although there was no influence of the sarin exposure on the diameter of the pupils, constricted pupils occurred over time in the persons with 12% ChE at the time of exposure, showing 2.9 mm one year later and 3.3 mm 3 years and 6 months after the attack. In addition, as shown in Table 3, for each item of reaction to light in each medical checkup, analyses of variances were conducted between each medical checkup and a control at different ages and Scheffé's multiple comparisons were conducted. In victims in their 40s including the severe victims, reductions in the constriction rate and the constriction velocity of the pupils were present. In the severe victims, it was inferred that the parasympathetic nerve stimulation might remain due to the sarin.

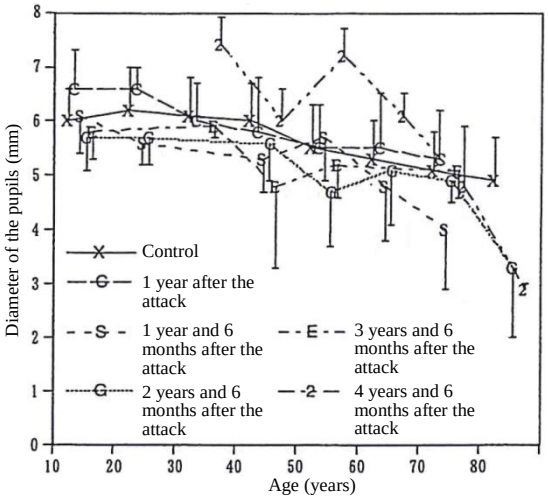


Fig. 17 Mean and standard deviation of the diameter of the pupils at different ages from each medical checkup

Table 3. Reaction to light using an electronic pupillometer at each medical checkup

(*P<0.05, **P<0.01)

Items by Iriscoder examination	Checkup	Overall	Ages							
			10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89
D1 (mm) (Diameter in the initial condition)	1 year after the attack	6.0 ± 0.9	6.6 ± 0.7	6.6 ± 0.4		6.0 ± 0.7	5.8 ± 1.0	5.5 ± 0.8	5.5 ± 1.0	5.3 ± 0.9
	1 year and 6 months after the attack	5.4 ± 0.9	6.1 ± 0.7	5.6 ± 0.4		5.3 ± 0.6	5.7 ± 0.8	4.8 ± 1.0	4.0 ± 1.1	
	2 years and 6 months after the attack	5.1 ± 1.0**	5.7 ± 0.6	5.7 ± 0.5		5.5 ± 0.7	4.7 ± 1.0	5.1 ± 1.0	4.9 ± 0.4	3.3 ± 1.3*
	3 years and 6 months after the attack	5.4 ± 0.8	5.8 ± 0.5		5.9 ± 0.2	4.8 ± 1.5	5.2 ± 0.6		5.1 ± 0.5	
	4 years and 6 months after the attack	5.7 ± 1.5			7.4 ± 0.5**	6.1 ± 0.6	7.2 ± 0.5**	6.1 ± 0.4	4.8 ± 1.1	2.9 ± 0.1*
D2 (mm) (The minimum diameter after light stimulation)	1 year after the attack	4.2 ± 0.8**	4.6 ± 0.7	4.6 ± 0.5**	4.2 ± 0.8	4.2 ± 0.9	3.8 ± 0.7	3.9 ± 1.0	3.9 ± 0.8	
	2 years and 6 months after the attack	3.6 ± 0.7	3.8 ± 0.6	3.7 ± 0.6		4.0 ± 0.5	3.6 ± 0.7	3.6 ± 0.9	3.4 ± 0.3	2.4 ± 0.6
	3 years and 6 months after the attack	3.6 ± 0.6	4.2 ± 0.4		3.7 ± 0.4	3.4 ± 0.8	3.3 ± 0.5		3.1 ± 0.3	
	4 years and 6 months after the attack	4.3 ± 1.1			5.4 ± 0.8**	4.4 ± 0.5	5.5 ± 0.2**	4.8 ± 0.7*	3.5 ± 0.8	2.4 ± 0.0
CR (Constriction rate of the pupil (D1 – D2/D1))	1 year after the attack	0.29 ± 0.07**	0.30 ± 0.06	0.29 ± 0.06**	0.29 ± 0.08	0.27 ± 0.07**	0.29 ± 0.06	0.29 ± 0.07	0.27 ± 0.09	
	2 years and 6 months after the attack	0.30 ± 0.07*	0.32 ± 0.06	0.34 ± 0.05		0.27 ± 0.05*	0.23 ± 0.05	0.29 ± 0.08	0.30 ± 0.08	0.32 ± 0.07
	3 years and 6 months after the attack	0.32 ± 0.08	0.27 ± 0.04		0.37 ± 0.08	0.27 ± 0.07	0.35 ± 0.01		0.40 ± 0.04	
	4 years and 6 months after the attack	0.24 ± 0.06**			0.27 ± 0.05	0.28 ± 0.04	0.22 ± 0.04	0.21 ± 0.07	0.27 ± 0.06	0.18 ± 0.05
A1 (mm^2) (Area of the pupil in the initial condition)	1 year after the attack	29.1 ± 8.1*	35.0 ± 7.4	34.7 ± 4.4	28.8 ± 6.0	27.8 ± 8.5	24.1 ± 7.1	24.9 ± 8.3	23.3 ± 7.8	
	2 years and 6 months after the attack	21.6 ± 7.2**	25.8 ± 5.1	25.9 ± 4.4		24.4 ± 5.6	18.3 ± 7.4	21.4 ± 8.2	19.4 ± 3.4	9.3 ± 6.7*
	3 years and 6 months after the attack	24.0 ± 6.5	24.4 ± 3.7		28.4 ± 1.8	19.8 ± 11.5	21.1 ± 5.3		21.3 ± 3.7	
	4 years and 6 months after the attack	27.9 ± 12.6			43.4 ± 5.8**	29.3 ± 5.4	41.6 ± 5.1**	29.8 ± 3.6	19.2 ± 8.4	6.8 ± 0.9
t1 (ms) (Time between light stimulation and constriction of pupils)	1 year after the attack	256.5 ± 25.9	264.1 ± 21.4	256.2 ± 35.0	257.5 ± 29.4	258.7 ± 37.6	256.4 ± 41.7	257.3 ± 27.2	235.4 ± 62.0	
	2 years and 6 months after the attack	257.3 ± 26.5	241.6 ± 27.5	233.3 ± 16.7		260.0 ± 27.4	275.0 ± 16.7	267.8 ± 24.0	253.7 ± 27.4	266.6 ± 0.0
	3 years and 6 months after the attack	257.3 ± 26.5	263.9 ± 19.5		250.0 ± 19.2	250.0 ± 13.6	275.0 ± 11.8		258.3 ± 28.9	
	4 years and 6 months after the attack	255.9 ± 36.3			245.8 ± 43.8	245.8 ± 15.9	266.6 ± 49.1	225.0 ± 44.1	260.0 ± 19.6	316.6 ± 0.0

t2 (ms) (Time until the diameter of the pupil changed by half)	1 year after the attack	294.6 ± 58.0	315.4 ± 83.2	310.4 ± 54.1	292.5 ± 56.8	290.5 ± 67.8	278.8 ± 54.9	287.5 ± 28.9	277.1 ± 43.6	
	2 years and 6 months after the attack	272.7 ± 60.7	321.6 ± 59.3	294.4 ± 41.9		276.6 ± 57.3	274.9 ± 114.2	246.4 ± 43.0	262.9 ± 40.6	200.0 ± 0.0
	3 years and 6 months after the attack	285.0 ± 50.1	286.1 ± 74.1		295.8 ± 36.9	270.8 ± 47.9	249.9 ± 47.2		304.1 ± 25.0	
	4 years and 6 months after the attack	250.0 ± 56.8**			279.1 ± 37.0	262.5 ± 47.7	304.1 ± 64.4	233.3 ± 70.7	233.3 ± 42.3	175.0 ± 35.4
t3 (ms) (Time when the pupil reached the minimum size)	1 year after the attack	1038.1 ± 172.2	1024.3 ± 183.0	1102.2 ± 119.1	1055.8 ± 217.2	979.0 ± 195.7*	1019.2 ± 180.3	1055.2 ± 139.5	933.3 ± 113.4	
	2 years and 6 months after the attack	1007.8 ± 199.2	1140.0 ± 110.6	1170.8 ± 130.1		1028.3 ± 146.8	849.9 ± 347.7	964.3 ± 180.8	974.0 ± 190.1	691.6 ± 106.1
	3 years and 6 months after the attack	1035.8 ± 178.4	1052.7 ± 156.8		1070.8 ± 232.3	925.0 ± 223.4	908.3 ± 129.7		1149.9 ± 65.3	
	4 years and 6 months after the attack	868.4 ± 268.8**			995.8 ± 102.2	991.6 ± 351.0	1000.0 ± 213.9	820.8 ± 401.7	805.0 ± 205.8*	516.7 ± 235.7*
t5 (ms) (Time between the minimum and 63% dilatation)	1 year after the attack	1685.8 ± 500.0**	1650.0 ± 316.2	1658.5 ± 473.4	1639.1 ± 445.0	1644.2 ± 501.9	1684.6 ± 499.3	1691.6 ± 474.7	2091.6 ± 911.5**	
	2 years and 6 months after the attack	1281.4 ± 357.6*	1410.0 ± 538.7	1024.9 ± 104.1		1328.3 ± 393.7	1208.3 ± 337.3	1353.5 ± 308.6	1090.7 ± 120.8	1416.6 ± 70.7
	3 years and 6 months after the attack	1360.0 ± 387.1	1288.9 ± 311.6		1629.1 ± 566.4	1141.6 ± 414.9	1308.3 ± 129.7		1441.6 ± 327.9	
	4 years and 6 months after the attack	1375.0 ± 409.0			1308.3 ± 137.1	1462.5 ± 510.0	1720.1 ± 748.8	1495.8 ± 359.4	1258.3 ± 251.3	983.3 ± 117.8
vc (mm/s) (The maximum constriction velocity)	1 year after the attack	4.0 ± 0.7**	4.2 ± 0.7	4.2 ± 0.6	4.0 ± 0.6	3.8 ± 0.7**	3.8 ± 0.7	3.7 ± 0.6	3.8 ± 1.6	
	2 years and 6 months after the attack	4.0 ± 0.9	4.4 ± 0.9	4.4 ± 0.1		3.8 ± 0.7*	2.9 ± 0.6	4.1 ± 1.0	4.1 ± 1.1	4.9 ± 0.2
	3 years and 6 months after the attack	4.2 ± 0.8	3.9 ± 0.7		4.9 ± 0.5	3.4 ± 1.0*	4.6 ± 0.0		4.7 ± 0.3	
	4 years and 6 months after the attack	4.0 ± 0.9			5.0 ± 1.0	4.3 ± 0.1	3.8 ± 0.3	4.0 ± 0.4	3.8 ± 0.9	2.3 ± 0.2*
vd (mm/s) (The maximum dilatation velocity)	1 year after the attack	1.8 ± 0.4	2.1 ± 0.5	1.9 ± 0.4	1.8 ± 0.4	1.8 ± 0.3	1.7 ± 0.4	1.6 ± 0.3	1.9 ± 0.7	
	2 years and 6 months after the attack	1.9 ± 0.6	2.3 ± 0.9	2.8 ± 0.8		1.8 ± 0.4	1.6 ± 0.2	1.6 ± 0.4	1.8 ± 0.5	1.9
	3 years and 6 months after the attack	2.1 ± 0.3	1.9 ± 0.3		2.4 ± 0.4	2.0 ± 0.3	2.0 ± 0.1		2.2 ± 0.2	
	4 years and 6 months after the attack	1.6 ± 0.5*			2.1 ± 0.3	2.2 ± 0.8	1.6 ± 0.4	1.5 ± 0.3	1.4 ± 0.4	0.9 ± 0.2
ac (mm/s^2) (The maximum acceleration velocity of constriction)	1 year after the attack	56.9 ± 15.7	58.8 ± 19.7	59.1 ± 14.9	57.9 ± 11.1	56.6 ± 16.0	50.9 ± 11.4	56.3 ± 15.9	63.0 ± 29.3	
	2 years and 6 months after the attack	60.0 ± 22.2	71.1 ± 24.2	72.0 ± 15.6		57.6 ± 22.1	56.3 ± 34.8	52.5 ± 18.1	57.0 ± 20.6	81.0*
	3 years and 6 months after the attack	58.1 ± 14.4	49.5 ± 7.5		67.5 ± 9.0	49.5 ± 18.7	63.0 ± 12.7		67.5 ± 15.6	
	4 years and 6 months after the attack	58.2 ± 23.9			72.0 ± 19.4	85.5 ± 40.6	47.3 ± 20.2	63.0 ± 18.0	49.5 ± 14.2	31.5 ± 6.4

2. Objective adjustment ability (measurement using an infrared optometer)

As shown in Fig. 18, the adjustment ability reduced with age, whereas there was no difference between the control and the results at each medical checkup. The measured values and subjective symptoms did not always correspond. In victims in their 40s, eye fatigue was frequently observed. As presbyopia progresses and the reduction in the objective adjustment ability is significant in their age, it was difficult to detect objective findings for subjective symptoms. On the other hand, in case a parasympathetic stimulation agent entered the eye and a measurement was conducted using an infrared optometer, a proximal deflection at an adjusting rest position was present, which inferred that the condition might be detected in the measurement in young victims at the early stage.

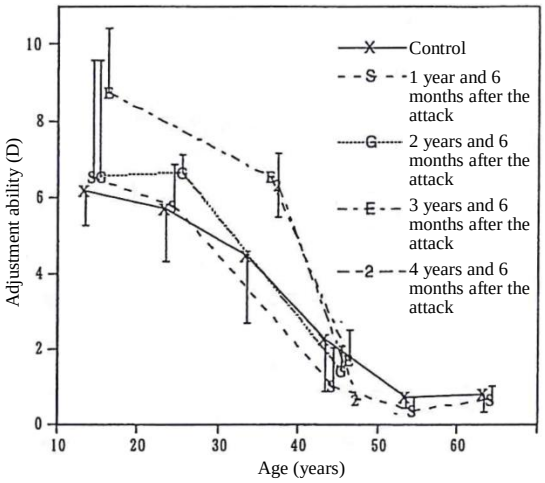


Fig. 18 Mean and standard deviation of the objective adjustment ability at different ages from each medical checkup

Major subject symptoms were eye fatigue and reduced visual acuity. In this measurement using an infrared optometer, the subjective symptoms and the results of the adjustment examination did not always correspond and abnormal adjustments were not detected. However, it was presumed that the parasympathetic nerves-dominant conditions remained owing to the sarin and, as with technostress ophthalmopathy, reduced visual acuity of the naked eyes and asthenopia induced by a proximal directional change at an adjusting rest position might be presented.

3. Visual acuity

At each medical checkup, only reduced visual acuity due to cataracts was detected in the elderly. The visual acuity in the other victims was favorable. Reduced visual acuity was not observed as an aftereffect due to sarin exposure.

4. Visual field (measurement using an automated perimeter)

In victims with 90% ChE at the time of exposure and in whom afferent constriction of the visual field was observed by a Humphrey Field Analyzer, the visual field measurement was repeated in the medical checkup 1 year after the attack. Although the condition was alleviated, the constriction remained. Subsequently, because the victim did not receive the medical checkup, the visual field examination was not conducted and it was thus unknown if the condition remained.

5. Electroretinogram (retinal electric reaction to light)

A mild reduction in the electroretinographic response remained in a victim with 12% ChE at the time of exposure, although the condition had gradually been alleviated. As the victim did not measure electroretinogram in medical checkups 1 year and 6 months and 2 years and 6 months after the attack, the case was not considered as Evaluation C during those years. However, if the victim had measured electroretinogram, it was inferred that a mild reduction in the electroretinographic response would have been detected and aftereffects of the sarin might remain in this severe victim.

6. Ophthalmoscopic findings

As 1 year or longer had passed from the sarin exposure to the medical checkups, for conditions such as conjunctival congestion, there was no finding from which the aftereffects of the exposure might be suspected. On the other hand, in the case of chronic phosphororganic poisoning, as it was reported that the retina in the eye ground might degenerate like retinal pigmentary degeneration, it was considered necessary to conduct regular examinations, especially in severe victims at the time of exposure having reduced electroretinographic response.

Summary

Overall, except for elderly, the diameter of the pupils, visual acuity and adjustment ability were normal. Thus, it was considered unlikely that the aftereffect might remain. On the other hand, although the measurement of the reaction to light was conducted through light stimulation only once, in the case of chronic phosphororganic poisoning, constricted pupils and prolonged recovery times were observed with repeated light stimulations. Moreover, because the disorder related to the Cajal nucleus and the central substance of the midbrain where the ChE value is high remains, it is reported that in the measurement of eye movement, when the smooth pursuit defect is measured by reduction in the gain to an indication pointer, remaining influence would be detected. In these checkups, if such a measurement was conducted, the overall remaining influence might be observed. However, the electronic pupillometer used in these checkups was portable, which could release light only once. In the measurement of the eye movement, a traced indication pointer and electronic measurement apparatus are necessary and it becomes specialized and large scale. Thus, it could not be conducted.

In the severe victims with 12% ChE at the time of exposure, reduction in the electroretinographic response remained and temporally constricted pupil was observed, which indicated that the influence of the sarin exposure might remain. Therefore, we considered that it would be necessary to continue the medical checkups mainly in victims who were considered to have remaining aftereffects.

Report on health surveys conducted after the toxic gas poisoning attack in Matsumoto City

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Report on health surveys conducted after the toxic gas poisoning attack in Matsumoto City
The 3rd survey

There were about 600 victims in the toxic gas (sarin) attack in Matsumoto City on the night of June 27, 1994. In a simple survey (of victims who had shown subjective symptoms three weeks after the attack) that was conducted about 4 months after the attack, 40 victims still noticed subjective symptoms caused by the toxic gas. During June 27–30, 1995, using the same survey method as the 1st survey, subjective symptoms caused by the toxic gas were investigated.

Survey method

The subjects were the same as in the 1st survey. Chairmen of neighborhood associations distributed and collected 2,052 questionnaire sheets. There were 1,237 responders (616 males, 609 females, and 12 people who did not specify), equivalent to a collection rate of 60.3%. Among the 1,237 responders, 318 felt subjective symptoms immediately after the attack and 919 didn't feel it.

Table 1. Distribution of the ages of subjects for the survey

Age groups	Number of people	%
0–4	16	1.3
5–9	31	2.5
10–14	39	3.2
15–19	48	3.9
20–29	123	9.9
30–39	134	10.8
40–49	183	14.8
50–59	180	14.6
60–69	198	16.0
70–79	163	13.2
80–89	77	6.2
90–	10	0.8
Unknown	35	2.8

Table 2. Subjective symptoms 1 year after the sarin exposure

Symptoms	Overall	Inpatients	Outpatients	People without the visit	Others
Easily fatigued	39	10	16	6	7
No patience	20	8	5	4	3
Stiff shoulder	20	3	9	6	2
Frequent nightmares	7	2	3	0	2
Difficulty in sleeping at night	9	2	4	1	2
Reduced visual acuity	34	6	11	9	8
Narrowed visual field	4	1	2	0	1
Eye fatigue	43	10	15	8	10
Cannot smoke cigarettes anymore	3	3	0	0	0
Cracking voice	8	0	5	2	1
Slight fever	3	2	1	0	0
Palpitations	6	2	3	0	1
Cough	1	0	1	0	0
Runny nose	2	0	1	1	0
Ocular hyperemia	0	0	0	0	0
Cannot easily write	1	0	1	0	0
Cannot sleep due to fear when alone	1	1	0	0	0
Feel that ocular aging has advanced	1	0	0	1	0
Shortness of breath when recalling the attack	1	0	1	0	0
Blush in one’s face unexpectedly	1	0	0	1	0
Increased blood pressure	1	0	0	1	0
Sneezing	1	0	0	1	0
Sore throat	1	0	0	1	0
Migraine headaches	3	0	2	0	1
Sweating	1	0	0	0	1
Numbness in the hands and feet	1	1	0	0	0
Poor gastrointestinal conditions	1	1	0	0	0
	58	10	25	13	10

Results and discussion

1. Results from the questionnaires

One year after the sarin exposure, the questionnaires inquired about subjective symptoms, which appeared to be caused by sarin. Fifty-eight people felt some subjective symptoms. The subjective symptoms included “Eye fatigue”, which was the most frequent, followed by “Reduced visual acuity”, “Easily fatigued”, “No patience”, and “Stiff shoulder”. Besides those, there were “Difficulty in sleeping at night”, “Cracking voice”, “Palpitations”, “Frequent nightmares”. “Eye fatigue” was the most common symptom in the survey 4 months after the attack as well as in the survey 1 year after the attack.

Inpatients had the highest occurrence of subjective symptoms 1 year after the attack followed by outpatients. In people who did not receive treatment, only a few had subjective symptoms 1 year after the attack. Although three people claimed not to exhibit any subjective symptoms immediately after the attack in the 1st survey last year, subsequently, they reported feeling subjective symptoms later. A 66-year-old woman reported, “Although I thought it was not sarin, I felt some subjective symptoms as if it was caused by sarin.” Although a 38-year-old woman reported that she felt subjective symptoms within one week, she filled in the questionnaire sheet last year affirming, “I do not feel any subjective symptom.” The remaining person aged 81 answered: “I felt subjective symptoms after 1 month or more passed.”

2. Methods for coping with subjective symptoms

Table 3. Methods for coping with subjective symptoms

Methods	Number	Methods	Number
Outpatient treatment	10	Unique health treatment	14
		Sleep well	3
Using commercialized drugs	14	Healthy foods	2
Saridon	1	Vankey treatment	1
Rokushingan	1	Light therapy	1
Eye drops	3	Early to sleep and wake-up	1
Nutritional supplements	1	Gargle	1
		Exercise at a gym	1
Isoscreen	1 (Taisho Pharmaceutical)	Regular meals and exercise after meals	1
		Wearing eyeglasses	1
Cold medicine	2	Replace electric lamps	1
Bufferin	2	Throat drops	1
		Nothing	

3. Symptoms one year later

In the 1st survey last year, 1,734 people participated. In the 3rd survey this year, 1,237 people participated. Of them, 1,016 people (58.3%: 28 inpatients, 70.0%: 115 outpatients, 73.7%: 175 people without the visit, 57.1%: 698 people without subjective symptom, 56.3%) have participated in the 1st survey. As shown in Table 4, most of the people who had subjective symptoms 4 months after the attack still did 1 year after the attack.

Figs. 1-3 show variation in the subjective symptoms in the participants in both 1st and 3rd surveys. Most of the subjective symptoms, which the subjects felt immediately after the sarin exposure, disappeared 4 months after the attack. However, the number of people with eye fatigue increased in the inpatients, outpatients, and people without a visit. All inpatients who had subjective symptoms had eye fatigue. It was present in more than half of the outpatients and the people without the visit who had subjective symptoms.

Initially, up to 4 months after the attack, complaints were rare. Frequent subjective symptoms in the survey 1 year after the attack were “Reduced visual acuity”, “Easily fatigued”, “No patience”, and “Stiff shoulders”. It should be noted that all inpatients were “easily fatigued” as well as had “eyes fatigue”. Two inpatients and three outpatients reported complaints of “Frequent nightmares” and “Palpitations”. The two inpatients were considered as “having aftereffects” in the medical checkup. The three people who reported that they could not smoke cigarettes anymore were all inpatients.

Figs. 4 and 5 show the complaint rate of subjective symptoms immediately and 1 year after the attack. The people who had subjective symptoms 1 year after the attack lived in a rectangular area with a long axis of 400 m from the spot of the attack. Most of the severe victims and 70% of all victims with sarin poisoning lived in the area, where was exposed to a relatively high concentration of sarin. These results indicate that the people exposed to the relatively high concentration of sarin have had subjective symptoms for 1 year since the attack.

Significance and problems of Health Survey Committee activities

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The Health Survey Committee commenced full-scale activities with an explanatory meeting for the regional representatives of the residents on July 14, 1994. At that time, the Committee explained about questionnaires for the residents and the medical checkups, and provided information on sarin at that time point. Subsequently, the health surveys were conducted continuously for the residents in the affected area. The results revealed that except for a very small number of severely affected victims any disorder caused by sarin had already disappeared. In this paper, the activities of the Health Survey Committee will be summarized.

The detailed results of the medical checkups conducted at the acute stage can be obtained from the report on surveys of the toxic gas poisoning in Matsumoto City, which has already been published. Furthermore, the results of the subsequent medical checkups can be obtained from the description by Yoshiki Sekijima, which is shown on the next page of this book.

Basic directions for the health surveys and its significance (Measures for the severely affected victims and health measures for regional residents)

The important objectives of the health surveys at the initial stage were to determine to what degree the residents had been affected by sarin and what aftereffects could be predicted. Therefore, in July, the erythrocyte acetylcholinesterase levels (true cholinesterase) were measured in all the residents who desired it. Furthermore, the inpatients who did not receive the medical checkup were each notified of the measurements through the hospital, and it was conducted individually.

Based on the results of this examination, medical checkups, and the medical care of the severely affected inpatients, the Expert Committee on Medical Cares Against Toxic Gas Poisoning Attack decided to implement the following basic directives for subsequent follow-up observation in the victims of the sarin attack.

1) The follow-up observations should be considered for severely poisoned victims and the others separately.
2) The severely affected victims were those who experienced serious effects such as consciousness disorders at the time of the attack, convulsion, or respiratory disorders. Presently, the fact that these victims may experience residual symptoms (such as electroencephalogram abnormalities and arrhythmia) or possible aftereffects (peripheral nerve disorder or unknown disorders which have not been reported) cannot be denied. Therefore,

careful follow-up observations are necessary.

3) The majority of victims with normal erythrocyte acetylcholinesterase levels cannot be considered to have absorbed a large amount of sarin. Since the local symptoms were alleviated, the possibility of subsequently new symptoms appearing may be considered low.
4) Handling the severely and mildly affected victims in a uniform manner and greatly publicizing issues such as the aftereffects of sarin will create unnecessary anxiety in the residents.
5) Therefore, it would be necessary to correspond with the residents without stirring up their anxiety and, in case unknown aftereffects appear, to develop and maintain a system to promptly deal with the situation.

Following the basic directives explained above, on August 31 a notification entitled "To: Residents affected by the gas poisoning attack" was circulated (refer to the report on surveys of the toxic gas poisoning in Matsumoto City (1995) 106-107). The notification emphasized that the mildly affected victims should not be unduly worried and if any cause for concern is noticed, it is recommended to consult the City Government (Citizens' Health Division) without any hesitation.

In dealing with the situation caused by the attack, it was noteworthy that efforts were made to avoid stirring up the residents' anxiety unnecessarily and the city government was involved in taking active measures to quell the anxiety of the residents about their health from the day of the attack. Furthermore, the medical checkups for the severely affected victims still continue at present. The Committee recommends that the residents of Matsumoto City should receive examinations at the Shinshu University Hospital and that individuals who have moved to distant places should continue to receive examinations as well and should be referred to appropriate medical institutions when necessary. As a result of these measures, subsequent progress in most of the severely affected victims have been favorable, and it was proven that the electroencephalogram abnormalities, which appeared to persist as an aftereffect of the sarin exposure, have been alleviated (Annals of Internal Medicine 127:1042,1997). However, presently, in some severely affected victims, there is a possibility that the disorders caused by sarin might remain at a high level and subsequent, continuous medical checkups are required. The details can be obtained by referring to the "Health survey results (3^{rd}–7^{th}) – long-term effects of sarin poisoning –" by Yoshiki Sekijima and the report on surveys of the toxic gas poisoning in Matsumoto City (Matsumoto City Council of Community-Based Integrated Care, 1995).

Various problems related to posttraumatic stress disorder (PTSD)

One of the problems associated with the attack is posttraumatic stress disorder (PTSD). It was not widely reported at the time of the Matsumoto sarin attack, and the concept was not well known compared with the current situation. However, it is commonly known that victims of great disasters

or attacks are likely to experience mental health problems. Therefore, it was easily presumed that this condition could occur.

In the early days after the attack, the Committee did not plan to conduct active counseling for such mental problems, and the emphasis was on providing the residents with accurate information and instituting measures to avoid stirring up their anxiety unnecessarily. However, there was evidence of mental instability in some victims, which was worsened when the subway sarin attack occurred and the court proceeding on the attack commenced. Taking these facts into consideration, the item on PTSD was included in the continuous health surveys for the residents (the primary screening by the distribution of medical interview sheets) and screening investigations were conducted in the victims who might have PTSD.

As a result, PTSD was suspected in several victims. However, in July 1999, some news media reported that dozens of residents experienced PTSD because of the Matsumoto sarin attack. The numerical value was based on the number of individuals who showed certain symptoms after the attack as the answer for some items on the medical interview sheet (such as “cannot sleep”). Therefore, these observations cannot be considered as PTSD. The screening process identified 10 individuals who were confirmed to meet the diagnostic criteria for PTSD based on the USA mental diseases classification (DSM-IV) (Among those identified, six individuals had received examinations at medical institutions at the time of the attack). Moreover, direct interviews were conducted with the affected individuals and more than a half of them were found to have PTSD which was not associated with the sarin attack. On July 19, 1999, the Health Survey Committee conducted a news briefing on this matter and explained the course of events and the current situation.

Moreover, physicians specializing in psychosomatic internal medicine conducted counseling sessions for victims who were likely to need to receive counseling and for those who desired it. Furthermore, in the case of individuals who needed to receive continuous counseling, specialized physicians were also referred. At that time, the individuals who desired the counseling requested strongly that the counseling should not be disclosed and be conducted in a situation devoid of any possible news reporting.

Considering these issues, it was recommended that the individual counseling sessions should be implemented from the earlier stage, but necessary measures to minimize the occurrence of PTSD have been taken.

Lessons for future similar cases

The Matsumoto sarin attack differed from the subway sarin attack because it occurred in a residential area and the victims could be identified easily by the city government. The neighborhood association was extremely well organized and cooperative, which facilitated the smooth

implementation of the health surveys.

Moreover, the linkage among the city government, Matsumoto City Medical Association, Matsumoto Healthcare Center, and Shinshu University School of Medicine, who constituted the Council of Community-Based Integrated Care, was very smooth at the level of the administrators and interested parties. This aspect was important for implementing the health surveys and providing immediate explanations to the victims. However, these were not prearranged as systems, and the discretions and cooperation of the interested parties contributed greatly to the success of the program. An example of these contributions was that of the mayor of Matsumoto City who recommended that residents should receive health examinations at medical institutions and subsidized the medical expenses on that day.

To minimize the development of PTSD, it is important to satisfy both of the needs to provide the necessary information and to avoid stirring up the residents' anxiety unnecessarily. As mentioned previously, in the medical checkups, necessary medical cares and counseling sessions, and information provided differed between the severely and mildly affected victims. In this regard, the number of the severely affected victims was fortunately extremely small in the Matsumoto sarin attack and, therefore, they could be treated individually.