

## Morbidity Follow-up Study of Yucheng Subjects Exposed to Polychlorinated Biphenyls and Dibenzofurans

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### 1. Introduction

Polychlorinated biphenyls (PCBs) and dibenzofurans (PCDFs) are widespread environmental pollutants<sup>1</sup>. Similar to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), they are known to cause health effects in many organ systems, including liver, skin, neurological, sex organs, thyroid, and other endocrine organs in addition to carcinogenesis. Human studies have focused on workers of electrical capacitor manufacturing plants<sup>2,3,4,5</sup>. 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 PCBs and their heat degraded products, mainly PCDFs and ter- and quarter-phenyls. Many of the exposed developed chloracne, hyperpigmentation, peripheral neuropathy, and other symptoms, referred to as *Yucheng* (oil disease)<sup>6</sup>. A registry was developed and maintained by the Taiwan Provincial Department of Health which also provided service and health care for the victims. The criteria used to identify victims included consumption of the rice bran oil produced in the factory known to be the source of the contamination, and the development of skin, eye, and other symptoms from January to October 1979. About 10% of the persons in the registry had a history of PCB exposure and had elevated serum PCB concentrations, but were asymptomatic. The average serum PCB level tested for 1246 exposed subjects between 1979 and 1983 was 54 ppb. This registry later included some children born to intoxicated mothers, who were considered to be affected by PCBs. The Yucheng Registry therefore followed a total of 2061 victims, including 53 prenatally exposed children.

In 1991-1992, we updated the Yucheng registry, identify controls, and started a long-term investigation regarding mortality and morbidity of the two groups. Here we report results of the morbidity investigation 14 years following the incident.

### 2. Methods

The details of the *Yucheng* incident and how subjects were included in the *Yucheng* registry have been described in previous papers<sup>6</sup>. All subjects included in the *Yucheng* registry who were born before July 1978, five months before the first recognized case,

were considered directly exposed subjects in this study. The subject list of 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 (LHRO). 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 LHROs. For each one of a subgroup of 101 blind *Yucheng* students boarded in a school for blindness in 1979, two age, gender-matched blind students from other blind schools were identified as his/her controls. No controls were identified for cohort members who live in remote areas that were hard to access<sup>7)</sup>.

In our assessment of morbidity, only the subjects born in 1964 or earlier were included. We obtained their telephone number from the local health stations and LHRO. The subjects were telephone interviewed for life-time health morbidity experience on an ever or never basis. To minimize recall bias due to previous exposure to toxic chemicals, the subjects were told that we were performing a survey of health in general population. Exposure to environmental chemicals was not mentioned by our interviewers. The following question was asked: "Have you ever had any of the following medical condition or diseases diagnosed by a licensed doctor (western medicine doctor)?" The diseases we asked included those of the eye, ear, nose, mouth, lung, cardiovascular, musculoskeletal, gastrointestinal, genitourological, hematological, neurological, endocrine, and skin systems (Table 1).

**Table 1. Diagnosed medical conditions or diseases in the questionnaire**

Organ or System	Medical Condition Questioned
Eye	cataract, glaucoma
ENT	chronic otitis media, sinusitis, hearing loss
Respiratory	lung diseases, pneumoconiosis, asthma, tuberculosis
Cardiovascular	hypertension, arrhythmia, coronary heart disease, other heart diseases
Musculoskeletal	rheumatic diseases, gout (or hyperuricemia), sciatica, fracture, arthritis, herniated disc or vertebral spur formation
Gastrointestinal	hepatitis, cirrhosis, hepatic or gall stone, peptic ulcer diseases, pancreatitis
Genitourological	renal problems, cystitis, urethritis, hernia
Hematological	aplastic anemia, anemia, purpura, agranulocytosis
Neurological	migraine, polyneuritis, epilepsy, Parkinsonism
Endocrine	diabetes, hyperthyroidism, hypothyroidism, goiter
Skin	abnormal nails, skin allergy, chloracne, hyperkeratosis
Oral	chipping of tooth, gum swelling, gum hyperpigmentation

### 3. Results and Discussion

A total of 1060 exposed and 1060 controls met our criteria for the morbidity study, and 801 Yucheng and 730 controls were actually interviewed (Table 2). The demographics of the study subjects are depicted in Table 3. Yucheng and control subjects who finished telephone interview had essentially the same age and sex distribution.

**Table 2. Study subjects interviewed for morbidity.**

<b>Total in list</b>	<b>2120</b>	
subject deceased	214	
wrong address	74	
no phone or wrong number	108	
<b>Total # of subjects with phone</b>	<b>1724</b>	
moved	53	
no person at home	61	
study subject is not at home (three efforts)	54	
refused interview	25	
<b># subjects finished interview</b>	<b>1531</b>	<b>Yucheng 801</b>
<b>(% of total subjects with phone)</b>	<b>(88.8%)</b>	<b>Control 730</b>

**Table 3. Demographics of Yucheng and control subjects who were successfully telephone-interviewed.**

Age	Men		Women	
	Yucheng	Control	Yucheng	Control
30-40	89 (26.1%)	74 (23.1%)	187 (40.7%)	165 (40.3%)
40-50	94 (27.6%)	91 (28.3%)	104 (20.6%)	88 (21.5%)
50-60	76 (22.3%)	79 (24.6%)	86 (18.7%)	84 (20.5%)
60-70	60 (17.6%)	54 (16.8%)	57 (12.4%)	47 (11.5%)
70-80	18 (5.3%)	21 (6.5%)	22 (4.8%)	20 (4.9%)
> 80	4 (1.2%)	2 (0.6%)	4 (0.9%)	5 (1.2%)
<b>Total</b>	<b>341</b>	<b>321</b>	<b>460</b>	<b>409</b>
<b>Mean age</b>	<b>50.4</b>	<b>50.8</b>	<b>47.0</b>	<b>47.3</b>

The occurrence of diagnosed medical conditions or diseases is summarized in Table 4. Yucheng men had significantly ( $p < 0.1$ ) higher rates of abnormal nails, skin allergy, chloracne, hyperkeratosis, rheumatism, arthritis, herniated disc, migraine, thyroid goiter, and gum pigmentation compared to their controls. Yucheng women had significantly ( $p < 0.1$ ) higher rate of having abnormal nails, skin allergy, chloracne, hyperkeratosis, liver disease, lung disease, anemia, migraine, thyroid goiter, broken tooth, gum swelling, and gum pigmentation compared to their controls.

Since the subjects were told that the purpose of this investigation was for general survey of health, and the previous episode of PCB/PCDF intoxication was 14 years ago, the effects of recall bias secondary to toxic exposure were expected to be minimal. This is supported by the results that Yucheng and control subjects reported similar occurrence of the following rather common diseases: sinusitis, hearing loss, hypertension, peptic ulcer diseases, and diabetes (Table 4). The fact that more Yucheng subjects reported thyroid goiter but similar proportions in the two groups reported occurrence of hyperthyroidism or hypothyroidism supported a real increased occurrence of thyroid goiter in Yucheng subjects. The increased occurrence of musculoskeletal diseases in Yucheng men is an interesting finding that can be related to calcium, hormone, or vitamin metabolism and warrants further investigation.

#### 4. Conclusion

**Table 4. Reported medical condition or diagnosed diseases in Yucheng men and women compared to their controls**

	Men			Women		
	Yucheng (341)	Control (321)	p-value	Yucheng (460)	Control (409)	p-value
abnormal nails	33	4	<0.0001	65	7	<0.0001
skin allergy	68	32	0.0004	103	38	<0.0001
chloracne	54	4	<0.0001	89	8	<0.0001
hyperkeratosis	13	2	0.006	23	4	0.0007
rheumatism	14	5	0.051	15	16	0.60
arthritis	13	1	0.0018	17	12	0.54
herniated disc	17	8	0.094	12	7	0.37
liver disease	28	20	0.33	25	12	0.070
lung disease	5	7	0.49	6	1	0.082
anemia	3	4	0.64	44	18	0.0037
migrane	19	7	0.025	41	20	0.022
thyroid goiter	5	0	0.030	15	4	0.023
broken tooth	28	17	0.14	38	10	0.0002
gum swelling	15	12	0.67	39	15	0.0038
gum pigmentation	7	1	0.041	30	1	<0.0001
sinusitis	6	3	0.36	9	6	0.58
hearing loss	16	12	0.55	13	10	0.73
hypertension	28	24	0.73	43	31	0.36
peptic ulcer disease	57	54	0.96	53	35	0.15
diabetes mellitus	15	11	0.53	16	11	0.52

People previously exposed to thermally degraded PCBs/PCDFs had more reported incidence of abnormal nails, skin allergy, chloracne, hyperkeratosis, arthritis, herniated disc, liver disease, anemia, migraine, goiter, broken tooth, gum swelling, and gum pigmentation than their matched controls.

## 5. References

- 1) Anderson HA. General population exposure to environmental concentration of halogenated biphenyls. In: Kimbrough RD, Hensen AA. (eds): Halogenated Biphenyls, Terphenyls, Naphthalenes, dibenzodioxin and Related Products. New York:Elsevier, pp.325-344, 1989.
- 2) Brown DP Mortality of workers exposed to polychlorinated biphenyls -- an update. Arch. Environ. Health 42:333-339, 1987.
- 3) Gustavsson P, Hogstedt C, Rappe C. Short-term mortality and cancer incidence in capacitor manufacturing workers exposed to polychlorinated biphenyls (PCBs). Am. J. Ind. Med. 10:341-344, 1986.
- 4) Bertazzi PA, Riboldi L, Pesatori A, Radice L, Zocchetti C. Cancer mortality of capacitor manufacturing workers. Am. J. Ind. Med. 11:165-176, 1987.
- 5) Sinks T, Steele G, Smith AB, et al. Mortality among workers exposed to polychlorinated biphenyls. Am. J. pidemiol. 136:389-398, 1992.
- 6) Hsu S-T, Ma C-I, Hsu S-K, et al. Discovery and epidemiology of PCB poisoning in Taiwan: a four year follow-up. Environ. Health Perspect. 59:5-10, 1985.
- 7) Yu ML, Guo YL, Rogan WJ, Hsu CC. The 13-year mortality experience of the Yucheng chort and their controls. In: H. Fiedler, et al., eds: The 14th International