RISK IV

FIFTEEN-YEAR FOLLOW-UP FOR NON-MALIGNANT HEALTH OUTCOMES AFTER DIOXIN EXPOSURE

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1. INTRODUCTION

The follow-up during 1976 to 1991 of the population involved in the Seveso incident (750 inhabitants in A-zone; 5000 in B-zone; 30,000 in R-zone; >200,000 in the surrounding non-contaminated territory adopted as reference) provided the opportunity to study non-malignant health outcomes in addition to cancer[1].

2. MATERIALS AND METHODS

Subjects' exposure was classified on the basis of their residence at the date of the accident (July 1976). Mortality follow-up was successful for over 99% of the study subjects and virtually all death certificates were available[2]. Two other end points were examined: endometriosis, based on the results of experiments in monkeys[3]; and the birth sex ratio, as a means to indirectly evaluate alterations of testosterone and gonadotropins levels in exposed subjects[4].Endometriosis was studied by means of direct evaluation of the relevant medical records in all Lombardy Region hospitals. The birth sex ratio estimate was based on the demographic information system we have established in the area.

3. RESULTS AND DISCUSSION

As shown in the TABLES, the clearest suggestions of unusual mortality from non-malignant causes were obtained in A-zone, the most heavily contaminated. Males had an increased mortality from cardiovascular disease, and particularly from chronic ischemic heart disease. Mortality from this cause was also increased in B and R zones, however with lower RR values. Although chance cannot be excluded as contributing factor to these findings, the accident experience itself is a very plausible explanation for the observed excess. Two components should be taken into consideration: the disaster experience with its burden of psychosocial stressors[5] and, possibly, the chemical exposure. Both might have contributed to the excess, most probably by precipitating already existing ill health conditions, as documented by the early post accident occurrence of the deaths, the old age of the affected people, and the prevalent type of cardiovascular disorder. Among A-zone males, respiratory tract disease mortality was increased as well. The excess mainly concerned chronic obstructive bronchial-pulmonary disease (COPD) and, similarly to the chronic ischemic heart disease excess, it occurred in the early post-accident period and affected the elderly. This pattern renders reasonable

MORTALITY 1976-1991 FROM NON-MALIGNANT CAUSES IN THE SEVESO POPULATION, FEMALES ALL AGES, BY CONTAMINATION ZONE (A = HIGHEST, R = LOWEST)..

CAUSE OF DEATH	A ZONE			B ZONE			R ZONE		
	Observ. Deaths	Rel. Risk	95% C.I.	Observ. Deaths	Rel. Risk	95% C.I.	Observ. Deaths	Rel. Risk	95% C.I.
All causes	31	1.1	0.7-1.5	193	1.0	0.9-1.1	1695	1.0	1.0-1.1
Infectious, parasitic disease	[0.1]			[0.5]			5	1.3	0.5-3.3
Diabetes	2	1.8	0.4-7.1	13	1.8	1.0-3.1	75	1.2	0.9-1.5
All circulatory disease	12	1.0	0.6-1.7	79	1.0	0.8-1.2	797	1.1	1.0-1.2
Chronic reumathic heart disease	3	15.9	5.0-50.8				12	1.3	0.7-2.4
Ischemic heart disease	1	0.3	0.0-1.9	25	1.0	0.7-1.5	224	1.1	0.9-1.2
Cerebrovascular disease	2	0.5	0.1-2.0	30	1.1	0.8-1.6	273	1.2	1.0-1.3
Respiratory diseases	2	1.3	0.3-5.3	10	1.0	0.5-1.9	84	1.0	0.8-1.2
Chronic obstructive pulmonary disease	1	2.0	0.3-14.5	8	2.5	1.2-5.0	37	1.3	0.9-1.9
Digestive disease	2	1.2	0.3-5.0	13	1.3	0.7-2.2	89	1.1	0.9-1.3
Cirrhosis of liver				4	0.7	0.3-1.9	46	1.0	0.7-1.4
Accidents	2	1.5	0.4-5.8	10	1.1	0.6-2.0	71	1.0	0.8-1.3

C.I. = Confidence Interval of the Relative Risk
[ ] = Number of expected deaths when observed = 0

MORTALITY 1976-1991 FROM NON-MALIGNANT CAUSES IN THE SEVESO POPULATION, MALES ALL AGES, BY CONTAMINATION ZONE (A = HIGHEST, R = LOWEST)..

CAUSE OF DEATH	A ZONE			B ZONE			R ZONE		
	Observ. Deaths	Rel. Risk	95% C.I.	Observ. Deaths	Rel. Risk	95% C.I.	Observ. Deaths	Rel. Risk	95% C.I.
All causes	39	1.0	0.7-1.4	275	1.0	0.8-1.1	2032	1.0	1.0-1.1
Infectious, parasitic disease	[0.2]			[1.3]			9	1.0	0.5-2.0
Diabetes				6	1.2	0.5-2.7	38	1.1	0.0-1.5
All circulatory disease	21	1.6	1.1-2.5	94	0.9	0.8-1.1	755	1.1	1.0-1.2
Ischemic heart disease	9	1.5	0.3-4.5	37	0.8	0.6-1.2	329	1.1	1.0-1.2
Myocardial infarction	4	1.5	0.3-2.5	18	0.6	0.4-1.0	194	0.9	0.8-1.1
Chronic ischemic heart disease	5	3.0	1.3-7.3	18	1.3	0.8-2.1	133	1.4	1.2-1.7
Cerebrovascular disease	5	1.5	0.6-3.7	32	1.2	0.8-1.7	199	1.1	0.9-1.3
Respiratory diseases	5	2.4	1.0-5.7	13	0.7	0.4-1.2	133	1.1	0.9-1.3
Chronic obstructive pulmonary disease	4	3.7	1.4-9.8	9	1.0	0.5-1.9	74	1.2	0.9-1.5
Cirrhosis of liver	2	0.9	0.2-3.6	12	0.8	0.5-1.5	114	1.1	0.9-1.4
Accidents	2	0.7	0.2-2.8	22	1.0	0.7-1.6	134	1.0	0.8-1.2

C.I. = Confidence Interval of the Relative Risk
[ ] = Number of expected deaths when observed = 0

to hypothesize that the same determining factors discussed for cardiovascular deaths could have precipitated respiratory disease as well. Women also experienced an excess respiratory mortality in A-zone (1 death only), and particularly in B-zone (8 deaths). A major explanatory factors might be the documented immunotoxic action possessed by dioxin. This might have impaired protection and defence mechanisms against respiratory infection episodes which play a major role in COPD natural history. Diabetes mellitus exhibited an increased mortality pattern in A- and B-zone females. These findings warrant attention in the light of the results of recent investigations in other dioxin exposed populations[6,7] .Question marks about the validity of the data collected in the first post accident period do remain. Mortality from cirrhosis of the liver was not increased. Accidents did not show remarkable departures from expectations. Results for endometriosis are presently available in the age range 40-54 years. No cases were observed in A-zone, 3 cases in B-zone, 12 in R-zone, and 86 in the reference population. Results of analysis are in the following table.

ZONE	RELATIVE RISK	95% CONFIDENCE INTERVAL
A+B	0.8	0.5-1.5
R	1.3	0.4-4.2

They failed to suggest an association between the occurrence of this disorder and contamination of the area of residence. Analysis of the M/F sex ratio is under way. Preliminary results are not suggestive of an excess siring of daughters in the post-accident period.

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4. REFERENCES

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