
原 著

A SURVEY OF ADULTS SUFFERING FROM MENTAL SEQUELAE TO
AN INCIDENT OF ACCIDENTAL MASS ARSENIC POISONING
DURING INFANCY OR EARLY CHILDHOOD

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Abstract : In 1955, about 13,000 babies in western Japan suffered from arsenic poisoning due to contamination of powdered milk supplies. The purpose of this report is to survey the social adjustment and neuropsychiatric characteristics of persons with mental disorders, epilepsy and mental retardation who are registered at the head office of a nongovernmental victims' relief agency, the Hilary Society, set up to serve survivors of this mass poisoning incident. The authors analyzed records for 578 survivors, of whom 79 have died in adulthood. By means of questionnaires completed by case workers in the society's field offices, demographic features, health problems in infancy, education and occupation, marital status and family history, medical history and levels of social adaptation were investigated. We estimated the prevalence of schizophrenia and other disorders (F2 category in ICD-10) in the population of survivors and concluded that the prevalence of these mental disorders among survivors is statistically higher than that in the general population. Survivors seeking the relief agency's support also appear to be characterized by lower educational achievement, lower marriage rates and lower levels of social adaptation. (奈医誌. J. Nara Med. Ass. 50, 63~73, 1999)

Key words : mental disorder, schizophrenia, prevalence, arsenic poisoning, disaster psychiatry

In the western part of Japan during the spring and summer of 1955, there was an accidental mass poisoning of infant with arsenic in the food supply. An infant formula preparation of dry milk, produced at the Tokushima Processing Plant of the Morinaga Milk Company, was contaminated with sodium arsenate, which came from the disodium hydrogen phosphate used

in the manufacturing process. According to an announcement of the Ministry of Health and Welfare at the time, 12,131 babies suffered from acute or chronic poisoning, of whom 130 died. Almost all of the arsenic-poisoned babies had displayed initial symptoms of high fever, diarrhea, vomiting and insomnia. They then showed typical symptoms of arsenic poisoning, such as exanthema, pigmentation, hepatomegaly and anemia. Many of them suffered cachexia or dehydration as a result of the intoxication and some of them displayed ascites, icterus and convulsions¹⁾. The frequency and the severity of these symptoms abated upon withdrawal of contaminated powdered milk supplies from the market.

In 1956, the Ministry of Health and Welfare instituted a survey of the arsenic-poisoned babies' conditions. At the time, nearly all of the babies were judged to have completely recovered from poisoning, because they showed no characteristic symptom or sign of arsenic poisoning other than slight hepatomegaly or incomplete recovery of the blood system.

The Ministry's ad hoc committee judged at the time that no sequelae would occur in the arsenic poisoned babies. However, in 1969, a group of public health nurses and school nurses noted adverse health consequences in the survivors of the arsenic poisoning²⁾. Following the report, a nationwide health screening of the survivors by physicians confirmed some sequelae: impairment of the central nervous system, such as cerebral palsy, epilepsy, mental retardation and minimal brain dysfunction syndrome, and dermatological findings, such as leukoderma and keratoderma^{3,4,5)}.

In 1974, a nongovernmental relief foundation, the Hikari Society, was established with funding by the milk producer and the Japanese government as a result of a court-ordered consent decree issued in response to a lawsuit filed by parents of the victims. The Society provides relief to all victims in the form of regular medical examination, health consultation, social services, underwriting special education needs and guaranteed employment.

As of July 1996, the number of victims totaled 13,418, of whom 679 have died. Of the remaining 1,2739 victims, 6,277 keep in regular contact with the Hikari Society, about 2,000 make contact only on occasions when victims or their families need help, and about 4,400 do not maintain contact with the Society at all.

SUBJECTS AND METHODS

The subjects of this report are victims registered at the head office of the Hikari Society as having had mental disorders, epilepsy or mental retardation.

Of those registered with these disorders, 499 are alive and 79 have died since initial registration. We prepared a questionnaire including items covering physical state during the early stage of the poisoning, the history of education, occupation and marital status, family structure, and family history of illness. The questionnaire also covered history of any present psychiatric illness, history of its therapy, present state of the illness, interpersonal relationship problems, level of daily living skills, current level of social accommodation and adaptation, economic or monetary circumstances and future life prospects.

The questionnaires were completed by case workers at the Society's 20 branch offices. Case workers have accumulated detailed data records concerning health conditions and life situations of the survivors for about 20 years. Data used in completing the questionnaires was restricted to those gathered from the autumn of 1993 to the spring of 1996. All of the

questionnaires were returned completely.

We analyzed the data using STATVIEW software for personal computers. Original diagnosis was made using a variety of diagnostic criteria by the clinician assigned to each patient. Using the data from the questionnaires, we categorized cases to conform to the International Classification of Diseases, 10 th edition (ICD-10). In those instances in which a subject had two or more diagnoses, we classified the case into one of three diagnostic groups according to the most salient feature of the subject's mental problems. For assessment of social function level and adaptation, we used Eguma's Social Adaptation Scale (ESAS)⁶.

RESULTS

(A) 499 living subjects

The 499 living subjects (survivors) can be divided on the basis of their primary diagnoses into three groups: mental disorders, epilepsy and mental retardation.

I Demographic features of the survivors

Table 1 shows the number of male and female subjects in each of the three diagnostic groups. Men outnumber women in this population of living survivors of the 1955 outbreak of infant arsenic poisoning who have registered with one of the three categories of neuropsychiatric disorders. The epilepsy group contained one of every nine survivors in this population. The remainder were about evenly split between the other two groups. The proportions of male subjects to female subjects in the three diagnostic groups are very similar to the proportion of total subjects.

Table 2 illustrates the year of their births. It is a matter of course that 90 % of the subjects were born in 1954 or 1955 when poisoned infant-formula powdered milk was marketed. Compared to the other two groups, survivors in the epilepsy group were more likely to have

Table 1. Sex of the survivors

Sex	Total		Mental Disorders		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
Male	296	59.3	128	59.8	32	55.2	136	59.9
Female	203	40.7	86	40.2	26	44.8	91	40.1
Total	499		214		58		227	

Table 2. Year of birth of the survivors

Year of Birth	Total		Mental disorders		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
1949	3	0.6	1	0.4	1	1.7	1	0.4
50								
51	4	0.8	1	0.4			3	1.3
52	12	2.4	7	3.3	3	5.2	2	0.9
53	30	6.0	9	4.2	3	5.2	18	7.9
54	218	43.7	100	46.7	18	31.0	100	44.1
55	231	46.3	96	44.9	33	56.9	102	44.9
56	1	0.2					1	0.4
Total	499		214		58		227	

been born in 1955 ($\chi^2=2.916, p<0.10$), suggesting that the survivors in the epilepsy group were exposed to the arsenic polluted milk sooner after birth than those in the other two groups.

II Health problems in infancy

The period of initial exposure to the arsenic-contaminated milk is listed in Table 3. Records exist of this exposure period for only about 40 % of the subjects. Most of the subjects for whom records exist were exposed to the milk within six months after birth. The epilepsy group particularly had a prominent tendency toward earlier exposure, although the difference in exposure latency from that of the other two groups is not statistically significant by the

Table 3. Period after birth in which survivors were first exposed to poisoned milk

Period (Month)	Total		Mental Disorder		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
1 ~ 3	142	28.5	57	26.6	26	44.8	59	26.0
4 ~ 6	34	6.8	14	6.5	4	6.9	16	7.0
7 ~ 9	22	4.4	13	6.1	3	5.2	6	2.6
10~12	6	1.2	3	1.4	1	1.7	2	0.9
13~18	1	0.2					1	0.4
19~24	1	0.2	1	0.5				
25~36	1	0.2	1	0.5				
Unknown	292	58.5	125	58.4	24	41.4	143	63.0
Total	499		214		58		227	

Table 4. Educational history of the survivors

Institution (Highest Level Entered)	Total		Mental disorders		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
School for the handicapped								
Graduated	67	13.4	5	2.3	16	27.6	46	20.3
Dropped out	10	2.0			3	5.2	7	3.1
Elementary School								
Graduated	5	1.0					5	2.2
Dropped out	9	1.8	1	0.5	3	5.2	5	2.2
Junior high school								
Graduated	145	28.5	39	18.2	21	36.2	82	36.1
Dropped out	5	1.0	1	0.5			4	1.8
High school								
Graduated	83	16.6	67	31.3	2	3.4	14	6.2
Dropped out	18	3.6	10	4.6	1	1.7	7	3.1
College								
Graduated	30	6.0	22	10.2	2	3.4	6	2.6
Dropped out	7	1.4	5	2.3	1	1.7	1	0.4
University								
Graduated	39	7.8	38	17.8			1	0.4
Dropped out	16	3.2	16	7.5				
Exemption from compulsory education	56	11.2	1	0.5	9	15.5	46	20.3
Unknown	12	2.4	9	4.2			3	1.3
Total	499		214		58		227	

Wilcoxon's Rank Sum Test.

Convulsion during infancy appeared at a higher rate (44.8 %) in the epilepsy group than in the other two groups. Ninety-six (19.2 %) of those 499 subjects were admitted to hospital during infancy, 16.8 % of subjects in the mental disorders group, 25.9 % in the epilepsy group and 19.8 % in the mental retardation group. The epilepsy group showed a somewhat higher relative frequency of admission during infancy compared with the other two groups.

III History of education and occupation

Educational history of the survivors are shown in Table 4. Although two-thirds of the same generation as the survivors graduated from high school in Japan, the survivors represented here suffered a much lower rate of graduation.

Three-hundred and forty-one subjects had obtained at least one job; 108 (31.7 %) of them did not change their jobs after their first employment. With regard to difference between these three diagnostic groups, 181 (84.6 %) of the subjects with mental disorders have worked before, while only 31 (53.4 %) of the epilepsy group and 129 (56.8 %) of the mental retardation group (56.8 %) have.

IV Marital status and social adaptation levels

Marital status is shown in Table 5. A greater percentage of subjects in the epilepsy group and the mental retardation group remained unmarried than in the mental disorders group.

Table 6 shows levels of social adaptation in these survivors. It appears that levels of social adaptation in the subjects of the mental disorders group tend to be better than those of this cohort as a whole.

Table 5. Marital status of the survivors

Marital State	Total		Mental Disorder		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
Unmarried	368	73.7	133	62.1	50	86.2	185	81.5
Married	107	21.4	63	29.5	7	12.1	37	16.3
Divorced	21	4.2	17	7.9			4	1.8
Widow or Widower	3	0.6	1	0.5	1	1.7	1	0.4
Total	499		214		58		227	

Table 6. Present level of social adaptation of the survivors

ESAS*	Total		Mental Disorders		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
Self-Supportive	118	23.6	68	31.8	8	13.8	42	18.5
Semi-Self-Supportive	8	17.6	27	12.6	12	20.7	49	21.6
Socially Adjusted to Family or Community	95	19.0	48	22.4	4	6.9	43	18.9
Maladjusted	53	10.6	26	12.1	11	19.0	16	7.0
Hospitalized	108	21.6	30	14.0	19	32.8	59	26.0
Unknown	37	7.4	15	7.0	4	6.9	18	7.9
Total	499		214		58		227	

* ; ESAS's Social Adjustment Scale. See Reference 6).

V Utilization of social services and support provided by the Hikari Society

Nearly two-thirds of the subjects received a public pension for the disabled, as shown in Table 7. About one-third of the survivors get a first-grade pension, and subjects in the epilepsy group or the mental retardation group receive larger amounts of pension than those in the mental disorders group. In addition, 295 (59.1 %) subjects receive an allowance as compensation paid by the Society, and the subjects of the mental retardation group and the epilepsy group similarly take a larger allowance.

Branch offices of the Society have assessed and planned support schedules for nearly all of the subjects (428, 85.5 %); nevertheless, living conditions of many subjects remain poor. Causes for difficulties in daily living include severe symptoms (20.6 %), lack of appropriate care (18.2 %) and lack of desire to improve themselves (10.0 %). Support schedules for many of them (406, 81.4 %) include plans to admit survivors into social facilities, such as residential facilities, in an effort to improve their living conditions.

(B) 214 survivors with mental disorders

Results here refer to conditions for 214 subjects with mental disorders. Table 8 shows the distribution and proportion of mental disorders in terms of ICD-10 diagnostic criteria.

Table 9 shows the age of onset of their mental illnesses. Although arsenic poisoning occurred during infancy, in about one-third of these subjects (101, 51.5 %), psychiatric symp-

Table 7. The number of pensioners among the survivors

Recipient	Total		Mental Disorders		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
Pension	327	66.5	99	46.2	49	84.5	179	78.9
1st Grade	166	33.3	26	12.1	33	56.9	107	47.1
2nd Grade	123	24.6	53	24.8	11	19.0	59	26
3rd Grade	11	2.2	11	5.1				
Unknown Grade	27	5.4	9	4.2	5	8.6	13	5.7
No Pension	172	34.5	115	53.7	9	15.5	48	21.1
Total	499		214		58		227	

Table 8. The number of the survivors with diagnoses by ICD-10 diagnostic criteria

Diagnostic Criteria	Number	%
F0 Organic Mental Disorders	51	23.8
F1 Substance Abuse	3	1.4
F2 Schizophrenic Disorders	110	51.4
F3 Mood Disorders	12	5.6
F4 Neurotic Disorders and Others	31	14.5
F6 Personality Disorders	5	2.3
Others	2	0.9
Total	214	

Table 9. Age of onset of the survivors' mental disorders

Age (years)	Number	%
Less than 5	4	1.9
5 to 9	6	2.8
10 to 14	25	11.7
15 to 19	56	26.2
20 to 24	29	13.6
25 to 29	23	10.7
30 to 34	15	7.0
35 or more	10	4.7
Unknown	46	21.5
(10 to 24)	110	51.5
Total	214	

toms first manifested in puberty and adolescence (from age 10 to 24), as observed in the general population. Only 59 (21.7 %) subjects had a record of a life event that could have induced the emergence of their mental disorders. Sixty-three (23.2 %) subjects commenced psychiatric treatment in the years from 1970 to 1975, the mode period in terms of therapeutic commencement.

Among 214 survivors with mental disorders, 137 had history of psychiatric hospitalization. Table 10 lists the frequency of admission, and Table 11 the total duration of hospitalization. In addition, types of present treatment for this group are shown in Table 12. Many of these survivors are outpatients at a psychiatric clinic; 15 % of them are now admitted or institutional-

Table 10. Frequency of admission of the survivors with mental disorders

Frequency of Admission	Number	%
1	32	23.4
2	18	13.1
3 to 5	41	30.0
6 to 10	38	27.7
11 to 20	7	5.1
Over 20	1	0.7
Total	137*	

* ; Only 137 survivors among 499 survivors experienced hospitalization

Table 12. Present treatment for the survivors with mental disorders

Type of Treatment	Number	%
Admission	32	15.0
Outpatient Clinic	125	58.4
Counseling	19	8.9
Rehabilitation	10	4.7
None	12	5.6
Unknown	16	7.5
Total	214	

Table 11. Total duration of admission of the survivors with mental disorders

Duration of Admission	Number	%
Less than 3 Months	19	13.9
3 Months to under 6 Months	16	11.7
6 Months to under 1 Year	17	12.4
1 Year to under 2 Years	20	14.6
2 Years to under 3 Years	10	7.3
3 Years to under 6 Years	18	13.1
6 Years to under 10 Years	13	8.8
10 Years to under 16 Years	9	6.6
16 Years or over	7	5.1
Unknown	8	5.8
Total	137*	

* ; Only 137 survivors among 499 survivors experienced hospitalization

Table 13. Present level of social adaptation of the survivors with mental disorders

ESAS*	Total		Diagnostic Criteria						
	Number	%	F0	F1	F2	F3	F4	F6	Others
Self-Supportive	68	31.8	33		9	7	17	1	1
Semi-Self-Supportive	27	12.6	5		16	3	2	1	
Socially Adjusted to Family or Community	48	22.4	4	1	36	2	3	2	
Maladjusted	26	12.1	3		18		4	1	
Hospitalized	30	14.0	2	1	25		2		
Unknown	15	7.0	4	1	6		3		1
Total	214		51	3	110	12	31	5	2

* ; ESAS's Social Adjustment Scale. See Reference 6).
Abbreviation of Diagnostic Criteria ; Table 8

Table 14. Age at death of the subjects who died

Age at Death (years)	Total		Mental Disorders		Epileps		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
13 to 15	1	1.3					1	5.3
16 to 20	3	3.8	1	2.6	1	4.5	1	5.3
21 to 25	12	15.2	7	18.4	5	22.7		
26 to 30	17	21.5	7	18.4	3	13.6	7	36.8
31 to 35	23	29.1	12	31.5	9	40.9	2	10.5
36 to 40	22	27.8	11	28.9	4	18.2	7	36.8
Over 40	1	1.3					1	5.3
Total	79		38		22		19	

Table 15. Cause of death

Cause of Death	Total		Mental Disorders		Epilepsy		Mental Retardation	
	Number	%	Number	%	Number	%	Number	%
Dis. of the Central Nervous Sys.	7	8.9			3	13.6	4	21.1
Dis. of the Cardiovascular Sys.	17	21.5	6	15.8	5	22.7	6	31.6
Dis. of the Respiratory Organs	13	16.5	1	2.6	7	31.8	5	26.3
Dis. of the Digestive Organs	4	5.1	2	5.3			2	10.5
Other Diseases	7	8.9	4	10.5	2	9.1	1	5.2
Accident	7	8.9	2	5.3	4	18.2	1	5.2
Suicide	21	26.6	21	55.3				
Unknown	3	3.8	2	5.3	1	4.5		
Total	79		38		22		19	

Dis. : Disease

Sys. : System

ized in a hospital or other residential facility, and about 9 % of them make use of a counseling service.

Table 13 shows levels of social adaptation of the subjects with mental disorders categorized by ICD-10 criteria.

(C) Subjects who died

Of the 79 registrants who died, 56 (70.9 %) were male and 23 (29.1 %) were female. More than half of the deceased subjects died at 31 years old or over (Table 14). Causes of death are shown in Table 15. The most frequent single cause was suicide, accounting for one in every four deaths of the combined groups, and for more than half of the mental disorders group.

38 deceased subjects of the mental disorders group comprised 2 (5.3 %) with organic mental disorder (F 0), 2 (5.3 %) with substance abuse (F 1), 21 (55.3 %) with schizophrenia, 6 (15.8 %) with mood disorder (F 3), and 4 (10.5 %) with neurotic disorder (F 4). There were three decedents whose psychiatric diagnoses were unknown.

DISCUSSION

Japan experienced many problems with environmental pollution during the period of industrial revolution after World War II; the arsenic milk poisoning accident counted among them. About 12,700 survivors, who are now 43 years old or more, are receiving social support through

the Hikari Society. Imaizumi and Kanazawa (1990)⁷⁾ and Kanazawa et al. (1990)⁸⁾ have reported on the psychiatric sequelae of this accident of food-chain contamination. We, the members of the psychiatric research group of the Hikari Society, investigated mental sequelae in these 499 survivors and 79 deceased subjects, and published our findings in Japanese (1997)⁹⁾. The present article reports some of these results in English for wider acknowledgement of this incident, and for its contribution toward preventing similar accidents.

I The influence of brain damage due to arsenic poisoning during infancy

A greater fraction of subjects in the epilepsy group were born in 1955 than in the other two groups ($\chi^2=2.916$, $P<0.10$). This finding probably suggests that babies exposed to arsenic earlier suffer from epilepsy afterwards more frequently than from mental disorders or mental retardation. However, there is no evident relation between exposure to arsenic during earlier periods and a higher risk of suffering from epilepsy afterwards. The reason might be that more precise (monthly) data about periods of first exposure to the milk are unknown for nearly 40 % of the survivors.

Concerning mental disorders found in the survivors, 110 subjects (51.4 % of the total number of the survivors with mental disorders) were classified in ICD-10's F 2 category (schizophrenia and other disorders). This might relate to branch-office case workers' capacity to find cases with mental problems, i. e., it is probable that the caseworkers are overlooking milder disorders, for example, mood disorder and neurotic disorder. Because survivors with such milder disorders do not consult a psychiatrist, and thus do not always report their mental problems to branch offices. In any case, schizophrenia and similar disorders, like schizotypal and delusional disorders, are more salient and reported more accurately to branch offices.

Therefore, we can compare the prevalence of F 2 disorders (in ICD-10) among the survivors with that of the general population in the same generation. With regard to prevalence, we cannot know the true prevalence of F 2 disorders among the survivors, and the Japanese government has not directly investigated the prevalence of schizophrenia and similar disorders nationwide for thirty years or more. Consequently, we will alternatively compare the "morbidity", the proportion of the population that is receiving psychiatric therapy, between survivors and the general population. The "morbidity" among the survivors is 0.86 % ; 110 survivors with F 2 disorders in all the survivors (12,739=13,418-679). However, the health status of only 6,277 victims is known accurately by the Hikari Society. Then, so far as these 6,277 victims are concerned, the "morbidity" among survivors is estimated at 1.96 % ; 110 survivors with F 2 disorders in 5,598 (=6,277-679) survivors. Therefore the "morbidity" of F 2 disorders among the survivors is presumed to lie within the range from 0.86 % to 1.96 %.

On the other hand, according to the Japanese "Patients Survey 1993" administered by the Ministry of Health and Welfare, the number of patients with schizophrenia and similar disorders, in treatment as of October 1993, is estimated at 114,100 in the age group from 35 to 44 years old¹⁰⁾. The population of the same age group is estimated at 18,063,000 in the "Vital Statistics in Japan 1993"¹¹⁾. Then the "morbidity" of schizophrenia and similar disorders (nearly equivalent to F 2 disorders), among the general population of the age group from 35 to 44 years old, is estimated at 0.63 % (114,100/18,063,000).

There is a statistically significant difference between 0.63 % and 0.86 % ($\chi^2=11.32$, $P<0.005$). Therefore, we can conclude that the "morbidity" of F 2 disorders among the survivors

is statistically higher than that of the general population. This finding might suggest that a baby exposed to arsenic during early periods after birth acquires vulnerability to schizophrenia afterwards. This is an interesting finding with special reference to the “neurodevelopmental disorder hypothesis on schizophrenia”^{12,13}. However, we need to do a case control-study for further evaluation.

II The social adaptation levels of survivors

The educational achievement of survivors in this survey is somewhat lower than that of the general population. The educational achievement (highest level attained) of Japanese in the same generation as the survivors, is as follows : 15.8 % graduated from junior high school, 53.3 % from high school, 11.9 % from college, and 19.9 % from university. Only one in one thousand was never enrolled in any school. Table 4 illustrates the educational experiences of the surveyed 499 survivors for comparison.

The marital status of these 499 survivors is very different from that of the general population in Japan, as well. In the same generation, 83.0 % of the general population people are married, 13.3 % are single, 3.2 % are divorced, and 0.5 % are widows or widowers. Accordingly, the marriage ratio is about 1 to 4, survivors to general population, and the ratio of being “single” is 5.5 to 1.

Levels of social adaptation of these 499 survivors are low: as shown in Table 6, only 23.6 % are able to support themselves.

These findings (Cover educational achievement, lower marriage rates, and lower levels of social adaptation) indicate that continuous support and case management will be much more important for the survivors in the future ; indeed, we predict that some kind of support will have to be continued for the remainder of the survivors’ lives.

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