

CANCER MORBIDITY (1977-1986) OF A YOUNG POPULATION LIVING  
IN THE SEVESO AREA

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## INTRODUCTION

2,3,7,8-tetrachlorodibenzodioxin (TCDD) is an established potent carcinogen in laboratory animals whereas its carcinogenicity in human is still controversial<sup>1</sup>. The town of Seveso is by now well known owing to an accident that occurred in a trichlorophenol plant in 1976. Due to a runaway reaction in one of the reactors a substantial quantity of TCDD was released into the environment and caused the contamination of a large inhabited area. Soon after the accident medical surveillance programs were initiated and the most relevant finding was the identification of nearly 200 cases of chloracne. The investigation of long-term effects started in 1983 and included mortality and cancer incidence studies. The results of the mortality studies in the adult population living in the contaminated area have been already published<sup>2,3</sup>. In the young population, aged 1-19 years, the suggestion of an increased mortality from leukemia came out<sup>4</sup>. The hint of an increased risk for non-Hodgkin lymphoma, biliary cancer, soft tissue sarcoma, multiple myeloma and myeloid leukemia was put forward by the cancer incidence study in the adult population<sup>5</sup>. We report here results of the cancer incidence study, 1977-1986, in the population aged 0-19 years.

## METHODS

Delimitation of the contaminated area was based upon measurements of TCDD levels in soil samples. Three zones with decreasing levels of contamination were identified (A,B and R)<sup>2</sup>. All persons having their residence in any of the three zones and in a surrounding non-contaminated territory, which was adopted as reference area, were followed up for cancer incidence. Incident cancer cases were ascertained through the hospital discharge registration system of the Lombardy Region where the study area is located. The system is known to cover nearly 95% of cancer occurrences and ad hoc evaluations confirmed this estimate. For each case, all relevant medical records (including histology when available) were reviewed. The collection of cancer cases included all malignant tumors of each site plus benign tumors of liver, bladder and central nervous system with a first diagnosis after the date of the accident (July 10, 1976). Relative risks (RR) and 95% confidence intervals (CI) were calculated using Poisson regression techniques.

## RESULTS

The tracing of the study subjects was successful in higher than 99% of the cohort members aged 0-19 years. The proportion of diagnoses histologically confirmed turned out

to be 87% of all cancers. The number of person-years of observations accrued during the study period were 1005 (males) and 1117 (females) in zone A, 9456 (M) and 8659 (F) in zone B, 55 933 (M) and 53 283 (F) in zone R, 304 932 (M) and 293 304 (F) in the reference area. The total number of cancer cases observed was 107, 23 in the contaminated area and 84 in the reference area. In zone A, the smallest but most polluted area, only 1 incident case was observed (0.298 expected) and turned out to be a mixed papillary and follicular carcinoma of the thyroid among females. In zone B two cancer cases occurred in the study period (2.531 expected) : one was a non-Hodgkin lymphoma among females and the other an acute myeloid leukemia among males. Given the rarity of the outcomes under study and the small size of the population in zone A and B, relative risks for specific cancer sites were calculated for the entire contaminated area (A+B+R). Table 1 reports relative risks comparing the exposed and reference populations only for cancers for which at least 2 cases were observed. The three incident cases not reported are: indifferetiate carcinoma of rino-pharynx, retinoblastoma of eye and ganglioneuroblastoma of adrenal glands. Overall cancer incidence was slightly increased in the contaminated area. None of the cause-specific relative risks departed dramatically from unity, with the only exception of thyroid cancer which exhibited, among females, a higher than four-fold elevated relative risk, albeit not statistically significant and based on only 2 cases. Two cases sustained the two fold increase for myeloid leukemia as well. Noteworthy, two ovary cancers occurred in the exposed population while no incident cases were detected in the reference one.

## DISCUSSION

The results of the cancer incidence study of this young population living in the Seveso area are far from being conclusive. Interpretation is hampered by the small number of events, short period of observation and exposure definition based on merely ecological basis. In addition, merging of people from zones with different levels of soil contamination, increased the population size but caused a dilution of exposure. None of the relative risks were statistically significant. Overall cancer incidence was only slightly above expectation. Of some interest, however, are the increased risks for thyroid cancer and myeloid leukemia. The two incident cases of thyroid were tumors of follicular cell origin : 1 mixed papillary and follicular carcinoma and 1 follicular carcinoma. The suggestion of a possible association between exposure to TCDD and thyroid cancer finds support in experimental and human data. TCDD, in fact, is known to increase the incidence of follicular cell adenoma and carcinoma of thyroid in rats<sup>1</sup>. Moreover a recent investigation of workers exposed to chlorophenoxy herbicides and chlorophenols showed an increased risk for thyroid cancer among subjects probably exposed to TCDD<sup>6</sup>. As regard to myeloid leukemia, the increased risk in this young population is quite consistent with the findings in the adult population living in the contaminated area. Both the mortality<sup>2</sup> and cancer incidence<sup>5</sup> studies suggested an excess for myeloid leukemia, particularly among subjects living in zone B. Overall, the results of this analysis should be viewed with caution because of the many limitations of the study, in particular, the very limited number of events involved and the absence of information on individual exposure. Other investigations are now under way: the incidence study will continue for a further decade; a case-control study has been initiated to delineate subjects' exposure better and to investigate the possible role of susceptibility factors in the pathogenesis of TCDD related cancers.

## REFERENCES

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Table 1. Cancer incidence, 1977-1986, in the population aged 0-19 years living in the TCDD-contaminated area. Results for selected cancers.

Cancer sites (ICD IX)	Observed	Expected	RR	CI <sub>95%</sub>
All (140-208)	23	18.2	1.26	0.8-2.0
Ovary and uterine adnexa (183)	2	0.0	-	-
Nervous system (191-192)	5	3.4	1.45	0.5-3.9
Brain (191)	4	3.0	1.32	0.4-4.0
Thyroid (193)*	2	0.4	4.66	0.7-33.1
Non-Hodgkin Lymphoma (200,202)	2	1.3	1.54	0.3-7.6
Hodgkin Lymphoma (201)	3	1.9	1.54	0.4-5.7
Lymphatic leukemia (204)	3	2.8	1.07	0.3-3.7
Myeloid leukemia (205)	2	0.9	2.30	0.6-9.2

\* Cases are restricted to females

