Exposure to PCBs/PCDFs in women resulted in prolonged time to pregnancy

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Abstract
This follow-up study investigated female reproductive effects of Yucheng women. These women had exposed from polychlorinated biphenyls (PCBs) and their pyrolytic product, mainly polychlorinated dibenzofurans (PCDFs) exposure episode, which occurred in Taiwan between 1978 and 1979, referred to as "Yucheng" exposure. In 2003, we conducted a follow-up study and invited all aged 25-45 years old from the Yucheng women cohort by telephone, and attempted to find finally 601 subjects of them. All 601 subjects, who answered a questionnaire to collect the time to pregnancy from fertile history, only 476 married women finish the part of fertile history (118 women singe status and 7 women incomplete their fertile history). Each woman was allowed to contribute only one pregnancy (the first pregnancy) to avoid interference from a correction with the TTP of subsequent pregnancies. Among analyzed results, we found the crude odds ratio was 2.28 (95 percent confidence interval (CI):1.42, 3.69) and adjusting for the other impotent confounders, the adjusted odds ratio was 2.20 (95 percent CI: 1.33, 3.68). However, we suggest exposure PCBs maybe prolong time to pregnancy of female.

Introduction
Polychlorinated biphenyls (PCBs) are a family of industrial compounds and human-made hazard chemicals that may be hormonally active agents. Recently, PCB congeners were reported can be estrigenic, antiestrogenic, androgenic, or antiandrogenic effect [1]. Among previous animal studies, PCB exposure has been suspected to affect the female reproductive system [2, 3]. In human studies, Axmon et al., didn't found the evidence of a hazardous effect associated with CB-153 in the general Swedish population[4, 5]. But, Buck et al., suggested that PCBs exposure increased time to pregnancy and reduce fecundability among the New York State Angler Cohort[6-8]. In addition, time to pregnancy increased with increasing serum PCB levels was found but the association was weak and inconclusive[9]. However, epidemiological information concerning the effects of PCBs exposure on female reproductive functions is still limited. The purpose of our study was to investigate the association of PCB exposure with time to pregnancy.

Materials and Methods
Population
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. The Yucheng registry was detail described elsewhere [10]. In 1993, we had taken place a health survey of the Yucheng women cohort and studied focus in menstrual characteristics and birth outcomes etc. These results of the 1993 survey were showed some reproductive problems from these Yucheng women [10]. Thus, we conducted a follow-up study in 2003 and invited all aged 25-45 years old from the Yucheng women cohort by telephone, and attempted to find finally 601 subjects of them. However, we followed to invite all Yucheng women 25-45 years old, who were maybe still menstruating, to realize whether prolong time to pregnancy for Yucheng women. All 601 subjects, who answered a questionnaire to collect the time to pregnancy from fertile history, only 476 married women finish the part of fertile history (118 women singe status and 7 women incomplete their fertile history). In addition, 11 Yucheng women were postpartum before exposed PCBs accident in 1969 and 23 control women reported also the first pregnancy before 1969. The detail flowchart in Fig. 1 shows the process of selection of the subjects included in TTP analysis.

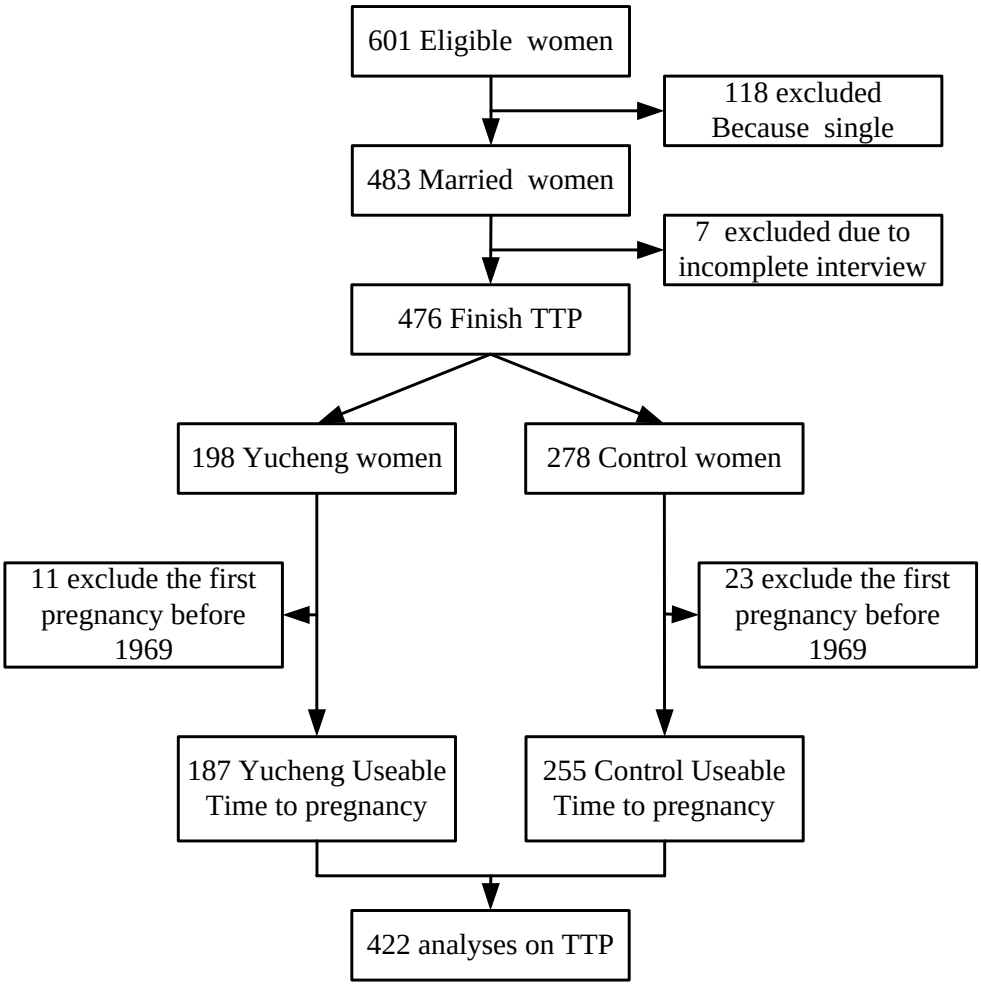

Fig.1. selection of the study population for the analysis of PCB exposure and TTP

Time to pregnancy

A questionnaire was administered in person by trained interviewers. Participating women were asked whether married. If, the answer was "yes", we collected the time to pregnancy (in months). The TTP was assessed for all of the women's pregnancies using a suite of questions: Did you get pregnant the first month of trying? If not, how many months did it take you to get pregnant? In order to collect accurately the information of TTP, we also asked their baby's birthday date and gestation duration of this pregnancy to determine the reasonable about the TTP's data. Then, we recheck double TTP by another researcher. To sum, TTP was defined as the duration between the dates of discontinuing contraceptive procedures and beginning of last menstrual period before pregnancy.

Data analysis

Each woman was allowed to contribute only one pregnancy (the first pregnancy) to avoid interference from a correction with the TTP of subsequent pregnancies. For analysis purposes, if TTP was reported as zero months, the answer was interpreted as 1 month. In the fecundability survival analysis, censoring of TTP was introduced, in order to reduce the effect of other medical causes on TTP. The censor was used for tree conditions. The tree conditions were more than 12 months of TTP, still not became to pregnancy in 2003 at the time of 2003 August, and sought for medical care or used medicine for pregnancy due to difficulty in getting pregnant. Therefore, the TTPs with censor due to more than 12 months and still not became to pregnancy were as 13 months and the TTP with censor due to sought for medical care or used medicine for pregnancy due to difficulty in getting pregnant were measured as the time to seek medicine.

We calculated the proportions of TTP greater than 9 months according to exposure status and the odds ratios. We used Kaplan-Meier survival curves to compare the TTP between the two exposure groups. Moreover, some potential biological and social confounders have been taken into account in the statistical analysis. These include mother's and father's age at conception, mother whether work,

father's work whether having risk exposure, mother's smoking, mother's alcohol habit, body weight, body height, body mass index, intercourse frequency before the first pregnancy, menstrual cycle days before the first pregnancy. Finally, the impotent confounders were mother's and father's age at conception in whole model.

Results

Table 1 summarizes the demographic characteristics of the Yucheng and control subjects. Yucheng women were shorter and thinner than control women. In addition, there was significant difference that Yucheng women were less frequency of intercourse before the first pregnancy than control women.
Compared with control women, the crude odds ratio was 2.28 (95 percent confidence interval (CI):1.42, 3.69). Adjusting for the other impotent confounders, the adjusted odds ratio was 2.20 (95 percent CI: 1.33, 3.68). However, table 2 showed a significant association with pregnancy delay in Yucheng women.

Discussion

There were inconsistent results of PCB exposure and time to pregnancy in previous studies. In the New York State Angler Cohort, increased time to pregnancy was found women exposed to PCBs when exposure was measured by using an index based on the total number of years eating Lake Ontario fish, portion size, number of species-specific fish meals, and species-specific PCB concentrations [8]. In the same cohort, simpler exposure measures, based on fish consumption quantified by duration and frequency, were not related to time to pregnancy[7, 11]. In the Swedish fishermen's families cohort, overall, there was no clear evidence of PCB back-calculated blood plasma or serum level exposure on fertility [4]. However, when data on fishermen's wives and sisters were combined, no indicated to prolong TTP for women with a high CB-153 concentration [5]. In the Collaborative Perinatal Project, suggested an association between increasing serum PCB levels and increased time to pregnancy based on third-trimester serum organochlorine levels [9]. In Yucheng cohort, we found evidence suggesting a relationship between Yucheng women compared to control women and increased time to pregnancy of women. Although our number of subjects was smaller than the Collaborative Perinatal Project and our dose no using measured PCB levels, our results were still acceptable to believe. Therefore, our Yucheng exposure status probably accurately reflected serum levels of PCBs.
The mechanism by which exposure to PCBs could prolong time to pregnancy is unclear. In previous studies, exposure organochlorine chemicals such as DDE or dioxin had been associated with spontaneous abortion and alter hormone level[1-3]. In our study, perhaps PCBs exposure altered a sexual desire further influence intercourse frequency.
In conclusion, evidence of an association between PCB exposure and time to pregnancy was significant from these data and suggested PCB exposure can prolong time to pregnancy of women in high exposure population among Yucheng cohort.

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Table 1 background characteristics of 442 Yucheng women cohort, studied in 2003

characteristic $	Yucheng (n=187) % or mean±SD	Control (n=255) % or mean±SD	P value
Current age (years)	39.5±4.6	39.2±4.6	0.41
B.H (㎝)	156.7±5.1	158.0±5.1	0.016
B.W (㎏)	55.9±8.1	57.6±9.0	0.055

BMI	22.8±3.4	23.1±3.2	0.40
Education			
＜high school	97 (52.7%)	105 (47.1%)	0.48
High school	63 (34.2%)	82 (36.8%)	
＞university	24 (13.0%)	36 (16.1%)	
Women's age at first pregnancy (years)	25.2±3.4	24.6±3.4	0.12
Husband's age at first pregnancy (years)	27.8±3.8	27.2±3.9	0.10
Intercourse before first pregnancy (times/week)	2.1±1.1	3.1±2.2	＜0.0001

$ The almost characteristics were tested by t-test or chi-square test.

Table 2. the crude odds ratio (OR) and adjusted odds ratio showed the association between PCBs and time to pregnancy based 442 women

PCBs exposure	N	TTP(months) medium	The crude OR		adjusted OR £	
			OR	95%CI	OR	95%CI
Yucheng	187	4	2.28	1.42-3.69	2.20	1.33-3.68
control	255	3	1		1	

£ : adjusted for women's age at first pregnancy and husband's age at first pregnancy