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A summary of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes

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Abstract

Altogether 22 347 men who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes in Australia and the Pacific Ocean between 1952 and 1967 were identified from the archives of the Ministry of Defence and followed up. Their mortality and incidence of cancer were compared with those in 22 326 matched controls selected from the same archives. The risk of mortality in the participants relative to that in the controls was 1·01 for all causes and 0·96 for all neoplasms. Thirty eight causes of death were examined separately. Significant differences in mortality were found for leukaemia, multiple myeloma, and other injury and poisoning, with higher rates in the participants, and for cancers of the prostate and kidney and chronic bronchitis, with higher rates in the controls. The mortality from leukaemia and multiple myeloma in the participants was slightly greater than would have been expected from national values (standardised mortality ratios of 113 and 111, respectively), but in the controls it was substantially lower (standardised mortality ratios of 32 and 0, respectively). Examination of the rates of leukaemia and multiple myeloma in groups of participants showed very little difference between groups characterised by recorded doses of external radiation or type of test participation and failed to indicate any specific hazard. Evidence obtained from participants who reported themselves voluntarily (or were reported by relatives or friends) suggested that 17% of participants may have been omitted from the main study group but that any resulting bias was small.

Most of the differences observed between the participants and controls were interpreted as due to chance, but some may be due to differences in smoking habits. Participation in the test programme did not seem, in itself, to have caused any detectable effect on the participants' expectation of life, apart from possibly causing small risks of developing leukaemia and multiple myeloma.

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Introduction

Between 1952 and 1958 the Ministry of Supply conducted a series of 21 atmospheric nuclear weapon tests in Australia and at islands in the Pacific Ocean. Other experiments in which radioactive materials were dispersed into the environment were also carried out by the Ministry of Supply in South Australia between 1953 and 1963. Survey and clean up operations continued until 1967. Staff from the United Kingdom also participated in American tests based at Christmas Island in 1962 and finally vacated the island in 1964.

The Ministry of Defence has always believed that only a small proportion of the staff from the United Kingdom who participated in these activities were exposed to ionising radiation by virtue of their participation and that those who were exposed received only a small dose. Some participants, however, have expressed concern that their health may have been affected. The Ministry of Defence therefore commissioned the National Radiological Protection Board to study the health of the participants and investigate whether any ill effects correlated with exposure to radiation.[1] This was not easy as a

complete list of participants was not compiled at the time. Many sources had to be consulted and over 100 000 records were examined; the description of the methods used to obtain accurate and unbiased information is necessarily long and is given in a report published by the National Radiological Protection Board.[2] Our paper summarises the investigation and its findings.

Methods

METHOD OF INVESTIGATION

We sought to identify as many as practicable of the servicemen and civilians from the United Kingdom who had taken part in the tests and then determine (*a*) whether they had subsequently suffered a greater incidence of cancer or mortality from cancer or any other cause than would have normally been expected and (*b*) if they had, whether the increase could be attributed to their participation in the tests and related to the recorded level of exposure to ionising radiation. We could not assume that the participants' mortality and incidence of cancer, in the absence of any effect of participation, would be identical to that of other men of the same ages in the population of the United Kingdom, so we therefore selected a control group of about an equal number of men who had not participated in the tests but who otherwise had similar characteristics. Both groups were followed up through their service records, or records of civilian employers, and national registers maintained by the Office of Population Censuses and Surveys and the Department of Health and Social Security (DHSS), including the central register of patients with cancer, which has been maintained since 1971. We were thus able to compare mortality in the participants with the corresponding national values and the mortality from and incidence of cancer in the participants with those in the control group matched for service or employment history.

DEFINITION OF A TEST PARTICIPANT AND SELECTION OF CONTROLS

The tests and associated experimental programme took place at the Monte Bello Islands in Western Australia, at the Emu Field and Maralinga Range in South Australia, and at the Malden and Christmas Islands in the Pacific Ocean. Visits to these five locations in connection with the testing programme were spread over 15 years. All servicemen from the United Kingdom and all male employees of the Atomic Weapons Research Establishment, Aldermaston, and the Atomic Energy Research Establishment, Harwell, and their preceding organisations, who could be discovered from Ministry of Defence records to have visited any of these locations during this time were included as test participants. Others included were staff from the United Kingdom who worked at RAAF Pearce in Western Australia and RAAF Edinburgh Field in South Australia, where the work included cloud sampling and dealing with contaminated aircraft. Men were not included if they had participated only in peripheral activities associated with the test programme at other locations. With this definition 22 347 men were identified, who constituted the participants in our study. Thirty per cent were in the Royal Navy (including the Royal Marines, the Royal Naval Volunteer Reserve, and the Navy, Army, and Air Force Institute); 28% in the Army; 39% in the Royal Air Force; and 4% employees of the Atomic Weapons Research Establishment, the Atomic Energy Research Establishment, or their forerunners (subsequently referred to as the Atomic Weapons Research Establishment).

The control subjects for the participants in the armed services were chosen from servicemen who did not participate in the weapon test programme but who had served in tropical or subtropical areas while the tests were being carried out. For employees of the Atomic Weapons Research Establishment control subjects were selected from employees who had not visited a test location or attended tests in the United States. Controls were matched with participants for age, type of armed service, rank (officers and other ranks; socioeconomic class for civilians), and date of entry to the study.

FOLLOW UP

We tried to follow up all who were accepted as participants or controls to 1 January 1984. We submitted details to the National Health Service (NHS) central registers at Southport and Edinburgh,[3] where a search was made to see if the subject had emigrated, died, or developed cancer. For those who had died, both the underlying and the contributory causes of death were coded according to the ninth revision of the International Classification of Diseases[4] by staff at the Office of Population Censuses and Surveys.

For servicemen who could not be traced on the NHS central registers help was sought from the DHSS records branch at Newcastle and the health departments in Belfast, the Isle of Man, and Jersey. For civilians the mechanism of follow up was similar to that for servicemen except for ex-employees of the Atomic Weapons Research Establishment who had left the establishment before 1 January 1983 because they had recently been followed up by the Medical Research Council's Epidemiological Monitoring Unit and the unit kindly allowed us to use their data. Eight per cent of participants and 6% of controls were found to have emigrated; 92% of participants and 93% of controls were found to have died or to be alive and resident in the United Kingdom, whereas less than 0·5% of each group were lost to follow up after discharge from full time service or leaving employment at the Atomic Weapons Research Establishment.

INCIDENCE OF CANCER

Fewer than half the number of cases of cancer that occur in the United Kingdom prove to be fatal and only a small proportion of the rest are referred to on death certificates as having contributed to death in an ancillary way. For some analyses we have therefore augmented the data on deaths attributed to cancer by adding (*a*) cases discovered from the reference to cancer as a contributory cause of death on the death certificate and (*b*) cases of cancer recorded in the NHS central registers.

VALIDATION

Checks were carried out to establish the accuracy of the data for each man, investigate whether any participants listed on the documents used by the Ministry of Defence to compile the study population had been omitted, and determine the completeness of coverage of the study. These are described in the National Radiological Protection Board's report.[2] The results were satisfactory, except for showing that some participants in the army and the Royal Air Force had been missed.

Failure to obtain information about all eligible men could have had a serious impact on the validity of the results if there had been a differential failure to discover men who had developed cancer. We therefore sought additional information about test participants from other sources and examined a sample of the claims for disabilities that had been received by the DHSS.

Firstly, the National Radiological Protection Board requested information from all organisations known to have compiled lists of participants independently from material in the Ministry of Defence's archives. In most cases the lists were made up of men who had contacted the organisation concerned or whose relatives had done so. They thus form a selected group and their morbidity is unlikely to be representative of participants as a whole. They can, however, be used to test the completeness and representativeness of the participants identified for the main study.

All such men (referred to subsequently as independent respondents) who were notified to the National Radiological Protection Board before 1 April 1986 were reviewed. Any who were obviously ineligible by the study's criteria or for whom there was sparse information were excluded. A total of 2161 well identified men remained, who, it seemed, should have been included. On checking against the main study list, we found that only 1707 were on it. The names of the other 454 men were forwarded to the Ministry of Defence with a request for full details of any postings that might have entailed participation in nuclear tests. Information thus obtained confirmed that 397 of the remaining 454 (87%) had been participants and left open the possibility that 17 others (4%) might have been. For 33 men (7%), over half of whom were in the Royal Navy, there was no indication that they had visited a test location during the relevant time or been posted to a ship or unit that was known to have participated in the tests; for 26 of these men the initial notification had come from a third party, such as a relative or friend. This contrasted with one third of the 397 men whose participation had been confirmed, and it seems unlikely that the 33 men (some of whom may have visited a different Christmas Island) were participants. For the remaining seven men (1·5%), no service records could be found.

The list of independent respondents whose participation was possible or confirmed enabled us to estimate the percentage of all eligible participants included in the study; table Im shows the results. All eligible independent respondents who were employees of the Atomic Weapons Research Establishment were included and almost all who had served in the Royal Navy. For the Army and the Royal Air Force, however, the proportions were 84% and 69%, respectively. After standardising service or employment category to the proportions observed in the main study this leads to the conclusion that about 83% of all eligible test participants had been included.

In its second check the National Radiological Protection Board sought the help of the archives of the DHSS, where records were held of all servicemen who had claimed a disability pension or for whom a claim had been made by a dependent. A one in 1000 sample of claims made since 1953 was selected from the ledgers and inquiries were made to see if the man's record was held in the relevant service records office. Eighty seven per cent of the records were complete and in their correct place (248 out of 285). The others, all relating to the Army, were either missing from the office (20) or incomplete and lacking details of postings (17). All the missing and incomplete records related to men for whom claims (or appeals) had been made before 1976. Before then it had been the practice to allow Army records to be sent to the DHSS without keeping a note of their removal or seeking their return. This is contrary to current practice and we had not appreciated it when the study was designed.

The evidence provided by these checks shows that the lists of participants used in our study are probably complete (or nearly complete) for the Royal Navy and employees of the Atomic Weapons Research Establishment but that an appreciable number of men who served in the Army and the Royal Air Force were probably missed. It shows, moreover, that the omission of some participants from the army may have biased the results by the differential exclusion of a small number for whom claims had been lodged.

METHOD OF ANALYSIS

Participants were entered into the study on the date that they first participated in a test. Controls were entered on the earliest date such that if they had died on that date they would still have been selected by the criteria used. For analyses of mortality subjects were removed from the study on their date of death or

emigration or 31 December 1983, whichever came earliest. For analyses of incidences of cancer the date of death was used for men for whom cancer was mentioned on the death certificate and for the others the date of cancer registration. Individuals were also removed from the study on reaching the age of 85. Standardised mortality ratios were calculated using national mortality statistics in five year age groups for each calendar year. Two sided tests were used for calculating the significance of standardised mortality ratios.

To compare the mortality of test participants with those of controls deaths and person years were stratified by age and calendar year into five yearly groups by service or employer (Royal Navy, Army, Royal Air Force, or Atomic Weapons Research Establishment) and by rank into officers (or social class I) and others. The relative risk was estimated by the method of maximum likelihood. We were specifically interested in testing the hypothesis that mortality and incidence of cancer were greater among test participants than among controls, and so one sided tests (in the direction of the observed difference) were used to calculate significance of the relative risks. In analyses of recorded dose of gamma rays the numbers expected in each dose category were calculated from the experience of all men for whom data on dosage were available, assuming that within any stratum the incidence of cancer was independent of dose. One sided tests for trend were then carried out using the score test.[5]

Results

COMPARISON OF MORTALITY IN TEST PARTICIPANTS AND CONTROLS

Table II shows the total mortality in the two groups and that from each of three broad groups of causes. Predictably, the mortality in both groups was less than average, partly because of the high proportion of scientists in the Atomic Weapons Research Establishment and officers in the armed services, whose mortality would be expected to be low because of their social class, and partly because servicemen who served in the tropics were selected for physical fitness.[6] We have not therefore given the significance of all the standardised mortality ratios but have cited it when it is of special interest. Mortality from all neoplasms and from all other diseases was substantially lower in both groups than in men of the same ages in England and Wales, but mortality from accidents and violence was considerably higher. Little difference was observed between participants and controls ($p>0{\cdot}1$ in all cases) and, in so far as there was any difference, the mortality from neoplasms was lower in the participants.

When the Army was excluded the mortality in participants relative to controls was slightly increased, but the mortality from cancer remained lower in the participants. Clearly, therefore, any bias introduced into the results from the retention of some Army records by the DHSS may have resulted in a slight underestimation of the participants' relative risk but it did not cause their mortality from cancer to be lower than that in the controls.

For some types of cancer mortality in participants was greater than in controls, although for others it was less (table III). The relative risk in participants was significantly greater than unity only for leukaemia and multiple myeloma ($p=0{\cdot}004$ and $0{\cdot}009$, respectively). For both diseases the numbers of deaths among participants were slightly greater than expected from national values, although the differences were not significant (leukaemia, standardised mortality ratio=113, $p=0{\cdot}57$; multiple myeloma, standardised mortality ratio=111, $p=0{\cdot}83$). Among controls the numbers of deaths were substantially less than expected (leukaemia, standardised mortality ratio=32, $p<0{\cdot}001$; multiple myeloma, standardised mortality ratio=0, $p=0{\cdot}006$). For cancer of the bladder the mortality in participants was estimated to be 2·79 times greater than in the controls, but the difference did not reach significance ($p=0{\cdot}06$). In contrast, the relative risk in test participants was significantly less than unity for cancers of the prostate and kidney ($p=0{\cdot}01$ and $0{\cdot}007$, respectively); it was also less than unity for cancer of the lung but the deficit did not reach significance ($p=0{\cdot}07$). For the remaining types of cancer there was little evidence that the mortality differed importantly ($p>0{\cdot}1$ for all types) and practically no difference in the value for all cancers other than leukaemia.

The four disease categories of Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, and leukaemia, which are shown separately in table III, together constitute the broad group of cancers of lymphatic and haematopoietic tissue. Altogether there were 51 such deaths in the participants and 28 in controls and the relative risk was estimated to be 1·65, which is significantly increased ($p=0{\cdot}02$; 90% confidence interval 1·08 to 2·51). The difference was not, however, due to a high mortality in the test participants, in whom the number of deaths was equal to that expected from national values (standardised mortality ratio=100), but to a low mortality in the controls, in whom the number was only just over half that expected (standardised mortality ratio=56, $p<0{\cdot}001$). When the analysis in table III was repeated excluding the army the results were similar.

The analysis shown in table III was also repeated limiting the period of follow up to that when any cancers attributable to ionising radiation were most likely to have occurred. For leukaemia this was assumed to have been from two to 25 years after first exposure[7 8] and for other cancers all times after the first 10 years. The results were hardly changed.

Not all types of leukaemia are equally readily induced by ionising radiation. We have therefore examined separately the deaths attributed to the four main types. For acute myeloid, chronic myeloid, and acute lymphatic leukaemias the numbers of deaths observed in the participants exceeded those expected from national values, and in comparison with the controls the relative risk among participants was greater than unity (relative risks 2·34, ∞, and 2·11, respectively). For chronic lymphatic leukaemia, which has not been shown to be increased in any irradiated population, there were two deaths; both occurred among participants and this was about the number expected from national values.

When the distribution of deaths from leukaemia was examined by type and time since each man's participation in his first test the number of deaths from acute myeloid leukaemia and all types combined exceeded that expected from national values in every five year time period apart from the first. Otherwise there were no clear trends with time.

Review of the evidence on which the leukaemia diagnoses were based had no material effect on these results.

Table IVm shows the results for specific causes of death other than neoplasms. For most the mortality was lower in both groups than in men of the same ages in England and Wales, but mortality from air and space transport accidents and from drowning and water transport accidents was raised. When the mortality of test participants was compared with that of controls the relative risk was in some cases less than unity and in some cases greater. Only for the category other injury and poisoning was the relative risk significantly greater than unity (relative risk=1·34; $p=0{\cdot}04$). Within this category no particular cause was outstanding. Only for chronic bronchitis was the relative risk significantly less than unity, the mortality among participants being less than 60% of that in controls (relative risk 0·55; $p=0{\cdot}02$). For no other non-violent cause of death did either the increase or decrease in relative risk reach significance ($p>0{\cdot}01$).

INCIDENCE OF CANCER IN TEST PARTICIPANTS AND CONTROLS

The relative risk of the incidence of cancer in participants and controls was estimated for the same 23 types of cancer. The patterns were similar to those for mortality. For both leukaemia and multiple myeloma the increased relative risks persisted. Twenty eight developed leukaemia compared with 11 controls, and the incidence in participants was 2·43 times greater than in

MINIPRINT TABLES I, IV, VI, AND VII

Im

TABLE Im—*Numbers (percentages) of independent respondents included and not included in main study by armed service or employer*

Service or employer	Independent respondents: Not included in main study	Independent respondents: Included in main study	Total
Royal Navy	13 (3)	484 (97)	497
Army	91 (16)	479 (84)	570
Royal Air Force	310 (31)	694 (69)	1004
Atomic Weapons Research Establishment	0 (0)	50 (100)	50
Crude total	414 (19)	1707 (81)	2121
Total standardised to service or employer distribution of main study	17%	83%	

VIIm

TABLE VIIm—*Relative risks of mortality and incidence of cancer with 90% confidence intervals in test participants compared with controls after adjustment for men not included in main study*

Cause of death	Relative risk of mortality (90% confidence interval)	Relative risk of incidence of cancer (90% confidence interval)
Neoplasms	0·99 (0·87 to 1·13)	0·99 (0·89 to 1·10)
Other known non-violent causes	1·07 (0·93 to 1·22)	—
Accidents and violence	0·89 (0·77 to 1·17)	—
All causes	1·05 (0·97 to 1·13)	—

IVm

TABLE IVm—*Observed deaths and standardised mortality ratios for specific causes other than neoplasms among test participants and controls with relative risks and 90% confidence intervals of mortality in test participants compared with controls*

Cause of death	Test participants: Observed deaths	Test participants: Standardised mortality ratio	Controls: Observed deaths	Controls: Standardised mortality ratio	Mortality in test participants relative to controls (relative risk (90% confidence interval))
Diseases related to smoking					
Coronary heart disease	460	74	505	78	0·94 (0·84 to 1·05)
Bronchitis, emphysema, and chronic obstructive lung disease	20	30	47	51	0·55 (0·34 to 0·91)*
Aortic aneurysm	16	104	15	92	1·20 (0·62 to 2·32)
Diseases related to alcohol					
Cirrhosis of liver, alcoholism, and alcoholic psychosis	20	108	20	107	1·05 (0·60 to 1·85)
Other diseases					
Infectious and parasitic diseases	15	71	15	70	1·01 (0·52 to 1·96)
Diseases of nervous system	13	39	14	42	1·03 (0·50 to 2·08)
Other diseases of circulatory system	166	71	153	63	1·13 (0·93 to 1·37)
Other diseases of respiratory system	51	61	42	48	1·31 (0·91 to 1·90)
Other diseases of digestive system	33	81	24	58	1·39 (0·86 to 2·25)
Remaining diseases other than neoplasms	34	44	29	38	1·20 (0·76 to 1·90)
Accidents and violence					
Motor vehicle traffic accidents	92	101	82	100	0·97 (0·74 to 1·27)
Drowning and water transport accidents	17	122	19	147	0·77 (0·40 to 1·47)
Air and space transport accidents	42	1285	54	1796	0·89 (0·61 to 1·28)
Suicide	69	101	62	95	1·12 (0·83 to 1·52)
Other injury and poisoning	101	122	74	94	1·34 (1·02 to 1·76)*
All known causes other than neoplasms	1149	78	1145	76	1·02 (0·95 to 1·09)

*p≤0·05 (one sided test)

VIm

TABLE VIm—*Observed deaths and standardised mortality ratios among independent respondents included and not included in main study with relative risks and 90% confidence intervals*

Cause of death	Not included in main study (n=407): Observed deaths	Not included in main study (n=407): Standardised mortality ratio	Included in main study (n=1707): Observed deaths	Included in main study (n=1707): Standardised mortality ratio	Mortality in those not included relative to those included (relative risk (90% confidence intervals))
Neoplasms	97	502	134	348	1·18 (0·82 to 1·67)
Lymphatic and haematopoietic tissue	7	830	27	683	1·08 (0·46 to 2·45)
Leukaemia	3	932	15	998	1·09 (0·27 to 3·89)
Multiple myeloma	0	0	3	735	0·00 (0·00 to 6·74)
Other	4	897	9	441	1·40 (0·41 to 4·55)
Other neoplasms	90	460	107	310	1·20 (0·81 to 1·79)
Other known non-violent causes	21	120	68	74	1·38 (0·85 to 2·23)
Accidents and violence	0	0	10	49	0·00 (0·00 to 9·07)
Unknown	1	—	6	—	—
All causes	59	199	218	145	1·22 (0·92 to 1·60)

controls (p=0·009; 90% confidence interval 1·27 to 4·70). Four further participants developed multiple myeloma, making 10 cases in the participant group compared with none in the control group (p=0·0007; 90% confidence interval 2·75 to ∝).

Similar results were again obtained when the analyses of incidence of cancer were repeated, first excluding test participants in the Army and then considering only the period when any cancers attributable to ionising radiations were most likely to have occurred.

The second (group B), totalling 15211 men, was selected by the investigators because they were thought to have been present for a major test or present for and directly concerned with the programme of minor trials at Maralinga. The third (group B[1]) consisted of 10172 men in group B who were thought to have attended a test on or near Christmas Island. The fourth (group C), totalling 1503 men, was selected because there was no reason to suspect that they could have been exposed to more radiation than the general public.

TABLE II—*Observed deaths and standardised mortality ratios among test participants and controls by broad cause of death with relative risks and 90% confidence intervals of mortality in test participants compared with controls*

Cause of death	Test participants		Controls		Mortality in test participants relative to controls (relative risk (90% confidence interval))
	Observed deaths	Standardised mortality ratio	Observed deaths	Standardised mortality ratio	
Neoplasms	406	80	434	83	0·96 (0·86 to 1·08)
Other known non-violent causes	828	68	854	68	1·00 (0·92 to 1·09)
Accidents and violence	321	124	291	121	1·07 (0·93 to 1·23)
Unknown*	36	—	28	—	—
All causes	1591	80	1607	79	1·01 (0·95 to 1·07)

* One death in a test participant was fully investigated and diagnosed only as natural causes; 63 causes of death were not discovered and 27 of these deaths were known to have occurred abroad.

TABLE III—*Observed deaths and standardised mortality ratios among test participants and controls for 23 specific types of cancer with relative risks and 90% confidence intervals of mortality in test participants compared with controls*

Type of cancer	Test participants		Controls		Mortality in test participants relative to controls (relative risk (90% confidence interval))
	Observed deaths	Standardised mortality ratio	Observed deaths	Standardised mortality ratio	
Tongue, mouth, pharynx	8	106	9	117	0·87 (0·35 to 2·18)
Oesophagus	23	156	18	118	1·37 (0·78 to 2·41)
Stomach	26	58	34	72	0·78 (0·49 to 1·23)
Large intestine and rectum	49	94	46	85	1·12 (0·78 to 1·61)
Liver and gall bladder	12	164	6	80	1·90 (0·76 to 4·95)
Pancreas	20	93	23	103	0·87 (0·50 to 1·50)
Larynx	3	67	8	172	0·40 (0·10 to 1·37)
Trachea, bronchus, lung, and pleura	119	65	156	81	0·82 (0·67 to 1·02)
Bone	2	63	1	33	1·34 (0·09 to 31·38)
Skin:					
Malignant melanoma	7	105	6	91	1·25 (0·44 to 3·59)
Other	0	0	0	0	—
Prostate	8	76	22	188	0·38 (0·17 to 0·80)**
Testis	9	112	9	122	1·01 (0·41 to 2·46)
Bladder	10	76	4	28	2·79 (0·94 to 8·94)
Kidney	6	54	20	176	0·30 (0·12 to 0·71)**
Tumours of central nervous system	30	98	22	73	1·33 (0·81 to 2·21)
Thyroid	1	92	1	90	1·01 (0·04 to 27·70)
Hodgkin's disease	7	58	8	70	0·81 (0·31 to 2·15)
Non-Hodgkin's lymphoma	16	114	14	101	0·90 (0·45 to 1·81)
Multiple myeloma	6	111	0	0	∝ (1·67 to ∝)**
Leukaemia	22	113	6	32	3·45 (1·50 to 8·37)**
Other:					
Specified	6	38	9	56	0·65 (0·24 to 1·72)
Unspecified	16	80	12	58	1·47 (0·73 to 2·96)
All neoplasms	406	80	434	83	0·96 (0·86 to 1·08)

*p≤0·05, **p≤0·01 (one sided test).

MORTALITY AND INCIDENCE OF CANCER WITHIN TEST PARTICIPANTS BY TYPE AND DEGREE OF EXPOSURE

Dosages of γ rays were available for 4453 men. The incidences of multiple myeloma and of all neoplasms combined tended to increase with increasing recorded dose, but for leukaemia the incidence tended to decrease. None of the trends, however, approached significance (p>0·25 in each instance).

Before the results were available four overlapping groups of test participants had been selected for special examination. The first group (group A), totalling 2314 men, was selected by the Ministry of Defence as consisting of men in whom any effect of exposure to radiation would, if present, be expected to be concentrated—namely, men thought liable to have been exposed to radiation as a consequence of their participation in tests, all participants employed by the Atomic Weapons Research Establishment, and all those known to be directly concerned with the programme of minor trials at Maralinga. According to the Ministry of Defence, any undocumented inhalation or ingestion of radionuclides was most likely to have occurred in the employees of the Atomic Weapons Research Establishment and those participating in the tests at Maralinga.

Table V shows the mortality from all neoplasms, leukaemia, and multiple myeloma observed in these four groups and in the 5633 men not included in groups B or C (group D). The relative risks for all neoplasms varied from 0·85 to 1·10 and only one difference was significant (p<0·05)—namely, the deficit of all neoplasms in group B[1]. The relative risks for leukaemia varied from 2·42 to 6·55 and for multiple myeloma they were all ∝ apart from those in group C, in which there was no case of death from this disease. The highest (or equal highest) relative risks were all in group D (other participants). In this group the significances of the results were most noticeable and the standardised mortality ratios the highest (leukaemia 181, p=0·15; multiple myeloma 250, p=0·12). The increases of both leukaemia and multiple myeloma were therefore concentrated in the group that was not selected by the Ministry of Defence or the investigators for special examination.

To see if there was any feature related to the participation of men in this group which distinguished those who developed leukaemia or multiple myeloma from those who did not the medical records were re-examined and the information compared with that of other participants in group D. For this purpose, one surviving man with leukaemia was added and one man who died of chronic lymphatic leukaemia was omitted. Six men in group D who

TABLE V—*Observed deaths, standardised mortality ratios, and relative risks compared with total control group for different groups of test participants. Groups B, C, and D are mutually exclusive*

Group	All neoplasms			Leukaemia			Multiple myeloma		
	Observed deaths	Standardised mortality ratio	Relative risk	Observed deaths	Standardised mortality ratio	Relative risk	Observed deaths	Standardised mortality ratio	Relative risk
A Men identified by Ministry of Defence as liable to be exposed to radiation, those employed by Atomic Weapons Research Establishment, and those directly concerned with minor tests at Maralinga (n=2314)	58	64	0·90	2	75	3·67	1	102	∝
B Men present at a major test or directly concerned with minor trials at Maralinga (n=15 211)	277	76	0·91	13	95	2·54*	3	78	∝
B[1] Men present at Christmas or Malden Island during major test (n=10 172)	158	71	0·85*	11	123	3·35*	2	86	∝
C Men unlikely to have been exposed to more radiation than the general public (n=1503)	28	90	1·09	1	78	2·42	0	0	—
D Men not in groups B or C (n=5633)	101	88	1·10	8	181	6·55***	3	250	∝**
All participants (n=22 347)	406	80	0·96	22	113	3·45**	6	111	∝**

*p≤0·05, **p≤0·01, ***p≤0·001 (one sided test).

were born in the same year as each affected man were randomly selected to serve as controls. The results failed to suggest any feature that distinguished the affected men from the controls.

MORTALITY AND INCIDENCE OF CANCER IN INDEPENDENT RESPONDENTS

To test whether there was any evidence that failure to achieve complete coverage of the study population had biased the findings we made inquiries about the state of all 414 independent respondents who were not included in the main study and for whom test participation was confirmed or inconclusive. Altogether 407 (98%) were successfully followed up. Table VIm shows the results in comparison with those obtained for the 1707 independent respondents who had been included in the study. In both categories the deaths from cancer were more than three times that expected from national mortality values and the increases were highly significant ($p<0·001$). Comparison of the mortality from neoplasms and from other non-violent causes of death showed that it was higher in the participants who were not included in the main study than in those who had been included (relative risk 1·18 and 1·38, respectively) but that the mortality from accidents was lower. For leukaemia and for all cancers of lymphatic and haematopoietic tissues the relative risks (1·09 and 1·08) were similar to those for all cancers, although for multiple myeloma the relative risk was lower (0·00). None of the risks observed for any of the nine causes listed in Table VIm was significantly greater or less than unity ($p>0·10$ in all cases).

Two other incident cases of leukaemia were also recorded in the 414 independent respondents who had not been included in the main study and two in the 1707 who had been. When these were also taken into account the relative risk of leukaemia in the independent respondents who were not included in the study increased to 1·83 ($p=0·23$). No other incident cases of multiple myeloma were recorded. When incident cancers were taken into account the relative risk for all neoplasms was 1·26 ($p=0·09$).

Discussion

GENERAL CONSIDERATIONS

On first inspection our results suggest that participation in nuclear tests was associated with an increased mortality from leukaemia, multiple myeloma, and other injury and poisoning and a decreased mortality from cancers of the prostate and kidney and chronic bronchitis; but not with any detectable effect on expectation of life or on the total risk of developing cancer. Interpretation of these results is not, however, easy.

One problem is the possibility of the introduction of bias. In this respect, the omission of some participants from the army was particularly worrying as past practices had allowed the records to be out of place for some of those for whom disability pensions had been sought. Exclusion of the army, however, had practically no effect on the results, and this feature did not seem to have biased the comparisons between participants and controls.

Another test of the effect of failing to include all participants is provided by the information obtained about participants from other sources. Most of this referred to men who were already in the study, but some did not. We could, therefore, test for bias in the construction of the lists by comparing mortality from specific diseases and incidence of cancer in those omitted and those included. Mortality from non-malignant disease and mortality from and incidence of cancer were all higher in the participants who had been omitted than in those who had been included, but the differences were not significant. An estimate of the extent of any bias that there may have been can be obtained from the observations on these two groups of independent respondents. For accidents and violence the estimated relative risk was lowered after adjustment for men not included in the main study, but for all causes of death, cancers, and other non-violent causes of death it was increased (table VIIm). The increases were not great and none made the difference between the participants and the controls significant.

A second problem is the low mortality observed in comparison with the corresponding national values. One reason was the high proportion of officers, in whom nearly a quarter of the deaths (24·1%) occurred; another was that all ranks who served in the tropics or subtropics had been selected for physical fitness. These reasons must have had a substantial effect on the mortality from neoplasms and from all non-violent causes of death in the early years and it is notable that the standardised mortality ratio for neoplasms in the combined group of participants and controls increased from 65 in the first five years after the start of observation to 86 after more than 15 years. Other minor reasons (such as the misclassification of men who had emigrated as being alive) might have resulted in underestimating all the standardised mortality ratios by about 3%.

A third problem is that when so many different causes of disease are examined some differences must be expected to occur by chance which are significant according to normal scientific standards. We examined 38 separate causes of death and five broad categories in which the individual causes were subsumed. It follows that if there were no real differences we might still expect to find by chance about four differences that would be so extreme that they would be significant, with about two increases in the participants and about two in the controls. In fact we found three examples of each: increased mortality from leukaemia ($p=0·004$), multiple myeloma ($p=0·009$), and other injury and poisoning ($p=0·04$) in the participants and increased mortality from cancer of the kidney ($p=0·007$), cancer of the prostate ($p=0·01$), and chronic bronchitis ($p=0·02$) in the controls. None of these was so extreme that no such difference would be expected to occur by chance once in 20 times when 38 different causes were examined (which would require a probability of 0·001 or less); on purely numerical grounds, it would be reasonable to categorise them all as due to random variation. The position is different, however, if there were a previous reason for looking for a specific increase in the group in which it occurred. For two of the increases—namely, those of leukaemia and multiple myeloma in the participants—there was such a reason: leukaemia is the type of cancer that has been most consistently increased

among populations known to have been exposed to high doses of radiation[9,10] and it was also increased among participants in the United States' shot codenamed SMOKY.[11] Similarly, multiple myeloma is the one type of cancer for which a dose related association has been shown in two large groups of radiation workers[12,13] in addition to having a higher incidence in many groups exposed to high doses of radiation.[14] These increases cannot therefore be lightly dismissed as chance findings.

CANCERS OF LYMPHATIC AND HAEMATOPOIETIC TISSUE

The differences between participants and controls in their mortality from leukaemia and multiple myeloma would have been easy to interpret if the mortality in the controls had been close to that expected from national experience and mortality in the participants had been substantially raised. This, however, was not so: mortality in the controls was unusually low (standardised mortality ratios 32 and 0) and the mortality in the participants was raised only slightly (standardised mortality ratios 113 and 111). No social, behavioural, or environmental factor is known that would lead to a low mortality from these diseases,[15,16] nor do any of the general considerations referred to earlier suggest that they could have been produced artificially. It is therefore difficult not to believe that, despite the previous reason for looking for an increase in mortality among the participants, some of the differences between the values was due to the chance occurrence of very low mortality in the controls.

There are, however, reasons for thinking that the increase in mortality in the participants was partly due to their participation in the programme. Firstly, the leukaemias from which the participants died were mostly of the types known to be produced characteristically by exposure to ionising radiation. For these types of leukaemia combined (including the contribution from unspecified types) the standardised mortality ratio was 115 and the relative risk for incident cases compared with controls 2·64, while the standardised mortality ratio for chronic lymphatic leukaemia, which does not appear to be induced by ionising radiations, was 102 and the relative risk for incident cases 1·84. Secondly, the omission of some participants from the main study may have led to an underestimation of the standardised mortality ratio and the real mortality in comparison with national values may have been somewhat higher.

More detailed examination of the distribution of cases with time and place fails to provide any clear evidence of a relation with radiation. The spread of the leukaemias with time gave no hint of the early peak that might have been expected from studies of populations exposed to external radiation for a brief period.[7,8] Nor was there any evidence of an accumulation of cases in groups which, it had been thought, were most likely to have been exposed to a radiation hazard if any existed.

An association between participation in the nuclear weapons test programme and the development of leukaemia and multiple myeloma, does not, of course, necessarily imply causation. The controls were, however, matched with the participants on so many features that we cannot think of any environmental or behavioural difference that might have influenced the development of these diseases. We conclude therefore that if a real association exists it is likely to reflect causality rather than confounding.

OTHER CANCERS

All cancers classed together caused a slighty lower mortality in the participants than in the controls irrespective of whether the army was included and the whole period of follow up examined or only the 10 or more years after entry. The inclusion of non-fatal cases, moreover, left the result essentially unchanged. It follows that the mortality from (and incidence of) cancers other than leukaemia and multiple myeloma would have been relatively even less in the participants as these two types of cancer were substantially increased. Even allowing for a slight underestimation of the mortality in participants owing to the omission of some participants from the main study, the results do not suggest that participation in the programme had caused any material increase in the risk of cancer in general. Nor does detailed examination of individual types of cancer suggest that there was a hazard of any type other than that of developing leukaemia and multiple myeloma.

For cancers of the kidney and prostate mortality was significantly different but in each case the mortality was higher in the controls and the differences can be attributed to chance. The data for cancer of the prostate were particularly notable as this cancer was the only type other than leukaemia for which an increase had been observed in the participants in any of the American series of tests,[11] and it was also higher in men employed by the United Kingdom Atomic Energy Authority.[17]

OTHER DISEASES

We observed little difference between the mortality in the participants and that in the controls for most of the other causes of death that were examined and for all other causes combined. The two differences that were significant (reduced deaths from chronic bronchitis in the participants and increased deaths from other injury and poisoning) could be attributed to chance. An alternative explanation of the decreased deaths from chronic bronchitis in the participants and its possible implications are considered below.

No information was obtained about the incidence of cataracts because they do not give rise to a recognisable increase in mortality. This, as far as we are aware, is the only somatic disease that has a very low fatality that is liable to be caused by exposure of adults to moderate doses of radiation.[10]

EFFECT OF POSSIBLE DIFFERENCES IN SMOKING HABITS

The lower mortality in the participants than in the controls from both chronic bronchitis and lung cancer suggested that the participants may have smoked less, perhaps as a result of a greater response to health education. That this may be so was supported by the fact that the mortality from other cancers related to smoking—that is, cancers of the tongue, mouth, pharynx, oesophagus, larynx, pancreas, bladder, and kidney—and that from the other principal non-malignant diseases related to smoking (coronary thrombosis and aortic aneurysm) were both also lower in the participants. The effects on health of participation in nuclear tests may therefore be better judged by examining the mortality from diseases less closely related to smoking. Such mortality was higher in the participants than in the controls (relative risk=1·16; p=0·03), but the mortality from the similar group of neoplasms other than leukaemia and multiple myeloma, which should provide a more sensitive indicator of any effects of radiation, were almost identical (relative risk=1·01).

CONCLUSION

We conclude that participation in the nuclear weapons test programme did not have a detectable effect on the participants' expectation of life or on their total risk of developing cancer, apart from a possible effect on the risks of developing multiple myeloma and leukaemia (other than chronic lymphatic leukaemia).

The evidence relating to multiple myeloma and leukaemia (other than chronic lymphatic leukaemia) was confusing, and on balance we conclude that there may well have been small hazards of both diseases associated with participation in the programme but that this has not been proved. The only carcinogenic agent that has been shown to cause an increased incidence of both diseases is ionising radiation, but we have no evidence that the participants who developed these diseases were exposed to unusual amounts.

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SHORT REPORTS

Microproteinuria: response to operation

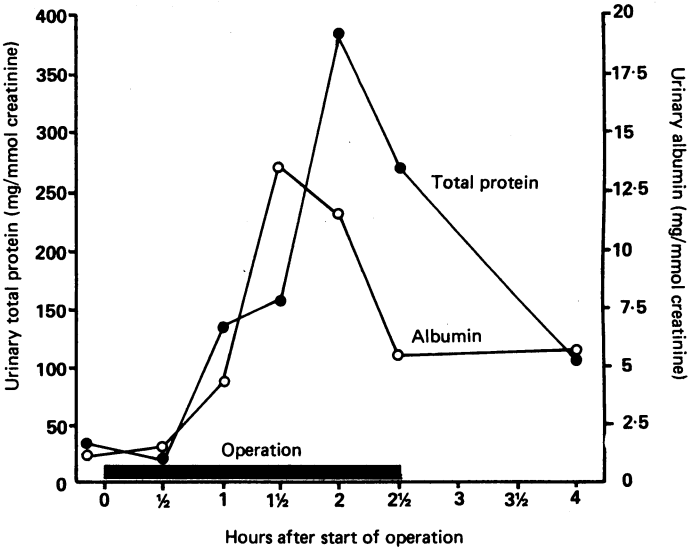
Microalbuminuria is accepted as a sensitive indicator of diabetic nephropathy. In diabetes proteinuria is associated with a greater incidence of arterial disease and higher mortality,[1] and microalbuminuria with a general increase in vascular permeability.[2] A transient increase in urinary excretion of protein and albumin occurs within four hours after burns and trauma.[3] It is proportional to the severity of injury, recurs with complications such as sepsis, and may reflect a general increase in vascular permeability as part of the acute phase response.[3,4] Vascular permeability increases within three hours of the start of operations[5] and might therefore be accompanied by an increase in urinary protein excretion. To establish whether this was so we measured protein excretion in patients before and after various operations.

Patients, methods, and results

We studied 33 patients, of whom 21 had indwelling bladder catheters. Eleven patients were having intraperitoneal operations (elective repair of an aortic aneurysm (five), resections of the large bowel (five) and cholecystectomy (one)); 13 were having extraperitoneal operations (femorodistal arterial reconstruction (11) and repair of an inguinal hernia (two)); and nine were having high ligation of the saphenous vein under local anaesthesia. Urine was obtained within the two hours before and three hours after the operation in all patients. Urinary total protein and albumin excretion was measured as described previously[4] and expressed as mg/mmol creatinine to correct for changes in dilution.

After operation the urinary total protein concentration increased in all 33 patients and urinary albumin concentration increased in 29 patients (four patients undergoing ligation of the saphenous vein did not show an increase). The geometric mean urinary total protein concentration increased 4·37-fold (95% confidence interval 2·28 to 8·34; geometric mean 6·5 (range 0·9-55·7) mg/mmol creatinine before operation and 28·6 (2·5-462) mg/mmol after). The geometric mean urinary albumin increased 3·10-fold (95% confidence interval 1·69 to 5·66; geometric mean 1·3 (range 0·4-8·5) mg/mmol before operation and 4·1 (0·3-62·6) mg/mmol after). The arithmetic mean urinary total protein concentration in the nine patients operated on under local anaesthesia increased from 4·4 (range 0·9-12·6) mg/mmol creatinine before operation to 7·2 (2·5-23·0) mg/mmol after operation, ($p<0·05$, Wilcoxon's signed rank test). The arithmetic mean urinary albumin concentration in these nine patients did not change significantly (mean 0·9 (range 0·2-2·4) mg/mmol creatinine before and 0·8 (0·3-2·0) mg/mmol after operation).

In two patients undergoing resections of the large bowel, one elective repair of an aortic aneurysm, and one axillobifemoral grafting with bilateral femorodistal arterial reconstruction urine samples were collected 15 minutes before the operation and every 30 minutes after the start of the operation. The mean time to significant increase in urinary total protein or albumin concentration was 1·5 (range 0·5-2·5) hours. The figure shows serial urinary concentrations of total protein and albumin in a 62 year old man with Crohn's disease who underwent resection for an enteroenteric fistula.



Excretion of urinary total protein and albumin during laparotomy and bowel resection. (Mean total protein and albumin concentrations in 20 healthy subjects were 3·9 (SD 1·3) and 0·5 (0·6) mg/mmol creatinine respectively.)

Comment

All 33 patients showed increases in urinary total protein concentration, and 29 in urinary albumin concentration, by three hours after their operation; the figure shows the rapidity and magnitude of the changes. Measurement of urinary proteins in four patients before and after catheterisation and induction of general anaesthesia showed no change in concentration. Three patients who had major operations but did not have catheters inserted showed appreciable increases in urinary total protein and albumin concentrations, suggesting that the phenomenon is independent of catheterisation. There were no differences between men and women or