PROLONGED EFFECT ON OFFSPRING'S SEX RATIO FOLLOWING PARENT'S INGESTION OF PCBs / PCDFs CONTAMINATED OIL

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Introduction

In 1979, over a 10 month period, about 2000 people in Taiwan were poisoned through cooking oil contaminated with heat-degraded polychlorinated biphenyls (PCBs). Those affected developed chloracne, hyperpigmentation, peripheral neuropathy and other visible symptoms; this syndrome was called *Yucheng* (oil disease)[1]. PCBs are a family of industrial compounds that until the 1970s, when they were banned, had been widely used as dielectric fluids in electrical transformers [2]. PCBs and PCDFs, like TCDD, are perisitent dioxin-like compounds which remain in the body for more than 20 years after they have been ingested [3,4]. These compounds bind to the Ah receptor and are hormone disruptors, able to alter the endocrine system thereby affecting reproduction [5].

Several environmental factors affect the fetus and thereby the outcome of pregnancy, including the sex of the offspring [6]. A recent study with the Seveso exposed population has shown a direct relation between higher TCDD serum concentrations and a lower sex ratio [7]. Our study group was exposed to PCBs and PCDFs. Our aim was to find if exposure to PCBs and PCDFs. would produce similar effects to TCDD. We investigated if there was any association between the 1979 exposure and the sex of the offspring of exposed and control parents of this cohort. Our study confirms a lowered sex ratio of the offspring of the fathers exposed to heat-degraded PCB / PCDF compounds in the Yucheng episode.

Methods and Materials

From 1979 to 1983 the Taiwan Provincial Department of Health registered 2,061 cases which showed signs and symptoms of the Yucheng syndrome or a history of consumption of contaminated oil. Registration was voluntary and those registered had access to free examinations and medical care. We renewed this registry and updated their addresses in 1993. In addition, unexposed controls were identified, matched to sex, age (within 3 years) and neighbourhood at the time of exposure. From this registration, which is constantly being maintained and updated, we gathered details on each of the participants and their offspring. This information included the number of children, date of birth of each of the children and sex. A more detailed description of the cohort and the selection of the controls is given by Guo et al, 1999 [8].

A data set was derived which included all births up to 1999. Stata Software (version 6) was used for all analyses. Initially the proportion of children of each sex was summarized. Logistic regression was used to determine the effect of exposure on the sex of the offspring. It was used for analyses with allowance for clustering by family; the analyses were repeated by conditional logistic regression to allow for the matching of exposed subjects and controls. In both sets of regression, year of birth was included as a linear trend.

Results and Discussion

Table 1 shows the number of children born from exposed and control parents from the Yu-Cheng cohort.

Table 1. Exposed Families with children born from 1980 to 1999.

1322 Children of exposed families

852 Children of Exposed Mothers	420 Children of Exposed Fathers	50 Children of Exposed Couples
429 boys	205 boys	26 boys
423 girls	215 girls	24 girls
Proportion of boys =0.50	Proportion of boys = 0.49	Proportion of boys = 0.52

3320 Children of unexposed families

1986 Children of Unexposed Mothers	1271 Children of Unexposed Fathers	63 Children of Unexposed Couples
1043 boys	689 boys	38 boys
943 girls	582 girls	25 girls
Proportion of boys =0.53	Proportion of boys = 0.54	Proportion of boys = 0.61

Table 2. Unmatched logistic analyses for mothers' exposure ORs for male birth, exposed versus unexposed.

	Exposed	Unexposed		
Time Period	**No. % male**	**No. % male**	**OR (95% CI)**	**P**
1960-1979	482 (64.1 %)	1517 (64.9 %)	0.90 (0.72-1.12)	0.34
1980-1999	902 (50.4 %)	2048 (52.7 %)	0.91 (0.78-1.06)	0.22
1981-1999	861 (49.7 %)	1863 (52.6 %)	0.89 (0.75-1.04)	0.14
1981-1984	285 (52.3 %)	687 (52.0 %)	1.01 (0.77-1.33)	0.95

1985-1989	283 (48.1 %)	599 (48.9 %)	0.96 (0.73-1.28)	0.80
1990-1994	223 (49.3 %)	409 (55.5 %)	0.78 (0.56-1.08)	0.14
1995-1999	70 (47.1 %)	168 (61.3 %)	0.57 (0.32-1.00)	0.05

Table 3. Unmatched logistic analyses for fathers' exposure ORs for male birth, exposed versus unexposed.

	Exposed	Unexposed		
Time Period	**No. % male**	**No. % male**	**OR (95% CI)**	**P**
1960-1979	424 (63.9 %)	1169 (62.9 %)	1.06 (0.84-1.35)	0.62
1980-1999	470 (49.2 %)	1334 (54.5 %)	0.80 (0.65-0.99)	0.04
1981-1999	444 (48.0 %)	1232 (54.9 %)	0.76 (0.61-0.94)	0.01
1981-1984	96 (46.9 %)	296 (54.7 %)	0.74 (0.47-1.18)	0.21
1985-1989	102 (45.1 %)	292 (55.1 %)	0.67 (0.43-1.06)	0.08
1990-1994	117 (53.8 %)	302 (51.7 %)	1.08 (0.71-1.66)	0.71
1995-1999	129 (45.7 %)	342 (57.6 %)	0.62 (0.41-0.93)	0.02

Tables 4 and 5 show results of matched analyses between exposed and control fathers and mothers.

The proportion of male births differed between exposed and control parents with statistical significance for fathers in the time band from 1980 to 1999, and more strongly in the time band from 1991. There was no evidence of any effect of mothers' exposure on the proportion of male births.

In the case of fathers, stronger effects were seen when the time is taken from approximately one year after the withdrawal of the contaminated oil (November 1979)

Table 4. Matched conditional logistic analyses for mother's exposure ORs for male birth, exposed versus unexposed.

Time Period	**OR (95% CI)**	**P**
1960-1979	0.85 (0.66-1.10)	0.22
1980-1999	0.92 (0.76-1.11)	0.38
1981-1999	0.90 (0.74-1.09)	0.28
1981-1984	0.82 (0.55-1.20)	0.30
1985-1989	1.11 (0.75-1.65)	0.60
1990-1994	0.82 (0.48-1.40)	0.47
1995-1999	0.33 (0.06-1.87)	0.21

Table 5. Matched conditional logistic analyses for father's exposure ORs for male birth, exposed versus unexposed.

Time Period	OR (95% CI)	p
1960-1979	1.16 (0.87-1.55)	0.32
1980-1999	0.75 (0.57-0.97)	0.03
1981-1999	0.69 (0.52-0.91)	0.01
1981-1984	0.70 (0.36-1.36)	0.30
1985-1989	0.84 (0.38-1.87)	0.67
1990-1994	1.18 (0.61-2.32)	0.62
1995-1999	0.70 (0.38-1.29)	0.25

Our findings add to similar lowered sex ratio studies of highly exposed populations, with the exposed fathers showing statistically significant associations. These results indicate a reduction in birth of male children to the exposed fathers. Also agreeing with previous findings, exposed mothers showed no effect on the sex ratio of their offspring.

These results support the use of an altered sex ratio as an initial and good indicator for the presence of human reproductive hazard, being inexpensive and easy to ascertain.

The difficulties of adequately measuring human reproductive health hazards in association with environmental pollutants have delayed the acquisition of our knowledge and therefore the implementation of preventative measures. It may now be possible to consider a lowered sex ratio as an initial sign of reproductive alteration in selected populations.

A further analysis in this population , including PCB / PCDF serum concentration levels, is currently in progress.

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