

### **Human health effects from PCBs and dioxin-like chemicals in the rice oil poisonings as compared with other exposure episodes**

Yueliang Leon Guo, MD, MPH, PHD

Environmental and Occupational Health  
National Cheng Kung University Medical College  
Tainan, TAIWAN

The human health effects of PCBs, PCDFs, and dioxin are important to understand since these polyhalogenated aromatic hydrocarbons (PAHs) have been found in the serum of all populations ever studied and the many of the PAH congeners have long half lives in the human measured in years. Many human health studies have been conducted in cohorts uniquely exposed to these PAHs. 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 effects found from these exposures and discuss potential mechanisms of the congeners, toxicity and the observed altered susceptibility of the cohorts.

The initial cohort to be discussed will be the cohort from Taiwan referred to as the Yucheng ("oil-disease") cohort. The Yucheng cohort are Chinese in Taiwan exposed to PCBs and their heat-degradation products from the ingestion of contaminated rice oil in 1979 (1). The health effects found in this cohort will be compared to the health effects found in the Yusho cohort of Japanese similarly exposed to PCBs/PCDFs in 1968; and to the Seveso cohort of Italians exposed to dioxin in 1976. Reference will also be made to several PCB-exposed cohorts in the United States. Differences in the study designs employed in each cohort will also be discussed. In Yucheng, exposed people had initial serum levels estimated to be 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.

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 (3). Of the 39 children in utero during the active exposure, 9 died at or around birth from primarily respiratory complications and perinatal conditions (1). 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 (4). 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 and increased chronic otitis media compared to matched controls (5).

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 (6). Possibility of loss in male advantage in visuospatial capability was suspected. No differences were identified when the exposed and none exposed females were compared. Differences in males genitalia growth was observed. In male subjects who have reached sexual maturity sperm analysis has been conducted and will be discussed at the meeting.

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 (7). These findings were different from Yusho and Seveso and will be discussed. A telephone health survey was conducted 14 years after the exposure (8), 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. Difference between these findings and those from other exposed population will be discussed.

The induction of cytochrome P450 1A2 was examined in most of the cohorts. In the Yucheng cohort, P4501A2 levels were markedly induced as monitored by the caffeine breath test. P4501A2 levels in the other cohorts were induced but to a much smaller degree.

These findings of intrauterine, developmental and chronic health effects found in the Yucheng cohort will be compared with Yusho and Seveso poisoning episodes and to a lesser extent the data from studies in the United States on the PCB exposed cohorts as well as other intoxication episodes. Follow-up of health effects for people involved in these untoward events has provided important information about the toxicities, health effects, and dose-response relationship of PCBs and dioxin-like chemicals in directly exposed and perinatally exposed humans. It has also been demonstrated that perinatal exposure to these chemicals caused more prominent health effects in several outcome measures.

### Reference

1. Hsu ST, Ma CI, Hsu SKH, Wu SS, Hsu NHM, Yeh CC, Wu SB. *Environ Health Perspect* **1985**, 59, 5.
2. Guo YL, Ryan JJ, Lau BPY, Yu ML, Hsu CC. *Arch Environ Contamin Toxicol*, **1997**, 33, 104.
3. Rogan WJ, Gladen BC, Hung KL, Koong SL, Shih LY, Taylor JS, Wu YC, Yang D, Ragan NB, Hsu CC *Science* **1988**, 241, 334.
4. Chen YC, Guo YL, Hsu CC, RoganWJ. *JAMA* **1992**, 268, 3213.
5. Chao WY, Hsu CC, Guo YL. *Arch Environ Health* **1997**, 52, 257.
6. Guo YL, Lai TJ, Chen SJ, Hsu CC. *B Environ Contam Toxicol* **1995**, 55, 8.
7. Yu ML, Guo YL, Hsu CC, Rogan WJ. *Am J Indust Med* **1997**, 31, 172.
9. Guo YL, Yu ML, Hsu CC, Rogan WJ. *Environ Health Persp* **1999**, in press.

