

## REPRODUCTIVE HEALTH IN YUCHENG WOMEN EXPOSED TO POLYCHLORINATED BIPHENYLS/POLYCHLORINATED DIBENZOFURANS

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### Introduction

Polychlorinated dibenzo-p-dioxins, dibenzofurans (PCDD/Fs) and polychlorinated biphenyls (PCBs) are environmentally persistent and bio-accumulate in human bodies. In 1979, a mass poisoning occurred in central Taiwan from cooking oil contaminated by heat-degraded PCBs<sup>1</sup>. Symptoms included chloracne, hyperpigmentation, and peripheral neuropathy, and the illness was referred to as "Yucheng" (oil disease). Patients used the contaminated cooking oil for an average of 8 months; they were estimated to have consumed about 1 gram of PCBs and 3.8 mg of PCDFs<sup>2</sup> (mostly the 2,3,4,7,8-penta-CDF and the 1,2,3,4,7,8-hexa-CDF) during that time, resulting in median serum PCB levels of 40 to 60 parts per billion wet weight, and serum PCDF levels of about 2.7 parts per trillion (ppt) wet weight for the penta-CDF and 10.8 ppt wet weight for the hexa-CDF. These levels are on the order of 10 to 20 times higher than background for PCBs and 100-1,000 times higher for the penta-CDF and the hexa-CDF<sup>3</sup>.

Laboratory evidence<sup>4,5</sup> and evidence from the Japanese Yusho poisoning<sup>6</sup> showed that that female reproductive function might be affected by exposure to PCDDs/PCDFs, and PCBs. Women in Seveso, Italy who were exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) before menarche were shown to have prolonged menstrual cycles<sup>7</sup>. Our previous study has demonstrated menstruation irregularity in Yucheng women exposed to PCBs and PCDFs at ages 17 years or older<sup>8</sup>. We carried out a survey on menstrual characteristics on Yucheng women exposed at younger ages, as compared with their controls.

### Methods and materials

This study was reviewed and approved by the Institutional Review Board at National Cheng Kung University Medical College. The *Yucheng* registry and the morbidity follow-up are described elsewhere<sup>9</sup>. From 1979 to 1983, the Taiwan Provincial Department of Health registered 2061 cases based on signs and symptoms of the illness or a history of consumption of the contaminated oil<sup>1</sup>. We acquired the registry from the Department of Health in 1991. Using the address listed in the *Yucheng* registry, we began in 1992 to locate the subjects' record at their registration office, and traced them through December 31, 2001. To identify controls, we used the 1979 addresses of the registry members as index addresses, and attempted to identify the persons who were of similar age (within 3 years) lived nearby in 1979 from the archives of the registration offices, and traced them through December 31, 2001. From December 2001 to April 2002, a telephone survey using structured questionnaire was conducted in women who were 0-20 years of age in 1979, when Yucheng episode occurred. Information on menstrual characteristics, reproductive functioning, and reproductive history including time to pregnancy were inquired. Only 216 Yucheng individuals and 220 controls who had correct phone number were included in our study.

Between 1980 and 1982, the Health Department measured serum PCB levels of many members of the *Yucheng* cohort. These results were used to stratify participating *Yucheng* women into high and low exposed groups.

### Results and discussion

A total of 192 Yucheng women and 188 controls completed the questionnaire interview satisfactorily. They were of similar age, body height, body mass index, education, family income, marital status, smoking and drinking habits. However, Yucheng women had smaller body weight than controls (Table 1). Yucheng women exposed to PCBs/PCDFs younger than 13 years of age had similar age at menarche, cycle length, and prevalence of dysmenorrhea (Table 2), but longer durations of menstrual flow as compared with their controls (5.8 days vs. 5.3 days,  $p=0.017$ ). Yucheng women exposed to PCBs/PCDFs older than 13 years of age had similar age at menarche, cycle length, duration of menstrual flow, and prevalence of dysmenorrhea as their controls.

Among those younger than 13 years of age in December of 1978, duration of menstrual flow was associated with serum levels of PCBs in 1980 to 1982 ( $p=0.017$  by analysis of variance),  $5.2 \pm 0.2$  days in controls,  $5.7 \pm 0.3$  days in

Yucheng women with serum PCBs of 42 ppb or lower, and  $6.1 \pm 0.3$  days in Yucheng women with serum PCBs of higher than 42 ppb (statistically different from controls by Tukey-Kramer HSD test).

Table 1. Demographic characteristics in women exposed to polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) and their controls

	Yucheng (n=192)	Controls (n=188)	P-value
<b>Age (year)</b>	$36.4 \pm 0.4^*$	$37.1 \pm 0.4$	NS
<b>Body height (cm)</b>	$156.7 \pm 0.4$	$157.8 \pm 0.4$	NS
<b>Body weight (kg)</b>	$55.1 \pm 0.6$	$57.2 \pm 0.6$	0.03
<b>Body mass index (kg/m<sup>2</sup>)</b>	$22.5 \pm 0.2$	$23.0 \pm 0.2$	NS
<b>Education</b>			NS
Elementary or lower	46 (24.4%)	39 (20.9%)	
Middle school	40 (21.2%)	48 (25.7%)	
High school	65 (34.4%)	59 (31.6%)	
College or above	41 (20.2%)	41 (21.9%)	
<b>Marital status</b>			NS
Single	30 (15.6%)	26 (13.8%)	
Married	159 (82.8%)	158 (84.0%)	
Divorced/separated	3 (1.6%)	4 (2.1%)	
<b>Ever worked full-time for longer than 3 months</b>	155 (80.7%)	152 (80.9%)	NS
<b>Smokers</b>	6 (3.1%)	2 (1.1%)	NS
<b>Regular drinkers</b>	12 (6.3%)	8 (3.2%)	NS

\*Items are mean  $\pm$  standard error

NS: non-significant statistically

Table 2. Menstrual characteristics in Yucheng women exposed to PCBs/PCDFs before and after age 13, and their controls.

	Yucheng	Controls	P-value
<b>Younger than 13 year old in December 1978</b>	(n=89)	(n=80)	
Age at menarche (year)	$13.9 \pm 0.1$	$13.9 \pm 0.1$	NS
Menstrual cycle length (day)	$30.4 \pm 0.6$	$29.8 \pm 0.6$	NS
Menstrual cycle duration (day)	$5.8 \pm 0.1$	$5.3 \pm 0.2$	0.017
Dysmenorrhea	54 (60.7%)	53 (67.1%)	NS
Mild	41 (46.1%)	41 (51.3%)	NS
Moderate	9 (10.1%)	9 (11.3%)	
Severe	2 (2.2%)	3 (3.8%)	
<b>Older than 13 year old in December 1978</b>	(n=103)	(n=108)	
Age at menarche (year)	$14.4 \pm 0.1$	$14.3 \pm 0.1$	NS
Menstrual cycle length (day)	$29.0 \pm 0.5$	$28.9 \pm 0.5$	NS
Menstrual cycle duration (day)	$5.1 \pm 0.1$	$5.3 \pm 0.1$	NS
Dysmenorrhea	70 (70.0%)	59 (60.2%)	NS
Mild	60 (58.3%)	48 (44.4%)	NS
Moderate	4 (3.9%)	9 (8.3%)	
Severe	6 (5.8%)	2 (1.9%)	

\*Mild: unaffected daily life and no medication required; moderate: daily life affected, and medication used for symptoms relief; severe: daily life severely affected, medication usually ineffective

Reproductive history was inquired in 135 married Yucheng women and 132 married controls. Among the married Yucheng women, 107 had serum levels measured in 1980-82, which was used to stratify Yucheng women into highly exposed and low exposed groups. More of the Yucheng women reported ever having premature birth (16.8% vs. 9.3%)

and stillbirth (6.1% vs. 2.3%). Number of pregnancies, number of children, ever having spontaneous abortion, and gender ratio of the offspring were not different between Yucheng and their controls (data not shown). Higher level of PCBs/PCDFs exposure had a higher stillbirth rate (Table 3).

Table 3. Reproductive history in Yucheng women and their controls.

	Controls (n=132)	Yucheng women with 1980-2 serum levels of < 38 ppb (n=54)	Yucheng women with 1980-2 serum levels of > 38 ppb (n=53)	P-value
Number of children	2.5 ± 0.1	2.3 ± 0.1	2.5 ± 0.1	NS
Number of pregnancy	2.8 ± 0.1	2.5 ± 0.1	2.9 ± 0.1	NS
Ever with history of premature birth, # (%)	12 (9.3%)	10 (18.9%)	8 (15.4%)	NS
Ever with stillbirth, # (%)	3 (2.3%)	1 (1.9%)	7 (13.5%)	0.003
Ever with spontaneous abortion, # (%)	13 (10.1%)	8 (15.1%)	4 (7.7%)	NS
Male offspring (%)	0.53 ± 0.03	0.57 ± 0.05	0.52 ± 0.05	NS

In conclusion, among Yucheng women exposed to PCBs and PCDFs at age of 0-20 years, duration of menstrual flow was increased, especially in highly exposed group. Stillbirth was also reported more frequently in Yucheng women exposed to higher levels of PCBs.

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