EXPOSURE OF CHILDREN WHOSE MOTHERS SUFFERED FROM YU-CHENG POISONING TO POLYCHLORINATED DIBENZOFURANS (PCDFS) AND POLYCHLORINATED BIPHENYLS (PCBS)

John Jake Ryan[a], Cheng-Ching Hsu[b], and Yue-Liang Leon Guo[b]
[a]Food Research Division, Health Protection Branch, Health and Welfare Canada, Ottawa K1A 0L2, CANADA
[b]Dept. Environmental Health, National Cheng Kung University Medical College, Tainan 70428, Taiwan (Republic of China)

In 1979 in central Taiwan, a food grade rice cooking oil was accidentally contaminated with an aged thermally degraded commercial PCB used as a heat exchange media. More than 2000 people consumed this toxic oil prior to the appearance of overt symptoms and withdrawal of the offending agent some 6 months later[1]. The illness, called yu-cheng (oil disease in Chinese), was characterized by severe acne, hyperpigmentation, neuropathy, eye discharge, and other signs. The outbreak was similar to one in 1968 in western Japan called yusho (oil disease in Japanese). In both cases the commercial PCBs were contaminated with elevated levels of PCDFs which, qualitatively, are similar in biological activity to the PCBs but, quantitatively, are much more potent[2]. It is now believed[3] that the PCDFs are responsible for most, if not all, the adverse effects of these two incidents.

Because these chemicals persist in human tissue and have been identified as transplacental poisons, offspring of female patients were and continue to be affected even though maternal exposure has ceased and the children themselves did not consume the contaminated oil. In early 1985, all living children born to women on the PCB oil disease registry were identified and matched with control children. These 118 exposed children were found to have lower birth size, hyperpigmentation, elevated bronchitis, and, most noticeably, developmental delay in a variety of tests[4]. Both the physical and cognitive symptoms are known to persist up to the age of 10 years[5]. From limited data, the relationship between the degree of symptoms in the children appears to be only weakly correlated with the serum PCB concentration of either the mother or child[6] although there was an indication that the child's *in utero* exposure was more important to developmental delay than was exposure through breast milk.

Since there are few incidents world-wide of human exposure to dioxin-like compounds, these human populations have immense importance for the study of human health effects without relying on extrapolation from laboratory animal experiments. The technology now exists to determine ultra trace amounts of chlorinated aromatic hydrocarbons in human blood samples. As the PCDFs have been associated with many of the adverse effects of yu-cheng, we used these more sensitive and specific techniques to study in a quantitative manner the current exposure of these children to both the PCDFs and PCBs.

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METHODS

Sampling

Human blood sera from individual children of the mother/child cohort were collected in Tainan, Taiwan in February, 1991 at the time of their recall visit for health assessment. Forty-five of these along with a single pooled sample from the matched control children were available for analysis. As the average age of the children was now 9.6 yr and their exposure was indirect *peri*natally through their mothers, the level of blood contamination was expected to be low. The average amount of serum obtainable for determination of the dioxin-like compounds (PCDFs/PCDDs/planar PCBs (pPCBS) and the classical PCBs in a congener specific fashion was 2.3 g with a range of 0.1 to 5.0 g. The average extractable lipid content was 6.8 mg corresponding to 0.31 % lipid in the sera.

Analysis

The dioxin-like compounds in the sera were determined simultaneously by isotope dilution gas chromatography-mass spectrometry (GC-MS) after extraction with ethanol-hexane, defatting with sulfuric acid, and chromatography on acid-base silica, Florisil (second fraction), and carbon columns as detailed recently[7]. The classical PCBs (up to 15 congeners) were monitored in the first Florisil fraction using capillary GC-EC. The toxic rice oil contained higher relative concentrations of PCDFs to PCBs than that in the commercial mixture (Kanechlor 400/500). Within the PCDFs, emphasis is placed on two congeners, 2,3,4,7,8-pentachlorodibenzofuran (PnCDF) and 1,2,3,4,7,8-hexachlorodibenzofuran (HxCDF), which are the most persistent in and toxic to humans. The detection limit of these two congeners with the small amount of sample used averaged 100 to 200 μg/kg (parts per trillion;ppt) on a lipid basis.

RESULTS AND DISCUSSION

The tissue data are somewhat difficult to interpret in that the limit of detection varies as a function of the sample size and many samples do not exhibit discrete detectable values. For the PCDFs, the total amount in these small serum samples varies from as high as 20 pg to as little as 1 pg -the latter quantity could still be distinguished from the small amount (< 0.5 pg) present in laboratory blanks. Detectable concentrations are found in about 1/2 the samples for the two PCDFs and in a little less than 1/2 for the PCBs as shown in Table 1.

Table 1. Chlorinated aromatic hydrocarbons in 45 sera and a single control pool of children from the yu-cheng cohort;
PCDFs in ng/kg (ppt) lipid and total PCBs in mg/kg (ppm) whole weight

Analyte	23478-PnCDF	123478-HxCDF	Total PCB
Number positive of 45	22	24	20
Detection limit	80-500	100-500	0.5-10
Average of positives	300	620	7.6
Median of positives	185	424	5.7
Range	89-1230	120-3040	0.9-36
Control serum value	19 ppt	23 ppt	0.56 ppb

HxCDF levels, which range up to 3 μg/kg, are about double those of PnCDF which in turn extend up to 1.2 μg/kg. These two analytes are highly correlated. Using only the positive values, the average and median of : a) the penta PCDF congener are 10 to 15 times higher than those of control sera and b) the hexa congener are 20 to 30 times higher. Total PCBs is about 10 to 15 times higher than control or background levels of PCBs. The correlation between the concentrations of the two PCDFs and total PCBs is low. Other PCDDs, PCDFs and planar PCBs (three congeners) are non-detectable in these samples. The results of the control sera also show that the background concentrations of PCDDs/PCDFs/pPCBs in Taiwan are similiar to those of many other industrialized nations e.g. circa 20 ng TEQ/kg blood lipid.

The mother's exposure to the toxic oil containing PCDFs and PCBs took place over 12 years ago and the children themselves were exposed secondarily. Nevertheless, concentrations of the analytes can still be quantified in about 1/2 the samples with these small volumes of sera. Using the positive values only, the levels found are still about 10 to 30 times greater than normal or background quantities.

As the cohort of children has demonstrated increased physical defects and developmental delays, the above quantitative exposure data now allows more detailed study of the relationship between dose and effect and, consequently, estimation of which individuals are at greater risk. In addition, knowledge of the blood concentration or body burden associated with an adverse effect permits a better judgement to be made of the health risk posed from the background or low levels of these contaminants found in the bodies of all people particularly in industrialized countries.

Present indications from demographic information on these individuals are that the serum concentrations could be affected markedly in infancy by feeding regime, bottle or breast. Therefore, it would be useful to obtain exposure data on the mothers themselves, an activity

presently under way.

ACKNOWLEDGEMENTS

The authors are grateful for the sample preparation techniques carried out by Luz Panopio and Nicole Beaudoin and the mass spectral determinations of Mark Boyle. This study has also benefited from the contributions of Yung-Chen Joseph Chen, National Cheng Kung University Medical College, Tainan. Collection of sera was supported by Taiwanese grants from the National Sciences Council #NSC 80-0421-B-006-05Z and 81-0421-B-006-03YZ and the Department of Health #DOH 82-HR-C13.

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