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Authors' reply—Hathaway draws attention to an apparent inconsistency in the classification of exposures in our study. This arose because, as explained in the paper, the method for assigning exposures in the nested case-control study differed from that in the cohort analysis. In the cohort analysis, factory specific job exposure matrices were used to classify people as never, possibly, or definitely exposed to acid mists. In the nested case-control study exposures were classified as zero, low, high, or uncertain, taking into account not only the jobs in which men had worked, but also the periods during which men had been employed. We questioned staff at the factories about these jobs in more detail than would have been practical for the full cohort. Among other things this caused one deceased case, originally classed as unexposed, to be assigned to the uncertain category; and another, whose exposure had been uncertain, to be classed as having low exposure.

We must stress that all exposures in the nested case-control study were assigned blind to the case or control status of the subject. Because they were assessed from more detailed information than could be incorporated into the cohort analysis, they should be more reliable.

Hathaway also questions our inclusion of cancers of the lip and mouth with those of the larynx and nasopharynx. This decision was made before the analysis was carried out, and was based on an assumption that if acids cause cancer of the upper aerodigestive tract, the most likely mechanism is by an irritant effect. High exposure to acid mists is known to cause dental erosion, and it seemed natural to include cancers of the lip and mouth. Hathaway points out that lip cancer is caused by sun exposure and pipe smoking, but there is no reason to think that within the workforce studied, men exposed to acid mists would have had higher exposure to sunlight or pipe smoking.

The statistical power of our study was limited, but we stand by our conclusion. The findings are consistent with those of other studies indicating a hazard of aerodigestive cancer from acid mists, but they suggest that any risk from exposure to sulphuric acid and hydrochloric acid below 1 mg/m^3 is small.

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Do occupational exposures in nuclear refineries contribute to mortality from brain cancer?

Editor—Mortality from brain cancer has been found more often than expected in several nuclear processing plants.[1] Exposure to chemicals and radiation were examined, one by one, but each alone was not the causative agent of the disease.[2-4] The possibility of an association between brain cancer and exposure to electromagnetic fields has been examined in several recent studies,[5] but definite conclusions about a causal relation have not yet been reached.

Brain cancer was noticed to occur more frequently than expected in uranium mill workers in Ontario (observed 5, expected 1·12, standardised mortality ratio (SMR) 446, 95% confidence interval (95% CI): 147 to 1054). This finding was unexpected. These 1190 uranium millers were included in a larger study of underground uranium miners to find out whether exposure to uranium dust in the mills could have increased mortality from kidney disease. The SMRs for all causes, all cancer, and most other specific cancer sites were below 100 for the uranium mill workers. No brain cancers were found (expected = 1·51) in men who worked in other mills in Ontario where ores such as gold, nickel, or zinc were processed. Nor was an excess of brain cancer found in Ontario uranium miners (observed 14, expected 23·72, SMR 59). An excess of mortality from brain cancer has also been found in men who worked in tank houses where nickel is electrolytically refined (observed 8, expected 2·19).[6]

Two of the deaths from brain cancer in the Ontario uranium mill workers occurred in men under the age of 35; the other three occurred in men over 55. Two of the cancers were glioblastoma multiforme, one a glioma, one a medulloblastoma, a rare tumour occurring in children and young adults, and the histology of the other brain tumour was unspecified. The work histories available to us were not detailed enough to identify characteristics in which the workers who died of brain cancer differed from the whole cohort. Three of the men who died of brain cancer did not work elsewhere in the mining industry in Ontario. One worked underground in a uranium mine and another was a painter for 28 months and gold mill worker for 141 months. Employments in the uranium mills ranged from four months to 74 months for these five men. Four of the five deaths from brain cancer occurred less than 10 years after the men last worked in the uranium mills. The date of diagnosis of brain cancer was not recorded on the death certificate for two men and ranged from two months to 6·5 years before death for the other three men.

Exposure records for external γ radiation have been included in the National Dose Registry[7] since the routine monitoring of the radiation exposures of uranium mine and mill workers was begun in 1981. We obtained exposure records from the National Dose Registry for 92% of the 1190 Ontario uranium mill workers. The average lifetime exposure to radon from all occupational sources was 20 working level months and the average cumulative external γ radiation exposure between 1981 and 1995 was 17 mSv. All of the men who died of brain cancer began working in the Ontario uranium mills in the late 1950s before external γ levels were routinely measured and recorded in the National Dose Registry. Exposure levels for all workers exposed to radiation in Canada have decreased since the 1950s but deciding whether this also occurred for uranium millers is difficult. In any case, the uranium millers' low levels of exposure to external γ radiation reflect the low levels of radioactive elements in the uranium ores mined in Ontario. Exposure to radon has not been associated with brain cancer,[8] but several studies have shown an association between brain cancer and exposure to γ radiation.[9] However, no association between brain cancer and exposure to radiation has yet been found in the survivors of the atomic bombings of Nagasaki and Hiroshima.

Recently, electromagnetic fields and extremely low frequency fields in two Ontario mines were surveyed but no measurements of the intensity of those fields in any of the uranium mills were made. The survey data showed that levels of electromagnetic fields around some heavy duty electrical machinery used in the mining industry was between 1 and 10 μT and levels of electromagnetic fields in the electrolytic nickel refineries were much higher. A recent United States study found a significant excess of brain cancer in workers in the highest exposure category. Exposure to magnetic fields two to 10 years before death was most strongly associated with mortality from brain cancer, the relative risk increasing by 1·94/μT-year.[10] This suggests that magnetic fields may act as a tumour promoter.[5] A Canada-France collaborative study found a non-significant increased risk of brain cancer in workers whose cumulative exposure to magnetic fields was above 15·7 μT-years (odds ratio 1·95, 95% CI 0·76 to 5·0).[11]

The question of whether or not the increase in brain tumours in nuclear processing plants is due to occupational exposures remains unanswered. It is unlikely that exposure to radon is directly related to the development of brain cancer as no excess has been found in uranium miners and the exposures in the uranium mills were much lower than in the uranium mines. Neither do the exposures to γ radiation seem to be large enough to produce an excess of brain cancer. The exposures to electromagnetic fields, however, may be larger than those found in other studies, in which excesses of brain cancer have been found. The case-control method should be used to investigate exposures that might be associated with brain tumours in nuclear processing plants and electrolytic metal refineries. Electromagnetic fields, radon progeny, γ radiation, and exposures to chemicals, including solvents, can be considered in the analysis. Several study populations would need to be combined to get one large enough for a valid statistical analysis.

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