FINDINGS FROM OUR SEVESO STUDY AND COMPARISONS WITH OTHER EXPOSED POPULATIONS

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Because of an industrial accident at the ICMESA plant on July 10, 1976, at least 1.3 kg of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) contaminated a populated area of about 2.8 km^2 near Seveso, Italy (Cerlesi et al., 1989). Based on dioxin soil levels, vegetation kill, and deaths of domestic animals, this area was divided into four zones: A Zone, 80.3 hectares, 736 residents; B Zone, 269.4 hectares, 4737 residents; R Zone, 1430 hectares, 31,801 residents; and the control non-ABR Zone, 7474 hectares, 182,843 residents. Because of the extreme toxicity of TCDD in certain species of animals, a large health monitoring project was established soon thereafter. All residents of A Zone, the most heavily contaminated zone, were evacuated within one month following the release. B Zone residents were asked not to eat their produce or poultry. From 1976 to 1982 residents of these zones underwent several medical examinations; some of the residents of the most exposed zones were followed until 1985. The most striking finding was that dermatologic investigations found skin lesions specifically attributable to the accident. These initial burns, characterized by erythema and edema, were attributed to the sodium hydroxide that was also released in the explosion (Gianotti, 1977). However, in September 1976, many cases of chloracne were diagnosed (Caramaschi et al., 1981); these were subsequently classified from the mildest type 1 to the most severe, type 4; all type 4 cases appeared in persons from the A Zone. Results

of the medical follow-up were periodically evaluated at Seveso by an International Steering Committee of experts; in its last meeting of February 19-21, 1984, the Committee again linked chloracne as the only clinical alteration with a positive association with soil levels of TCDD; no conclusion was yet possible with regards to cancer, but a registry was established and is still active. Preliminary results (Bertazzi et al., 1989) after 10 years of observation of cancer mortality do not permit any conclusion; however the latency period of 20 years that was used by Fingerhut et al. (1991) has not yet been reached.

Although these health effect data are reassuring, we knew little about the extent of actual TCDD exposure. In 1981, Facchetti et al. reported the TCDD levels in autopsy samples of adipose tissue, blood and other organs from a 55 year old woman who had died from pancreatic adenocarcinoma 7 months after the explosion. Her TCDD whole-weight levels varied from 6 parts-per-trillion (ppt) in blood to 1840 ppt in adipose tissue.

In 1988, a group of U.S. and Italian scientists convened in Milan to further examine the Seveso incident. Since more than 30,000 serum or plasma samples (volumes of <1-3 mL) from the medical examinations had been stored at -30°C, the group agreed to assess whether we could measure TCDD in these samples. Ten samples from chloracne cases and from non-chloracne cases, all from A Zone, were sent to CDC. The TCDD levels in the chloracne cases ranged from 828-56,000 ppt (lipid-adjusted) and in the non-chloracne cases from 1770-10,400 ppt. Although the mean levels were much higher in the cases, there was some overlap in the TCDD levels between the two groups. One striking difference between these two groups was that the chloracne group was primarily children and the non-chloracne group was primarily adults (Mocarelli et al., 1991). No difference in the levels of the other polychlorinated dibenzo-p-dioxins or polychlorinated dibenzofurans was seen (Mocarelli et al., 1990). The 56,000 ppt level from this acute exposure is the highest TCDD level ever reported in an individual; this sample was drawn in October 1976, from a 4 year old girl. During the examination period from 1976 to 1985, no clear pathological effects were observed in these 20 people, although a few of the clinical chemistry tests were transiently outside the normal range.

Our protocol was later expanded to include the following:

> Determine if B Zone residents were overtly exposed, and if so, did the exposure occur primarily at the time of the explosion or did it continue years

after the incident.

- Investigate the relationship between TCDD blood levels with prevalence and development of cancer.
- Determine the half-life of TCDD in these adults and children, both sexes.

These studies are still in progress, but our findings to date are summarized.

Residents of B Zone were also overtly exposed to TCDD, but to a lesser degree than A Zone residents, as a result of the 1976 explosion; however, those B Zone residents who lived in B Zone for a few years, but who moved into B Zone after the explosion, did not have elevated levels.

The results to date indicate no difference in the TCDD levels in cancer mortality cases versus non-cancer cases.

The half-life data are still being analyzed, but some of the initial data show a sharp decrease following the initial sampling, which was taken within a month or two following the explosion.

These results and other comparisons will be presented.

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