# The 13-year Mortality Experience of the Yucheng Cohort and Their Controls

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## 1. Introduction

Polychlorinated biphenyls (PCBs) are widespread environmental pollutants[1)]. It can cause hepatocellular carcinomas (HCC) in rats[2-4)] and mice[5-6)]. Human studies have focused on workers of electrical capacitor manufacturing plants[7-10)]. These studies have found an excess of liver and biliary tract cancer, cancer of the rectum, hematopoietic malignancies, lung cancer, malignant melanoma, and cancer of the brain and nervous system.

In 1979, a mass poisoning occurred in central Taiwan from cooking oil contaminated by heat-degraded polychlorinated biphenyls (PCBs) and related compounds. Many of the exposed developed chloracne, hyperpigmentation, peripheral neuropathy, and other symptoms, referred to as ***Yu-cheng*** (oil disease)[11)]. A registry developed and maintained by the Taiwan Provincial Department of Health includes 2008 exposed subjects. The average serum PCBs level among 1246 exposed subjects between 1979 and 1983 was 54 ppb.

In 1991-1992, we updated the Yucheng registry, identify controls, and started long-term investigation regarding mortality and morbidity of the two groups. Here we report results of the mortality investigation 12 years following the incident.

## 2. Methods

### Study Subjects

All subjects included in the *Yucheng* registry who were born before July 1978 were included in this study. The registry was acquired from Taiwan Provincial Department of Health and the information updated from data kept in local health stations and local household registration offices (HRO). For each Yucheng subject, three age (within 1 year for those under 10 years of age in 1979, and within 3 years for those older), gender, and 1979 neighborhood-matched controls were identified

from the 1979 household register kept in local HROs. For each one of a subgroup of 101 blind *Yucheng* students, two age, gender-matched blind students from other blind schools were idenfitied as his/her controls. No controls were identified for cohort members who live in remote areas that were hard to access.

Follow-up Procedures

Information on basic demography for every study subject was abstracted from records kept at local HROs. All subjects were traced and vital status up to December 31, 1991 were ascertained. It is mandatory to register deaths within one month of death occurrence in the HRO, and reporting of death in Taiwan is believed to be complete. The HROs always update individual changes of residence within the precinct and maintain forwarding addresses for persons who have moved from their precinct, so subjects who had changed their residence could be followed in the new HRO. For the deceased cases, a copy of death certificate was acquired and information on date, place, and causes of death was abstracted. Cause of death was coded according to the ninth revision of the International Classification of Diseases by two nosologists.

Data Analysis

Overall and cause-specific mortality rates of the *Yucheng* cohort were compared with that of the controls. Person-years at risk of dying were calculated for each subject from the date of the incident, January 1, 1979, through the end of study, December 31, 1991, or the date of death, whichever occurred first. The age, gender-adjusted rates were compared using the Cox proportional hazard regression model, and were computed with the PHREG program in the SAS package.

3. Results

A total of 1837 *Yucheng* subjects (91% of the original 2008 subjects in the registry) were located and 5247 controls identified, and fifty-four percent of both group was female. Vital status was successfully ascertained for 99.5% of the 7084 identified subjects (Table 1), among which 82 Yucheng subjects (4.5%) and 132 controls (2.5%) died before January 1, 1992.

**Table 1 Gender and vital status of Yucheng and control group in 1979**

| | *Yucheng* | Control |
|---|---|---|
| Gender | | |
| Female | 986 (54%) | 2822 (54%) |
| Male | 851 | 2425 |
| Total | 1837 | 5247 |
| Final Vital Status | | |
| Alive | 1755 | 5115 |
| Deceased | 82 (4.5%) | 132 (2.5%) |

When the age- and gender-adjusted mortalities were compared directly between the Yucheng and control groups, mortality among the Yucheng cohort tended to be

increased for most causes except for mortality due to malignant neoplasms of respiratory system, disease of the nervous system, and accident (Table 2). Overall mortality in the Yucheng cohort was almost twofold that of the control group (rate ratio (RR) = 1.9, 95% confidence interval (CI) = 1.4-2.5). Yucheng cohort had significantly increased mortality rates than the controls in deaths due to disease of the circulatory system, disease of the respiratory system, and disease of the digestive system. Most of the increase in circulatory system mortality was due to heart disease (RR = 3.7, 95% CI = 1.9-6.9), and most of the digestive system mortality was due to chronic liver disease and cirrhosis (RR = 5.3, 95% CI = 1.9-14.7). Mortality due to all malignant neoplasm and cancer of selected sites were also increased in the Yucheng cohort except for cancer of respiratory system, but none of the rate ratios were statistically significant.

**Table 2. Mortality after the Yucheng incident. Rate ratio (RR) for specific causes of death between the Yucheng and control groups, 1979-1991.**

| Underlying cause of death | RR* | 95% CI |
|---|---|---|
| All causes | 1.9 | (1.4- 2.5) |
| All malignant neoplasms | 1.3 | (0.6- 2.7) |
| lip, oral cavity, and pharynx | 6.2 | (0.6-68.9) |
| digestive organ and peritoneum | 1.1 | (0.4- 3.5) |
| liver and intrahepatic bile duct | 1.6 | (0.4- 6.5) |
| respiratory system | 0.7 | (0.1- 6.0) |
| lymphatic and hematopoietic tissue | 3.2 | (0.4-22.4) |
| Disease of the circulatory system | 2.7 | (1.6- 4.5) |
| Disease of the heart | 3.7 | (1.9- 6.9) |
| Disease of the respiratory system | 3.3 | (1.2- 9.4) |
| Disease of the digestive system | 4.0 | (1.9- 8.2) |
| Chronic liver disease and cirrhosis | 5.3 | (1.9-14.7) |
| Disease of the nervous system | 1.0 | (0.1- 9.4) |
| All accidents | 0.8 | (0.3- 2.0) |
| Suicide amd homicide | 1.9 | (0.3-11.6) |

* adjusted for age and gender

4. Discussion

Thirteen years after the Taiwan Yucheng incident, the mortality of the Yucheng cohort was compared with that of the age, gender, and 1979 neighborhood-matched controls. The Yucheng cohort experienced higher mortality than their controls in overall death and deaths due to several major causes.

In 1983, when the original Yucheng cohort was last followed up for vital status, 24 deaths were reported and almost half of them were due to hepatoma, liver cirrhosis or liver diseases with hepatomegaly[11]. After nine more years of follow-up, the Yucheng cohort was found to have a 5.3 fold increased mortality from liver disease and cirrhosis, a picture pretty consistent with the previous one.

At the 15-year follow-up of the Japanese Yusho cohort of 1761 subjects, six fold and three fold increased liver cancer mortalities were found in exposed men and

women, respectively; and a significant excess of lung cancer mortality was also seen in men[12]. Although mortality due to liver and intrahepatic bile duct cancer was increased in the Yucheng cohort (RR = 1.6), this increase was not statistically significant. This can be due to the fact that the Yucheng cohort was young (58% was younger than 30 years of age in 1979) , and after 13 years of observation, only a small number of liver and intrahepatic bild duct cancer deaths had been reported. Another possibility is that liver cancer is the number 1 cause of cancer death in Taiwan[13], with a high background rate, it is very unlikely for the cohort members to develop a substantial number of cancer cases to show a significant increase within 13 years.

Studies on workers of electrical capacitor manufacturing plants have yielded a variety of results. Some studies have found an excess of liver and biliary tract cancer[7,8], some found an excess of mortality due to cancer of the gastrointestinal tract, hematopoietic malignancies and lung cancer[9], and some found increased mortality due to malignant melanoma and cancer of the brain and nervous system[10]. The Yucheng cohort had an increased mortality due to malignant neoplasm of lymphatic and hematopoietic tissue (RR = 3.2), but the increase was not significant. They did not show an excess of malignant neoplasm of digestive organ and peritoneum, and there were no cases of both skin cancer and malignant neoplasm of the brain and nervous system. The observed discrepancies between the Yucheng cohort and the occupational cohorts were probably due to the different doses of PCBs exposed and the virtual absence of polychlorinated dibenzofurans in the occupational cohorts.

None of the human studies mentioned above have shown an excess of mortality due to disease of circulatory system or heart disease as the Yucheng cohort does. This peculiar experience is similar to a 10-year mortality of the population involved in the seveso incidenct, which found an increased mortality from cardiovascular disease[14]. The speculative interpretation of that finding was that the Seveso cohort underwent powerful stresses which might have precipitated preexisting conditions of cardiovascular disease[14]. The same mechanism might probably cause the Yucheng cohort, who had underwent great stresses during and after the Taiwan Yucheng incident, to have an increased mortatlity due to heart disease.

One limitation of the study is that the whole cohort has only been followed for 13 years, and since the cohort was young in 1979, there have only been relatively few deaths developed and reported in the cohort, and the small number of observed deaths resulted in risk estimation with broad confidence intervals. Another limitation is that the lack of accurate measurements of serum PCB levels prohibited us to conduct dose-effect analyses.

The findings of this study provided a comprehensive data on the 13-year mortality experience of the Yucheng cohort and their controls. In summary, the Yucheng cohort had a significantly increased overall mortality than their controls, and mortalities due to disease of the circulatory system, disease of the respiratory system, and disease of the digestive system were also significantly elevated in the Yucheng cohort.. For causes of special interest, Yucheng cohort had a 3.7 fold (95% CI = 1.9-6.9) and a 5.3 fold (95% CI = 1.9-14.7) increased risk of dying from heart disease and chronic liver disease and cirrhosis, respectively. Yucheng cohort also had increased mortalities due to all and site-specific malignant neoplasms, but because of the small numbers of the cancer cases, the confidence intervals of these differences were broad and the findings inconclusive. The cohort subjects

and their controls will continually be followed and their mortality and morbidity be studied. We are also collecting blood samples from the study subjects for serum PCB and PCDF measurements. These biologic markers will help us to characterize individual exposure better, and may allow us to conduct dose-effect analyses in the future. These on-going projects may shed lights on the long-term health effect of PCB and PCDF exposure.

5. References


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