REPRODUCTIVE EFFECTS OF PCBS/PCDFS IN YUCHENG PATIENTS

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Introduction

Polychlorinated biphenyls (PCBs), dibenzofurans (PCDFs), and dibenzodioxins (PCDDs) are known ubiquitous contaminants and found in animal studies to disrupt the endocrine systems. Many human health studies have been conducted in cohorts uniquely exposed to these polychlorinated aromatic hydrocarbons. In this discussion the human health effects identified in several cohorts will be compared and contrasted in an attempt to better understand the scope and severity of the reproductive effects found from these exposures and discuss potential mechanisms of the congeners, toxicity and the observed altered susceptibility of the cohorts.

Methods and Materials

Taiwan Yucheng ("oil-disease") cohort consisted of approximately 2000 Taiwanese exposed to PCBs and their heat-degradation products from the ingestion of contaminated rice oil in 1979[1]. The exposure levels, mortality and morbidity, reproductive history in women, findings of children at birth and later development will be compared with findings from high accidental exposures, Yusho ("oil-disease") of Japan, 2,3,7,8-TCDD exposure in Seveso, Italy, as well as those from cohorts with background levels of exposure. Evidence related to endocrine and reproductive effects will be specifically discussed.

Results and Discussion

Exposed Yucheng people had initial serum levels estimated to be higher than 20,000 ppb lipid base for PCBs and 40,000 ppt lipid base for PCDFs. Fourteen years after the exposure, the Yucheng female adults had serum levels of PCDF up to two hundred times as high as found in the unexposed, closely matched controls, and serum levels of PCBs up to more than ten times the control subjects[2]. Lactation by breast-feeding reduced the serum levels in the Yucheng mothers, but increased serum levels in their children[3]. This level of exposure was similar to the level in Japan Yusho cohort[4], except that the levels of toxicants in the contaminated oil were lower in Taiwan, and the duration of exposure was much longer. The median exposure level in cohort from Seveso was lower than the two Asia episodes in terms of dioxin toxic equivalencies[5]. The Yucheng cohort exposed as adults was found to have increased mortality secondary to chronic liver diseases and cirrhosis, but similar rate of liver cancer as compared to the national death using

standardized mortality ratio 12 year after the exposure[6]. These findings were different from Yusho and Seveso cohorts. A telephone health survey was conducted 14 years after the exposure[7], which showed that Yucheng men reported increased prevalence of having skin allergies, chloracne, headache, spine and joint diseases, and goiter. Yucheng women reported increased prevalence of having skin allergies, chloracne, headache, anemia, and goiter. These findings were to some extent similar to those from other exposed populations. Reproductive history of the women was compared with unexposed controls in a retrospective study on Yucheng cohort[8]. Among Yucheng women, 4.2% reported a stillbirth since 1979, as compared to 1.7% in unexposed controls (P=0.068). Sex ratio in the offspring of Yucheng mothers was not different from the unexposed population[9]. This is similar to the findings from Seveso, that maternal exposure did not result in sex ratio difference, as was shown in paternal exposure[10]. Initial analysis in Yucheng men showed reduced sex ratio in their offspring, as reported in exposed men in Seveso. More Yucheng women reported that one of their offspring had died during childhood (10.2% vs. 6.1%, P<0.05). Similarly, Hsu et al. reported that of the 39 Yucheng babies in utero during the time the mothers ingested the contaminated oil, 8 died in the first few years of life, mostly from perinatal conditions and respiratory infections[1]. Children of Yucheng women were born growth retarded, with dysmorphic physical findings, and delayed cognitive development as compared with unexposed children. The dysmorphic features included cola-colored hyperpigmented skin, hyperpigmented oral mucosa, chloracne, Meibomian gland swelling, natal teeth and fragile teeth, and deformed and pigmented nails[11]. Children born to the cohort after the initial exposure have been followed from birth to the present day. From 4 to 11 years of age, Yucheng children had reduced intelligence quotients compared to the unexposed controls[12]. Those children born immediately after maternal exposure were similarly affected in neurocognitive developments as those born 6 years after the exposure. In their age 8-14, Yucheng children had increased nail deformities[13]. The main nail findings were transverse coarse grooves and irregularly concaved depression in approximately one quarter of Yucheng children, with predilection for thumbs, followed by big toes and other fingers. Those children born closer to the mothers' intoxication had more nail deformities than those born later. The Yucheng children not only had increased respiratory infections reported by parents[14], but also increased chronic otitis media compared to the matched controls by examination in 1993[15]. In regards to endocrine disruption in the transplacentally and lactationally exposed subjects, Yucheng adolescent males had decreased capacity to understand spatial relationships as compared to their long-term closely matched males control subjects[16]. Possibility of loss in male advantage in visuospatial capability was suspected. No differences were identified when the exposed and none exposed females were compared. In prenatally exposed young men who had reached sexual maturity, sperm analysis showed increased abnormal morphology, reduced motility, and reduced capability of penetrating hamster oocytes[17].

It was concluded that long-term follow-up of Yucheng cohort and their offspring, when compared with other poisoning episodes, has been able to provide valuable information concerning the reproductive health effects of PCBs/PCDFs. It has also been demonstrated that exposure to these chemicals caused prominent health effects in several outcome measures. People exposed perinatally are found to be one of the most susceptible groups of humans to the toxic effects of these persistent organic pollutants.

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