

## MORTALITY AMONG YUSHO PATIENTS -A 28-YEAR FOLLOW UP STUDY-

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### Introduction

In 1968, a mass accidental exposure to dioxin-like compounds occurred in western Japan by ingestion of a commercial brand of rice oil contaminated with PCBs and PCDFs (1,2). As a result, about 1800 registered patients had and have been suffering from several clinical symptoms; acneiform eruptions, pigmentation of the skin, nails and conjunctivas, increased discharge from the eyes, and numbness of the limbs, named as "Yusho"(oil disease) in Japan (1,2). Preliminary and interim reports regarding mortality of the Yusho patients were published in 1987(3) and 1996 (4). Standardized mortality ratios (SMRs) of liver cancer in males were reported to have significantly increased compared with the general population in Japan in both reports, though those of major causes of death were not significant.

In this study, in order to update the results in the follow-up studies and reevaluate the effect of PCBs and PCDFs on mortality, the risks of major causes of death were calculated using data of our follow-up survey conducted in 1996.

### Materials and Methods

The total number of officially registered patients of Yusho by March 31, 1990 was 1870. Of these, 1815 patients who registered by March 31, 1983; 917 males and 898 females, have been followed up since then regarding their survival. According to their names, date of birth, sex, address, date and place of registration, vital status for all cases were obtained at the municipal health departments. To date, three follow-up surveys have been conducted; in 1983, 1990 and

1996. Underlying causes of death were identified by death certificates collected by the department up until the survey of 1990. In the latest survey, underlying causes of death were newly obtained by collation of the two datasets; Yusho patient follow-up data and the national death file between 1978 and 1995 provided by the Statistics Bureau, the Management and Coordination Agency (MCA) of Japan.

The amount of person-years (PYs) at risk contributed to a given age group-calendar-period category by each patient were calculated from the officially registered date as a Yusho patient to the date of death, last vital status confirmation date for lost-to-follow-up, or January 31, 1996 for those who had been completely followed up. In addition, the total number of PYs in each category was calculated according to the prefecture where patients were registered, in order to adjust for the geographic variations of mortality pattern of liver cancer and diseases in Japan.

Expected numbers of deaths were computed by accumulation of the expected number of deaths in each category, which were obtained by multiplying mortality rates in the general population at the third year of each calendar period corresponding to the category according to causes of death and sex. Expected numbers of deaths were also computed based on mortality rates in the local population as references. Standardized mortality ratios (SMRs) were calculated by observed and expected deaths obtained as stated above.

## Results and Discussion

A total of 292 deaths; 177 males and 115 females, among 1815 patients was identified during the 28-year follow-up. Until January 31, 1996, 19,884 PYs for males and 20,023 PYs for females were accumulated. Sixty-three patients, whose vital status had not been confirmed since the second survey in 1990, were treated as a censor.

The risk of liver cancer in males were five times higher than that of the general population in the first three calendar periods; however, the risk had been decreased down to 2.93 times in the calendar period between 1968 and 1996. The risk of liver cancer in females followed the same trend as that in males, though they were not significant.

Based on mortality in the local population as references, SMRs were calculated. The risk of liver cancer in males throughout the follow-up period between 1968 and 1996 was still 1.97 times higher than that of in the local general population; however, the risks have decreased gradually according to time. The SMRs of liver cancer and liver cirrhosis/chronic hepatitis during the last 13 years were 1.56 (95 % CI: 0.75, 2.87) and 1.20 (95% CI: 0.33, 3.07) for males, and 1.38 (95% CI: 0.28, 4.04) and 0.76 (95% CI: 0.02, 4.25) for females, respectively.

Carcinogenicity of PCBs and PCDFs in the liver is still uncertain, because the elevated risk of liver cancer (3, 4) had been suspected to be due to the geographical variations of the hepatitis B/C virus infection in Japan, and this elevated risk has not been observed in the Yucheng incident (5,

6). However, the mortality risks of liver cancer or diseases had elevated during several years immediately after the incidents, and they have been gradually reducing both in Yusho and Yucheng incidents.

In summary, our results suggest that liver cancer risk due to prolonged exposures to PCBs and PCDFs remained in the body have been reduced, though a direct effect of PCBs/PCDFs or their interaction with hepatitis viruses to cause liver cancer/cirrhosis in the acute period immediately after the incident could not be denied.

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### Notes

Permission to use of the national vital information recorded on a magnetic tape, and inspection of copied death certificate records in regional health centers were officially granted by the Management and Coordination Agency of Japan, and announced in the Bulletin No.69 in the Government Newsletter: 2372 on April 30, 1998.

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