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June 30, 1986

Drs. Arthur O.S. Chiu, David Bayliss,
and Charli Hiremath
Office of Research and Development
Environmental Protection Agency
Washington, D.C., 20460
USA

Dear Drs. Chiu, Bayliss, and Hiremath :

Please forgive my delay in answering you which was caused by waiting for our latest results of analysis.

As shown on the separate sheets of paper, our analysis of the deaths seen among the patients with Yusho showed an excess mortality from cancer of the liver (including those not specified as primary) particularly in men as compared with the national average mortality. Such excess mortality was also confirmed by comparing with the expected deaths calculated by the male mortality rate from liver cancer in Fukuoka and Nagasaki prefectures where about 70 % of the patients live and where are known to be most prevalent in liver cancer in the nation. Thus, the excess death from liver cancer among male patients seems real. However, this cannot readily be considered to be due to the poisoning because in Nagasaki prefecture where more than 550 patients live only one male and no female death from liver cancer has been seen, indicating no elevated mortality from liver cancer among them at all. We are also examining the medical records of the decedents in order to know the accuracy of diagnosis of liver cancer appearing on the death certificates. Therefore, we are not yet certain whether or not Yusho causes liver cancer. Anyway, I shall be glad if our findings which are still tentative could serve your purpose in some ways.

Sincerely yours,

Masanori Kuratsune
Masanori Kuratsune, M.D.
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Analysis of Deaths seen among Patients with Yusho

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(Department of Public Health, Faculty of Medicine, Kyushu University)

and

Masanori Kuratsune
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The total number of patients officially recognized as Yusho by the Ministry of Health and Welfare by the end of 1983 was 1,821. They were followed from the time when they were officially recognized to the end of 1983. Death certificates of the decedents seen among them during the observation period were collected by the government. Excluding 9 patients who had been officially recognized as Yusho after death and 51 who could not be confirmed for survival, 1,761 patients (97.5% of the whole patients) were completely followed, and 120 deaths (79 males and 41 females) seen among them were compared with the expected number of deaths calculated by applying the national age-class (5 years)- and sex-specific mortality rates in 1970, 1975, and 1980. Table 1 shows the main results of such comparison, while Table 2 the secular trends of SMR for some main causes of death.

One death seen among the male patients in Nagasaki prefecture whose cause had not been confirmed when the above calculation was made was recently turned out to be due to liver cancer. Adding this death to the above 8 male deaths from liver cancer, 9 male deaths from liver cancer were compared with the expected number of death obtained by applying the death rates in Fukuoka and Nagasaki prefectures. The results are shown in Table 3.

Table 1. Observed and Expected Number of Death and SMR by Cause of Death

Cause of death	Male			Female		
	Observed	Expected	O/E	Observed	Expected	O/E
Total	79	66.13	1.19	41	48.90	0.84
Tuberculosis	1	1.26	0.79	0	0.50	0.00
Malignant neoplasms	33	15.51	2.13**	8	10.55	0.76
Esophagus	1	0.77	1.30	1	0.18	5.45
Stomach	8	5.69	1.40	0	3.26	0.00
Rectum, sigmoid colon, and anus	1	0.63	1.60	0	0.46	0.00
Liver	8	1.61	4.98**	2	0.66	3.04
Pancreas	1	0.71	1.41	1	0.46	2.18
Lung, trachea, and bronchus	8	2.45	3.26**	0	0.85	0.00
Breast	0	0.01	0.00	1	0.66	1.46
Uterus				1	0.58	1.71
Leukaemia	1	0.45	2.23	0	0.32	0.00
Diabetes	1	0.75	1.34	0	0.69	0.00
Heart diseases	10	9.46	1.06	9	7.65	1.18
Hypertensive diseases	0	1.20	0.00	0	1.39	0.00
Cerebrovascular diseases	8	14.61	0.55	5	12.03	0.42*
Pneumonia and bronchitis	3	3.17	0.95	0	2.33	0.00
Gastric and duodenal ulcer	0	0.73	0.00	1	0.34	2.96
Chronic liver diseases and cirrhosis	6	2.26	2.65	2	0.73	2.74
Nephritis, nephrose syndrome and nephrose	0	0.79	0.00	2	0.71	2.81
Accidents	5	4.66	1.07	2	1.32	1.52

* : P < 0.05

** : P < 0.01

Table 2. Secular Trend of Standardized Mortality Ratio for Major Causes of Death by Sex

Cause of death	Male			Female		
	Year			Year		
	~ 72	73~78	79~83	~ 72	73~78	79~83
Total deaths	1.42	1.18	1.13	0.69	0.95	0.80
Malignant neoplasms	2.68	2.07	2.04	2.01	0.50	0.59
Liver	5.99	5.60	4.42	10.66	0.00	3.11
Trachea, bronchus, and lung	3.98	2.18	3.92	0.00	0.00	0.00
Heart disease	1.86	1.44	0.61	0.00	1.43	1.35
Cerebrovascular lesions	0.90	0.48	0.48	0.00	0.41	0.59

Table 3. Standardized Mortality Ratios for Liver Cancer and Cerebrovascular Diseases among Yusho Patients as Calculated by National Average Death Rates and by Death Rates in Fukuoka and Nagasaki Prefectures

Cause of death	Male			Female		
	Observed deaths	Expected deaths	O/E	Observed deaths	Expected deaths	O/E
Liver cancer	9	1.61 (2.34)	5.59** (3.85)**	2	0.66 (0.79)	3.04 (2.53)
Cerebrovascular lesions	8	14.61 (14.20)	0.55 (0.58)	5	12.03 (11.21)	0.42* (0.45)

Figures for expected deaths and O/E ratio in parentheses are those derived from the death rates in Fukuoka and Nagasaki prefectures, while figures not in parentheses from the national average death rates.

Subject: Kuratsune's reply on the Yusho incident

From: Arthur Chiu

To: David Bayliss and Charles Hiremath

Kuratsune has stipulated in the letter (6/30/86) that

1. "Cancer of the liver in man showed an excess of mortality....
2. However.....not due to poisoning.....because in Nagasaki prefecture where 550 (out of 1821) only one..... death.....
3. We are examining therecords.....accuracy of diagnosis....."

I have read the letter and have the following thoughts:

A. From table 1:

1. We notice a marked elevation of cancer deaths 33 observed vs. 15.51 expected. There are 8 cases of liver cancer vs. 1.61 expected in the male.
2. From the same table, we observe 2 cases of liver cancer in the female vs. 0.66 expected.
3. There is a problem in this table, the sum total of all neoplasms is 28 cases (sum of line 4 to line 14) in the male, and the female 6 cases (line 4 to line 14). These are different from the 33 and 8 cases listed in the table (line 3).
4. We also gather the following information from this table.
 - a. Tuberculosis 1 case vs. 1.26 expected. Pneumonia and bronchitis 3 cases vs. 3.17 expected. This suggests to us that there is no overt increase of (pulmonary) infections secondary to a generalised suppression of the immune systems.
 - b. Heart diseases 10 vs. 9.46 expected; diabetes 1 vs. 0.75 expected; Cerebral vascular diseases 8 vs. 14.61 expected. This indicates to us either younger age group or one very similar to that in chronological age in the Yusho patients in comparison with those in the rest of Japan.

- B. From table 2, we see a trend of decreasing mortality throughout the years. This includes malignant neoplasms (and liver cancer) from 72 to the 5 years interval of 79-83. Similar can be said of heart diseases and CVA. We suspect that this can be due to improvement of hygiene throughout the years.
- C. From table 3, the liver cancer incidence is markedly elevated among the Yusho patients in comparison with Japan or the people living in the same prefectures.