

YUCHENG: STUDIES IN CHILDREN

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Abstract

In 1979, a mass poisoning occurred in Taiwan due to cooking oil contaminated by thermally degraded polychlorinated biphenyls. These chemicals persist in human tissue, and so children born to female patients after the outbreak were exposed in utero. In 1985, we examined 118 children born to affected women and unexposed controls, and have followed the children since. The exposed children are shorter and lighter than controls; they had abnormalities of gingiva, skin, nails, teeth and lungs more frequently than controls. The exposed children showed delay of developmental milestones, deficits on formal developmental testing and abnormalities on behavioral assessment. At 18 months of follow up, the developmental delay persists, but does not show a strong relationship to the physical findings.

Cooking oil contaminated by polychlorinated biphenyls and dibenzofurans led to an outbreak of illness (called yucheng, "oil disease") in Taiwan. The illness consisted of chloracne, hyperpigmentation, and Meibomian gland dilatation among other findings. The epidemic was noted in May, 1979 and the oil was removed from the market in October; cases were identified retrospectively from as far back as December, 1978 (1). There is a registry of about 2000 persons who were exposed to the oil. A similar outbreak (yusho) had occurred in Japan in 1968.

Because these chemicals persist in human tissue, offspring of female patients continue to be born affected, even though maternal exposure has ceased. By 1983, 8 of 39 hyperpigmented children born to case mothers had died. In April, 1985 we performed a field survey (2) of all living children who were known to have been in utero during or after the period of oil contamination. These children would have had transplacental exposure and possibly exposure through breast milk, but would not themselves have consumed the contaminated oil.

Seventy four women in the health department's registry had living children born between June 1978 and March 1985. Chinese-speaking nurses interviewed the mothers in their homes. The women reported 159 pregnancies in this time; 3 were ongoing, 5 miscarried, 8 were aborted, 6 were stillborn, and 5 liveborns later died, leaving 132 living children. We obtained usable information on 128. One more child died between interview and examination. 29 families had 1 eligible child, 34 had 2, 9 had 3, and 2 had 4. Controls came from 96 families who lived in the same neighborhoods. These 96 mothers reported 205

pregnancies in this period; 3 were ongoing, 8 miscarried, 4 were aborted, and 190 produced live births; we obtained data on 115. The exposed children averaged 32 months old, range from 1 to 82; the controls averaged 31 months, range 3 to 98.

Exposed mothers reported lower birthweight (mean \pm SE, N: 2749g \pm 46g, 128 vs 3228g \pm 40g, 115), hyperpigmentation (54/127 vs 2/114), conjunctivitis (32/108 vs 5/113), nail changes (30/122 vs 1/113), and natal teeth (11/127 vs 0/113) in the children at birth. The largest difference in the medical histories was the higher rate of bronchitis in the exposed children (30/124 vs 5/115). There was consistent reported developmental delay in the exposed children; of the 33 milestones that we asked about, the exposed children were behind in 32 (the null value would be 16.5).

The physical examinations were carried out over 11 days in April 1985, at four local clinics. 117 exposed children and 108 control children attended. The exposed children were smaller than controls, averaging 93% (95% CI 90-96) of control weight and 97% (95% CI 96-99) of control height, adjusted for age and sex. The gum hypertrophy or swelling noted by the mothers at birth was still apparent on examination (7/116 vs 0/107). Neither acne nor conjunctival cysts were much more common in the exposed, but the differences in hyperpigmentation (perineal/genital: 50/117 vs 29/106; head/face: 13/117 vs 4/106) and nail deformities and pigmentation (fingers: 19/117 vs 1/106; toes: 74/117 vs 22/106) are large. The marked differences in eyebrow flare (25/117 vs 4/106), hypertelorism (24/117 vs 10/106) and clinodactyly (47/117 vs 25/106) were not anticipated. There were no abnormal reflexes or any localizing findings in the neurologic exam; however, the exposed children were delayed compared to controls in the age at which they performed tasks such as saying phrases and sentences, turning pages, carrying out requests, pointing to body parts, holding pencils, imitating drawn circles, or catching a ball. The neurologists had an overall clinical impression of developmental or psychomotor delay in 12 (10%) of the exposed vs. 3 (3%) of the control children, and of a speech problem in 8 (7%) vs. 3 (3%).

We did age-appropriate testing of cognitive development in the home at 6, 12, and 18 months after the survey, using new controls matched for neighborhood, sex, age, sib order, and family socioeconomic status (3,4,5). Except for verbal IQ on the WISC, the exposed children always score lower than the controls on the three developmental/cognitive tests. These differences are stable over 18 months of follow-up (Table 1). We have also seen relatively weak relationships between the degree of symptoms in the mother, the growth retardation in the child, and the level of PCBs in the child and developmental delay; however, none of the physical findings present on exam are related to the presence or persistence of low scores on developmental testing.

Thermally degraded PCBs were identified as human teratogens in the Japanese epidemic in 1968. Children born to yusho mothers had low birthweight, hyperpigmentation of gums and nails, conjunctivitis, dysplastic nails, wide fontanels, metastatic scalp calcification, diffuse dark skin pigmentation and natal teeth: 2/13 were stillborn (6). Four of these children were reported as normal at ages 8-19 months (6,7) but Harada (7) reported that the thirteen children he examined up to 7 years after the exposure were apathetic

and dull with IQs in the 70s.

In Taiwan, Wong and Hwang (8) noted skin desquamation, deformed, pigmented nails, hypersecretion of the Meibomian glands, hyperpigmentation of the nose, and acne in 6 offspring of yucheng mothers. Four of these children weighed 2500 grams or less at birth. Lan et al. (9) added another case with diffuse skin hyperpigmentation and low birthweight who died at 22 months. Law et al. (10) reported twins seen at 3 months of age for respiratory distress and pneumonia. They weighed 1800 and 2820 grams at birth, and had wide fontanels, hyperpigmentation, and persistent conjunctival swelling.

These children have been exposed only by transplacental passage of the chemicals or by breast milk exposure. It is impossible to separate cleanly effects that persist because of structural changes during the fetal period from those that persist because of continued internal exposure. The kinds of toxicities seen are consistent with PCBs, but the exposures are relatively low. The children of workers exposed to PCBs uncontaminated by PCDFs do not show nearly so much toxicity, but the mothers achieve blood PCB levels that are comparable to those seen in the outbreaks (11). The most likely reason is the presence of the very toxic PCDFs in the cooking oil. Qualitatively, the PCBs and PCDFs are similar in toxicity, but the PCDFs are active at much lower doses. The oil in Taiwan had about 100 ppm PCBs, and about 0.1 ppm PCDFs (12). Although there has not been a human exposure to PCDFs in the absence of PCBs, it is reasonable to assume that much of the toxicity seen in both outbreaks is due at least in part to PCDF contamination.

TABLE 1. Mean Developmental Scores Among Exposed and Controls

Instrument	Fall '85		Spring '86		Fall '86	
	exposed	control	exposed	control	exposed	control
	mean (n)	mean (n)	mean (n)	mean (n)	mean (n)	mean (n)
Bayley Mental	100 (45)	106 (45)	101 (28)	102 (28)	100 (19)	104 (19)
Bayley Psychomotor	101 (45)	108 (45)	104 (28)	106 (28)	106 (19)	110 (19)
Stanford-Binet IQ	85 (52)	89 (52)	98 (25)	106 (25)	92 (69)	97 (69)
WISC Verbal IQ	82 (21)	82 (21)			85 (30)	86 (30)
WISC Performance IQ	90 (21)	97 (21)			97 (30)	102 (30)
WISC Full Scale IQ	84 (21)	88 (21)			90 (30)	93 (30)

WISC = Wechsler Intelligence Scale for Children

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