"Seveso: human health effects"

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Introduction

We have conducted the follow-up (from 1976 to 2004) by monitoring health conditions of thousands of people affected by the fallout of TCDD over Seveso and the nearby area that occurred on July 10, 1976[1,2]. These data present advantages in that: (1) they were derived from individuals of both sexes covering all age ranges; (2) since the accident, serum samples have been kept frozen and we have been able to measure (at CDC, Atlanta, USA) the TCDD blood lipid content. Therefore, we can directly correlate exposure with health effects over the years[3].

Results

The results indicate that:

- serum TCDD levels in residents showed a highly elevated exposure (up to 56 000 ppt lipid basis)
-chloracne was the only clinical alteration that positively, even if incompletely, correlated to TCDD contamination levels, and with differing individual susceptibility
- miscarriages, perinatal mortality, low birth weight, or congenital malformations did not significantly increase
- clinical monitoring of children and adults did not prove any clear association between morbidity (except chloracne) and TCDD exposure
- laboratory results with relation to liver function tests, complement haemolytic activity, white blood cells, lymphocytes, and haemoglobin showed minimal differences between exposed (even if highly exposed) individuals and controls in the period of acute exposure (1976-1977).

These differences initially were subclinical, then faded and disappeared with time[4]. A follow up of mortality cases of the Seveso population has shown an increased mortality and incidence of lymphatic and hematopoietic neoplasms both in males and females of zones A and B. In males an increased mortality for rectal and lung cancer and in females an increased mortality for hepatobiliary cancer has been found[5, 6].

Part of the exposed subjects were matched with controls during the period from 1992-2004 and the results showed that:

- no clear pathological laboratory results were related to TCDD levels in both the acute and chronic phase
- cytochrome P450 1A2 seemed to be induced after about 17 years in exposed individuals compared to controls as measured by the caffeine breath test
- the half-life of TCDD was longer in women (about 9 years) than in men (about 7.5 years), while in children it was much shorter.

A follow-up of a cohort of about 900 women showed a two fold, non-significant risk for endometriosis among those women with serum TCDD levels of 100 ppt or higher, but no clear dose response. Unavoidable disease misclassification in a population-based study may have led to an underestimate of the true risk of endometriosis[7]. Among women who were premerarcheal at the time of the explosion, a 10-fold increase in serum TCDD level was associated with a lengthening of the menstrual cycle by 0.93 days and a reduction in the odds of low menstrual flow[8]. However, among women who were postmenarcheal at the time of the explosion, TCDD was not associated with menstrual cycle length or sparse flow. In both menarche groups, TCDD levels were associated with decreased odds of having irregular cycles but were not related to days of flow. These results are consistent with effects noted in some animal species of TCDD on ovarian function and with greater sensitivity to TCDD during development. In the same cohort a breast cancer risk study[9] showed that the hazard ratio for breast cancer associated with a 10-fold increase in serum TCDD levels ($\log_{10}$ TCDD) was significantly increased to 2.1. Covariate-adjusted results were not different. Individual serum TCDD is significantly related with breast cancer incidence among these women. Continued follow-up of the cohort will help shed light on the possible role of TCDD in the pathogenesis of breast cancer[9].

A striking skewing of the sex ratio at birth (males/males+females) with an excess of females ($p<0.001$) from parents exposed to TCDD has been described for the period 1977-96. This effect has been shown to be permanently related only to exposure of the father (especially during the pre and puberty period)[10]. This effect has been recently confirmed in a dioxin induced chloracneic Austrian cohort and in exposed male workers producing phenoxy herbicides in Ufa, Russia. The TCDD concentrations by which this lower sex ratio is induced in males of the Seveso

group are only about 20 times the estimated average concentration currently found in human beings of industrialized countries[10]. Thus, it has been demonstrated for the first time that the human male reproductive system is very sensitive to dioxin. Developmental dental aberrations were associated with childhood exposure to TCDD, supporting the hypothesis that dioxins can interfere with human organogenesis. These facts can have important public-health implications due to the different individual sensitivity in humans.

References

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