

Historical Perspective On Yu-Cheng Incident

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Polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are two classes of manmade chemicals which occur as contaminants in certain industrial chemicals and can be produced in thermal processes. Neither class of compounds has any known beneficial use. However, there is much concern about their effect on human health. This concern stems from the results of a multitude of acute and long-term toxicity tests in experimental animals and more recently from epidemiologic studies that examined cancer mortality in occupational workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), presumably the most toxic compound in these two classes. This human health concern is heightened by the knowledge that almost all humans in the industrialized world have measurable levels of many of the congeners of these two classes. Of particular concern are populations that are deemed "more susceptible." These include the very young (developing fetuses and breast fed children), people who subsist on contaminated fish, and populations that have been overtly exposed because of some incident. The relationship between exposure, as measured by the internal dose of these compounds, and health effects in overtly exposed populations should be studied extensively. From such studies, we will gain valuable data, which when coupled with data from animal studies, will give regulatory and public health agencies improved information for risk assessment and risk management.

Three general populations, that have been exposed to PCDDs and PCDFs, exist. These are Yusho (1968, Japan), Yu-Cheng (1979, Taiwan), and Seveso (1976, Italy) populations. The first two populations of about 2,000 people each consumed food grade rice oil that had been contaminated with thermally degraded polychlorinated biphenyls (PCBs), which had given rise to PCDFs and polychlorinated quaterphenyls (PCQs). Samples of the Japanese

oil reportedly contained about ten times more PCBs, PCQs, and PCDFs than did the Taiwanese oil, but the Taiwanese population on average consumed about ten times more oil; thus the exposures were remarkably similar in terms of the amount of total exposure to the contaminants and the number of people exposed. The primary etiologic agent in these incidents is believed to be the PCDFs, even though their concentrations are 100-500 fold less than the PCBs and PCQs. Although many PCDFs have been measured in the oils, the PCDFs that primarily persist in the victims are 2,3,4,7,8-pentachlorodibenzofuran; 1,2,3,4,7,8-hexachlorodibenzofuran; and 1,2,3,4,6,7,8-heptachlorodibenzofuran. The most notable manifestations of the Yusho and Yu-Cheng populations were dermal lesions such as chloracne and comedones. However, many other overt symptoms, including babies born with unusually brown colored skin, gingiva, nails and eye discharge continued. Subsequent testing has shown that these victims' offspring suffer neurotoxic and developmental effects. These studies will be discussed during this symposium.

The third general population that has been overtly exposed to these classes of compounds is that in and around Seveso, Italy. That population will also be described in this and other sessions at the meeting. As mentioned previously, the Yusho and Yu-Cheng populations were exposed to a mixture of chlorinated aromatics; on the other hand, the Seveso population was exposed to only 2,3,7,8-TCDD and the starting materials used and products produced in the synthesis of 2,4,5-trichlorophenol. This exposure was the result of an accidental release of these materials from a manufacturing plant. The main route of exposure to the nearby residents is believed to be by inhalation of and dermal contact with the contaminated fall-out and ingestion of contaminated food products.

All three of these episodes led to extremely high levels of PCDFs or 2,3,7,8-TCDD in the exposed populations. In fact, the toxic equivalency based on 2,3,7,8-TCDD per kilogram of body weight in selected chloracne cases showed remarkable agreement (Figure 1). Yet other adverse health effects in these populations differ. Perhaps the talks in this session will better define reasons for this apparent difference.

Body Burden Levels (TEQ) In Chloracne Cases

<u>INCIDENT</u>	<u>Levels ($\mu\text{g}/\text{kg bw}$)</u>
Yusho*	3.0
Yu-Cheng*	2.0
Seveso+	3.0

*Exposure primarily to 23478-PCDF and 123478-HxCDF Levels from Ryan et al. Fund Appl Toxicol 1990;15:722-731.

+Exposure to 2378-TCDD. Calculated level from Needham et al., Banbury Report 1991;35:229-257.