AECL-9442

ATOMIC ENERGY OF CANADA LIMITED

L'ENERGIE ATOMIQUE DU CANADA, LIMITEE

A STUDY OF THE HEALTH OF THE EMPLOYEES OF ATOMIC ENERGY OF CANADA LIMITED

IV. ANALYSIS OF MORTALITY DURING THE PERIOD 1950-1981

UNE ETUDE DE LA SANTE DU PERSONNEL DE L'ENERGIE ATOMIQUE DU CANADA, LIMITEE

IV. L'ANALYSE DE LA MORTALITE AU COURS DE LA PERIODE 1950-1981

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Whiteshell Nuclear Research Establishment

Etablissement de recherches nucléaires de Whiteshell

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RÉSUMÉ

On a mené une étude de postobservation de 13 570 personnes employées par l'Énergie Atomique du Canada, Limitée en établissant le rapport entre les données de dossier médical de ce groupe et les statistiques de mortalité du Canada pour la période entre 1950 et 1981. À peu près 60 pour-cent des personnes du groupe ont reçu quelque irradiation enregistrée au cours de leur emploi. On a observé 150 cas mortels au total dus au cancer chez les hommes ayant reçu quelque irradiation par rapport à 166 cas mortels prévus - ce qui donne un rapport de mortalité normalisé de 0,90. Aucun cancer particulier ne présente un taux de mortalité considérablement accru par rapport au taux de mortalité de la population. En général, ces résultats fournissent l'indication utile que les valeurs de risque admises actuellement pour le cancer dû à l'irradiation sont raisonnables à faible dose et faible débit de dose reçus.

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ABSTRACT

A follow-up study of 13 570 individuals employed by Atomic Energy of Canada Limited has been conducted by linking the records for the cohort to Canadian mortality data for the period between 1950 and 1981. Approximately 60 percent of the individuals in this cohort had some radiation exposure recorded during their employment. A total of 150 deaths from cancer were observed in those males with some radiation exposure, compared to 166 expected, giving a standardized mortality ratio of 0.90. No individual cancer shows a significantly increased death rate compared to the population rate. In general, these results provide useful evidence that the currently accepted risk estimates for radiation-induced cancer are reasonable for low dose and low dose rate experience.

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1. INTRODUCTION

The association between exposure to high doses of low Linear Energy Transfer (LET) radiation and increased risk of certain cancers has been recognized for many years. The evidence is particularly compelling for some of the leukemias and for cancers of the thyroid, the female breast, and the lung; for some other cancers, suggestive evidence is accumulating (BEIR III, 1980). The growth of nuclear power programs in many countries and exposure of the general population to medical x-ray procedures, such as mammography, have led to an increased interest in the long-term biological effects of exposures to low doses of radiation delivered at low dose rates over long periods of time. Therefore, long-term studies of the health of radiation workers have been established in several countries, including the United Kingdom (Beral et al., 1985; Darby, 1981; Smith and Douglas, 1986), the United States (Checkoway et al., 1985; Marks et al., 1978), and Canada (Abbatt et al., 1983). Such studies generally lack the power to detect any significant effect of radiation exposure on cancer risk if the currently accepted estimates of risk (Reissland et al., 1976) are valid, but they should serve in estimating reasonable upper bounds for these risk estimates and provide reassurance that radiation workers and the general population are not being exposed to unreasonable levels of risk. Concerns have been raised over the adequacy of the present occupational standards by observations suggesting a possible increase in risk for cancers of the prostate in a follow-up study in the United Kingdom (Beral et al., 1985), and of myeloma amongst workers at the Hanford Nuclear Energy Research Laboratory in the United States (Mancuso et al., 1977; Gilbert and Marks, 1980). In addition, Smith and Douglas (1986) have recently published a report of their findings on the mortality of workers at nuclear fuel plant in the United Kingdom. Among the radiation workers in the study, there were excess deaths from myeloma and prostatic cancer, but the findings were not of statistical significance. There was a statistically significant association with risk of bladder cancer for radiation workers.

This report describes a follow-up study of 13 570 employees of Atomic Energy of Canada Limited (AECL). The company is a Crown Corporation and was incorporated in 1952 to carry out research and development of the Canadian nuclear power program and related technologies. Prior to 1952, the Chalk River Nuclear Laboratories, which had been established in 1944, were under the control of the National Research Council. A total of 7865 (58%) study subjects had some radiation exposure recorded during their employment, i.e., are defined for the purpose of this report as radiation workers. The mortality experience of the cohort between 1950 and 1981 has been determined by record linkage to the Canadian National Mortality Database. Further linkages to update the mortality data for this cohort are planned for the future.

2. METHODS

2.1 STUDY SUBJECTS

Those eligible for study included 7548 individuals currently employed by AECL at sites across Canada as of July 1, 1980 (subsequently referred to as "current employees"). The cohort also included 7074 employees who had worked at Chalk River Nuclear Laboratories and at the Whiteshell Nuclear Research Establishment, but had left AECL prior to January 1, 1980. These past employees were known to be alive as of January 1, 1950. The majority of AECL employees worked at these two sites, where most of the recorded radiation exposures occurred. Of the current employees, 586 did not give their consent to participating in the study and, for a further 455 individuals, errors were detected in their records, which could not be corrected, and these two groups were excluded from analysis. The cohort whose mortality was monitored and analyzed thus consisted of 13 570 individuals, 92.8 percent of those originally defined as eligible for the study.

2.2 RADIATION EXPOSURE

Radiation exposure records have been maintained by AECL since its inception, but, because of a fire in February 1956, many individual records prior to that year were lost. Several methods were used to attribute dose to individuals employed before 1956. For some, notably those involved in the clean-up of the 1953 NRX reactor accident, individual doses have been reconstructed. For others, for whom the total cumulative doses to the end of 1955 were available, individual yearly doses have been calculated by dividing the total doses by the number of years individuals were employed by AECL. Where such a total was not available, but the employee continued to be employed after 1955, the average subsequent yearly exposure was allocated to all years of employment before 1956. For those who did not continue in employment after 1955 and for whom no total dose was available, a value of 2.25 mSv (10 mSv = 1 rem) for each year of employment was used. This represents the mean between what appeared to be reasonable limits on the likely average annual exposure, namely, 0.5 and 4.0 mSv. The assumptions involved in attributing dose in this way are considered to be valid , and their application leads to only minor variations in the results obtained.

The mean and standard deviation of the cumulative whole body dose for the 6626 men with some exposure recorded were 46.8 mSv and 107 mSv, respectively, with the values for the 1239 females exposed being 3.86 mSv and 5.51 mSv. The maximum accumulated dose recorded for any one individual was 1150 mSv for men and 112 mSv for women, and very few doses exceeded fifty mSv in any one given year, the currently accepted occupational standard.

2.3 MORTALITY ASCERTAINMENT

Identifying characteristics for all members of the cohort, such as surname, given name, and date of birth, were collected from present employees by a self-administered questionnaire, and for past employees, from company records. A total of 32 such identifying items were potentially available and, for the great majority of the cohort, the quantity of available identifying data was large. These identifiers were used to link the records of the cohort to the Canadian National Mortality Database maintained by Statistics Canada. This database contains, in machine-readable form, records of all deaths recorded in Canada since 1950 and of deaths of some Canadian residents who died in the U.S. The probabilistic techniques used for the computerized linkage of such records have been described in detail by Newcombe (1973), and Howe and Lindsay (1981). After linkage had been completed, individual records from the cohort were classified as definitely linked, possibly linked, or definitely not linked, depending on the total probability weights calculated during the linkage. The small number of possible links was inspected, and a decision was made as to whether or not the link was a valid one. In subsequent analyses, deaths were defined to include those identified in the resolution of the possible links, together with the definite links. All computer linkages were carried out at Statistics Canada under the protection of the Official Statistics Act for confidentiality reasons. When the linkage had been completed, the identifiers were removed and the analysis carried out on the unidentified records at the Epidemiology Unit of the National Cancer Institute of Canada.

2.4 STATISTICAL ANALYSIS

An individual entered the study either on January 1, 1950, if employed before that date, or else at the midpoint of the first year of employment. Subjects excited the study at the end of 1981, or, if they died between 1950 and 1981, at the midpoint of the year in which they died. Person-years at risk were then computed, classified by 15 age groups (0-19, 20-24, ...80-84, ≥ 85) and by six periods of calendar year of observation (1950-54, 1955-59, 1960-64, ...1975-81). The person-years were further classified by cumulative radiation dose to the end of the year prior to the one under consideration, and by time since first recorded exposure. For person-years accumulated prior to any exposure, time since first employment was treated as "time since first exposure". Analyses were also conducted using lagged doses, in which the relevant year of exposure for assigning person-years at risk was defined as 15 years before the year under consideration. The observed number of deaths were classified by age at observation, calendar year of observation, dose, and time since first exposure in the same way as for person-years, and also by 64 individual causes of death (Howe and Lindsay, 1983). The observed number of deaths in any subgroup was then compared to the expected number of deaths calculated from Canadian National Mortality rates between 1950 and 1981, again specific for the 15 age groups and 6 calendar year periods. The ratio of observed to expected deaths, the standardized mortality ratio (SMR), is then the maximum likelihood estimator of the relative risk for the subgroup of the cohort compared to the population (under the assumption of constant relative risk across strata). Tests of significance of the departure of the SMR from 1.0 and confidence intervals were computed by treating the observed number of deaths as a Poisson variable. Where direct comparisons were made between the exposed and non-exposed experiences, maximum likelihood estimates of the relative risk were computed (Howe, 1986), with tests of significance based on the Mantel-Haenszel procedure (Mantel and Haenszel, 1959), and confidence intervals from a modification of Cornfield's method (Howe, 1983). The significance of linear trends was assessed using the Mantel extension (Mantel,

1963) of the Mantel-Haenszel procedures, treating the person-years as a non-stochastic denominator. All p-values quoted are one-tailed, since only associations in the direction of prior hypothesis were considered as possibly significant.

3. RESULTS

Table 1 shows the observed and expected deaths for males from all cancers and all other causes combined for the "non-exposed" and "exposed" experiences. "Non-exposed" refers to years accumulated with no recorded dose, and "exposed" to years accumulated with some recorded dose. It should be noted that in this report the term radiation worker refers to individuals who at some point have some recorded exposure. Thus, the "exposed" experience corresponds closely with the experience of radiation workers, but differs in that years accumulated by radiation workers prior to exposure are allocated to the "non-exposed" experience. This difference is much more marked when doses are lagged. The observed mortality is less than expected both for cancers and all other causes for the non-exposed, and similar deficit is seen for the exposed. For both experiences, the deficit is greater for other causes than for cancer, and this pattern is very consistent with the expected healthy worker effect, and similar to that seen in other Canadian occupational cohort studies (Howe and Lindsay, 1983).

The corresponding data for females are shown in Table 2. Again, the expected healthy worker effect is seen in both exposure experiences, and this seems greater for females than for males. However, the total number of deaths observed for females with some exposure is only 29, of which 14 are cancer deaths. This number precludes any further meaningful analysis of the data for females, and they are considered no further in the present analysis. Subsequent mortality updates, which are planned for the cohort, will provide increased numbers of years at risk for the females, and thus should enable their mortality from individual causes to be further assessed.

Table 3 shows observed and expected numbers of deaths for males for specific cancers, again classified by exposure experience. The cancers included were those in which the observed or expected number of deaths in the exposed experience were at least two, or in which there was particular interest in the cancer because of its previous association with radiation exposure.

None of the cancers show a significantly increased death rate compared to the population rate. Direct comparison of the exposed and non-exposed experiences also yields no significant differences. It should be noted that there is no excess from all leukemias combined, nor with multiple myeloma, but these observations are inevitably based upon very small numbers. For cancer of the prostate, previously reported to show an excess risk for radiation workers (Beral et al., 1985), there are eight observed with 8.43 expected, yielding an SMR of 0.95, 95% confidence interval 0.41 to 1.87.

If low LET radiation acts purely as an initiator in carcinogenesis, radiation received for a number of years prior to the clinical appearance of a tumour would be irrelevant, and for death from that tumour, this period would be even greater. Following Smith and Douglas (1986), we have computed observed and expected deaths using a lag period of 15 years for exposure, and the results are shown in Table 4. Leukemias, which can arise within three years of exposure, are excluded from this analysis. Again, there is no significant excess for any cancers in the exposed experience.

Cancers in which there were at least five observed deaths in the exposed experience in Table 3 are examined in Table 5, with the exposure experience classified as 0, up to 100 mSv, and greater than 100 mSv whole body dose. Relative risks for the two exposed experiences are compared to those of the non-exposed; doses for this analysis were not lagged. For none of the cancers is the dose-response relationship significant, though for pancreas risk it increases with increasing exposure. When doses are lagged by 15 years (Table 6), the risk for pancreatic cancer in the highest dose group is increased (Table 5), but, again, there is no significant dose-relationship for any individual cancer.

4. DISCUSSION

The present study provides evidence that the currently accepted risk estimates for cancer induced by radiation, based on populations exposed at much higher doses, are not largely in error for those exposed at the low doses currently accepted as occupational standards. The exclusion of relatively few members of the original cohort, the quality of the follow-up, and the individual detailed monitoring of radiation doses lends credibility to these conclusions. It must be recognized, however, that the generally small numbers of expected and observed deaths means that the study has little power for detecting small elevations in risk that could occur if the currently accepted estimates are in error by a moderate amount. Nevertheless, they are generally adequate to indicate that these risk estimates are not in error by a large amount.

Previous studies of radiation workers have suggested possible increases in risk for cancers of the prostate, bladder, and for multiple myeloma. The present observations do not support the hypothesis that risk estimates for these cancer sites have been greatly underestimated in the past. Further, in view of the large number of comparisons made in the present as well as previous studies, chance seems a reasonable explanation of these previously observed excesses, in the sense that results indicating such increased risks are not consistent among the studies reported. There may be a similar explanation for the few isolated increases in risk seen in the present data.

It is of considerable importance to monitor cohorts with occupational exposure to low levels of radiation. As discussed above, and as discussed by Reissland et al. (1976), these studies may not contribute to the estimation of the specific risk coefficients for radiation due to cancer, but can provide estimates of a reasonable upper bound on those estimates. They can also provide reassurance both for those exposed to radiation by virtue of occupation, and for the general population exposed through such means as medical radiation.

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TABLE 1

MORTALITY (1950-1981) BY EXPOSURE STATUS FOR MALES

Cause of death	Non-exposed[1] Obs	Non-exposed[1] Exp	Non-exposed[1] SMR[3] (95% CI[4])	Exposed[2] Obs	Exposed[2] Exp	Exposed[2] SMR[3] (95% CI[6])
All cancer	49	58	0.85 (0.63-1.12)	150	166	0.90 (0.77-1.06)
All other	167	230	0.73[5] (0.62-0.84)	515	613	0.84[5] (0.77-0.92)
All	216	288	0.75[5] (0.65-0.86)	665	779	0.85[5] (0.79-0.92)

[1]Non-exposed - no recorded exposure, person-years = 48 935
[2]Exposed - some recorded exposure, person-years = 110 859
[3]SMR - the standardized mortality ratio
[4]CI - the confidence interval
[5]p ≤ 0.0001

TABLE 2

MORTALITY (1950-1981) BY EXPOSURE STATUS FOR FEMALES

Cause of death	Non-exposed[1] Obs	Non-exposed[1] Exp	Non-exposed[1] SMR (95% CI)	Exposed[2] Obs	Exposed[2] Exp	Exposed[2] SMR (95% CI)
All cancer	16	21.5	0.74 (0.42-1.12)	14	23.6	0.59[3] (0.32-1.00)
All other	20	97.0	0.21[4] (0.13-0.32)	15	92.5	0.16[4] (0.09-0.27)
All	36	118.5	0.30[4] (0.21-0.42)	29	116.1	0.25[4] (0.17-0.36)

[1]Non-exposed - no recorded exposure, person-years = 33 452
[2]Exposed - some recorded exposure, person-years = 21 296
[3]p ≤ 0.05
[4]p ≤ 0.0001

TABLE 3

MORTALITY (1950-1981) BY EXPOSURE STATUS FOR MALES

	Non-exposed[1]			Exposed[2]		
Cause of death (cancer)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
Stomach	2	5.31	0.38 (0.05-1.36)	13	14.98	0.87 (0.46-1.48)
Colon	3	5.17	0.58 (0.12-1.69)	13	14.79	0.88 (0.47-1.50)
Rectum	3	2.42	1.24 (0.26-3.62)	10	6.83	1.46 (0.70-2.69)
Liver	1	1.06	0.94 (0.02-5.26)	3	3.05	0.98 (0.20-2.88)
Pancreas	2	3.28	0.61 (0.07-2.20)	10	9.65	1.04 (0.50-1.91)
Lung and trachea	18	16.32	1.10 (0.65-1.74)	50	50.23	1.00 (0.84-1.31)
Prostate	4	3.30	1.21 (0.33-3.10)	8	8.43	0.95 (0.41-1.87)
Bladder	0	1.57	0.00 (0.00-2.35)	1	4.34	0.23 (0.01-1.28)
Brain	3	2.13	1.41 (0.29-4.11)	2	6.06	0.33 (0.04-1.19)
Non-Hodgkins lymphoma	1	1.86	0.54 (0.01-3.00)	8	5.41	1.56 (0.67-3.07)
Myeloma	0	0.72	0.00 (0.00-5.11)	1	2.14	0.47 (0.01-2.60)
Lymphatic leukaemia	1	0.58	1.73 (0.04-9.64)	0	1.56	0.00 (0.00-2.37)
Myeloid leukaemia	1	0.89	1.12 (0.03-6.24)	2	2.33	0.86 (0.10-3.10)
Other leukaemia	1	1.01	0.99 (0.03-5.52)	1	2.60	0.38 (0.01-2.14)

[1]Non-exposed - no recorded exposure, person-years = 48 935
[2]Exposed - some recorded exposure, person-years = 110 859

TABLE 4

MORTALITY (1950-1981) BY CANCER SITE AND EXPOSURE STATUS FOR MALES (DOSES LAGGED BY 15 YEARS)

	Non-exposed[1]			Exposed[2]		
Cause of aeath (cancer)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
Stomach	8	11.29	0.71 (0.31-1.40)	7	9.00	0.78 (0.31-1.60)
Colon	4	10.08	0.40 (0.11-1.02)	12	9.88	1.21 (0.63-2.12)
Rectum	5	4.83	1.04 (0.34-2.42)	8	4.43	1.81 (0.78-3.56)
Liver	3	2.05	1.46 (0.30-4.28)	1	2.06	0.49 (0.01-2.71)
Pancreas	4	6.37	0.63 (0.17-1.61)	8	6.56	1.22 (0.53-2.40)
Lung and trachea	24	30.45	0.79 (0.50-1.17)	44	36.11	1.22 (0.89-1.64)
Prostate	4	5.09	0.79 (0.21-2.01)	8	6.65	1.20 (0.52-2.37)
Bladder	0	2.85	0.00 (0.00-1.30)	1	3.07	0.33 (0.01-1.82)
Brain	5	5.00	1.00 (0.32-2.34)	0	3.20	0.00 (0.00-1.15)
Non-Hodgkins lymphoma	4	3.97	1.01 (0.27-2.58)	5	3.03	1.65 (0.54-3.85)
Myeloma	1	1.38	0.72 (0.02-4.03)	0	1.48	0.00 (0.00-2.49)

[1]Non-exposed - no recorded exposure, person-years = 121 751
[2]Exposed - some recorded exposure, person-years = 38 042

TABLE 5

MORTALITY (1950-1981) FROM CANCER SITE BY WHOLE BODY DOSE FOR MALES

Cause of death (cancer)	Dose (mSv)						
	0		> 0, < 100		> 100		
	RR	(Obs)	RR	(Obs)	RR	(Obs)	p(trend)
Stomach	1.00	(2)	3.24	(13)	0.00	(0)	0.229
Colon	1.00	(3)	1.28	(11)	1.00	(2)	0.393
Rectum	1.00	(3)	0.67	(6)	2.05	(4)	0.166
Pancreas	1.00	(2)	1.53	(8)	2.29	(2)	0.173
Lung and trachea	1.00	(18)	0.75	(40)	0.83	(9)	0.709
Prostate	1.00	(4)	0.63	(7)	0.60	(1)	0.765
Non-Hodgkins lymphoma	1.00	(1)	2.58	(7)	2.13	(1)	0.238
Other cancers	1.00	(3)	1.44	(9)	1.29	(2)	0.236

TABLE 6

MORTALITY (1950-1981) FROM CANCER SITE BY WHOLE BODY DOSE FOR MALES
(DOSES LAGGED FOR 15 YEARS)

Cause of death (cancer)	Dose (mSv)						
	0		> 0, < 100		> 100		
	RR	(Obs)	RR	(Obs)	RR	(Obs)	p(trend)
Stomach	1.00	(8)	3.18	(7)	0.00	(0)	0.158
Colon	1.00	(4)	2.04	(12)	0.00	(0)	0.317
Rectum	1.00	(5)	0.74	(5)	5.26	(3)	0.116
Pancreas	1.00	(4)	2.06	(7)	6.59	(1)	0.090
Lung and trachea	1.00	(24)	1.43	(40)	1.17	(4)	0.151
Prostate	1.00	(4)	1.14	(7)	2.93	(1)	0.336
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