Health Physics Pergamon Press 1977. Vol. 33 (November), pp. 369–385. Printed in Great Britain

RADIATION EXPOSURES OF HANFORD WORKERS DYING FROM CANCER AND OTHER CAUSES*

THOMAS F. MANCUSO, ALICE STEWART and GEORGE KNEALE
University of Pittsburgh, Pittsburgh, PA 15261

(*Received* 24 *February* 1977)

Abstract—Data from the Hanford study have shown that sensitivity to the cancer-induction effects of radiation is at a low ebb between 25 and 45 yr of age. Nevertheless, at younger and older ages there is probably a cancer hazard associated with low level radiation which affects bone marrow cancers more than other neoplasms and cancers of the pancreas and lung more than other solid tumors.

INTRODUCTION

HANFORD Works in Richland, Washington is one of the largest atomic plants in the United States, and most of the staff are in some way concerned with the manufacture of radioactive substances. For these workers, who are predominantly white males, there is systematic recording of data under the following headings as part of a study of the lifetime health and mortality experience of employees of ERDA contractors (Ma71):

(1) Sex, date of birth, date of hire and social security number.

(2) Dates of entering and leaving specified occupations.

(3) External and internal radiation.

(4) Date and cause of death.

The wearing of radiation badges in all workshops and laboratories is obligatory, and the badges are read at frequent intervals to ensure that no worker ever receives more than the maximal permissible dose of 5 rems/yr (BRPC71). In several high risk occupations the workers are also examined (at regular intervals and following accidents or radiation "leaks") for internal depositions of radioactive substances. Therefore, there are both records of the total amount of external penetrating radiation received by each worker by the end of each calendar year (annual doses in centirads) and similar records relating to intakes of radioactive materials (positive urine analyses or internal radiation).

Deaths of Hanford employees are identified through death benefit claims by a nationwide system of social security numbers. These numbers probably provide better identification of males than females but the method of death identification has two major advantages: intervals between discharge and death may be of long duration and there is coverage of all deaths in any U.S. state or territory. Finally, certified causes of death are taken direct from death certificates, copies of which are obtained from official sources and filed with the other records.

Radiation monitoring has been in operation since 1943 and sufficient time has now elapsed for most of the non-survivors to be men who died 10 or more years after leaving the industry. Therefore, from the records of men with certified causes of death we should be able to discover whether NCRP recommendations for protection of radiation workers (BRPC71)—which are strictly enforced by all ERDA contractors—have succeeded in eliminating the cancer hazard or, failing that, are keeping the risk within reasonable bounds. As a first approach to this problem we have examined the records of workers who died within 29 yr of Hanford Works going into full production (1944).

*Under Contract No. E(11-1)-3428.

PRELIMINARY FINDINGS

Death benefit claims on behalf of men who died before 1973 totalled 3710 and included 3520 certified deaths for the period 1944–1972 (Table 1). Compared with the much larger number of survivors from the same work force, these deaths were strongly biased in favor of the first and largest work cohort. Among the men who were hired during 1944 were some workers who, strictly speaking, were not members of the monitored population (é.g. construction workers). Nevertheless, these men have always been so regarded (Ma74), since, in the early records, there is difficulty in distinguishing between workers in monitored occupations who never received any radiation (non-exposed workers) and workers who were not obliged to wear radiation badges (non-monitored occupations).

The high proportion of non-exposed workers in the 1944 cohort and the relatively low doses recorded before 1954 and by men with short periods of employment (Tables 5 and 6), are reasons why we would expect non-survivors to have lower radiation doses than survivors. This has been a constant feature of earlier analyses of Hanford data (Ma74) and will be mentioned again after we have completed the analysis of certified deaths (see discussion). Meanwhile, it should be noted that division of the certified deaths into cancers (670 cases) and non-cancers (2850 cases) left both groups with the same proportions of men hired in 1944 (48%) and men hired later than 1948 (16%).

In spite of their cohort resemblances the two groups of certified deaths had dissimilar radiation records, also ones which showed that men who eventually developed fatal cancers had been more often and more intensively exposed to external radiation than men with other causes of death (Table 2). Thus the proportion of exposed workers (or men who had one or more positive badge readings) was 66% for cancers and 61% for non-cancers, and for these workers the mean cumulative radiation dose was higher for the cancers (210 centirads) than for the non-cancers (162). Therefore, the "all-worker dose" was appreciably higher for cancers (138) than non-cancers (99).

A classification of the deaths by ICD Nos. showed that for none of the Main Orders of non-malignant diseases was the level of radiation dose higher than the level for all cancers (Table 3). But within the group of malignant diseases there was wide variation in the dose level, also higher doses for RES neoplasms (ICD Nos. 200–209) than solid tumors (ICD Nos. 149–199), and exceptionally high doses for a small group of bone marrow cancers (ICD Nos. 203 and 205). For example, the "all-worker" dose averaged 94 for accidents, 105 for cardiovascular diseases, 114 for digestive diseases, 130 for solid tumors, 219 for RES neoplasms and 449 for bone marrow cancers. Other malignant dis-

Table 2. External radiation records for two groups of non-survivors: cancers and non-cancers

Non-survivors	Cases (Nos.)	Exposed* workers (Nos.)	Cumulative radiation dose (centirads)	Exposed workers %	Mean radiation† dose in centirads A	B
Cancers	670	442	92657	66.0	210	138
Non-cancers	2850	1742	282961	61.1	162	99
All certified deaths	3520	2184	375618	62.0	172	107

*Men with one or more positive badge readings.
†A = Mean cumulative radiation dose for exposed workers.
B = Mean cumulative radiation dose for all workers.

Table 1. Hanford workers; survivors and non-survivors from 1944 to 1971 work cohorts

Cohort*	% Survivors*	% Non-survivors* Uncertified deaths	Cancers	Non-cancers	Totals Nos.	Early discharges*
1944	16.4	41.3	48.7	47.8	5256	49.4
1945	4.7	14.7	12.5	14.5	1524	42.7
1946	2.3	2.0	2.1	3.1	597	19.9
1947	10.3	11.3	12.5	11.0	2615	34.5
1948	7.8	10.7	8.2	7.5	1.927	48.6
1949–71	58.5	20.0	16.0	16.1	13,020	32.3
Total Nos.	21,206	213	670	2850	24,939	9410
Total %	85.0	0.9	2.7	11.4	100.0	37.7

*Cohort = year of hire.
Survivors = alive in 1973.
Non-survivors = pre-1973 deaths.
Early discharges = men discharged during the calendar year of hire or the following year.

Table 3. External radiation records for stated causes of certified deaths

Certified causes of death (ICD Nos.)	Totals (Nos.)	Exposed workers* (Nos.)	Cumulative radiation dose (centirads)	Exposed workers* (%)	Mean R dose (centirads*) (A)	(B)
Non-cancers:						
Infective (000–136)	29	16	1258	55.2	79	43
Benign neoplasms (210–39)	10	4	155	40.0	39	15
Endocr. & blood (244–89)	54	34	5199	63.0	153	96
C.N.S. (290–389)†	36	20	3389	55.6	169	94
C.V.S. (390–458)‡	1837	1149	191,987	62.5	167	105
Respiratory (460–519)	194	108	14,330	55.7	133	74
Digestive (520–577)	139	83	15,807	59.7	190	114
Accidents (800–999)	450	271	42,244	60.2	156	94
Residue (580–796)	101	57	8592	56.4	151	85
RES neoplasms:						
Lymphomas (200–2)	34	28	4049	82.4	145	119
Lymphatic Lk (204)	3	2	57	66.7	29	19
Myelomas (203)	11	8	8530	72.7	1066	775
Myeloid leukemia (205)	11	6	1337	54.5	223	122
Residue (206–9)	5	3	58	60.0	19	12
Solid tumors:						
Mouth & pharynx (140–9)	24	14	2134	58.3	152	89
Stomach (151)	38	26	2227	68.4	86	60
Large intestine (153)	61	48	8222	78.7	171	135
Rectum (154)	19	16	1887	84.2	118	99
Other intestinal (150; 152)	18	10	581	55.6	58	32
Liver & gall bl. (155–6)	18	10	557	55.6	56	31
Pancreas (157)	49	31	12,377	63.3	399	253
Lung (162–3)	192	130	32,384	67.7	249	169
Prostate (185)	43	21	1817	48.8	87	42
Kidney (189)	21	14	3935	66.7	281	187
Other G.U. (186–8)	15	10	1225	66.7	123	82
Brain (191)	18	11	3967	61.1	361	220
Residue	90	54	7313	60.0	135	81
Totals:						
Non-cancers	2850	1742	2829.61	61.1	162	99
RES neoplasms	64	47	140.31	73.4	299	219
Solid tumors	606	395	786.26	65.2	199	130

*See footnotes to Table 2.
†C.N.S. = Neurological diseases.
‡C.V.S. = Cardiovascular diseases.

eases with high radiation doses were cancers of the pancreas (253), brain (220), kidney (187), lung (169) and large intestine (135).

In Table 4, the various neoplasms are listed in accordance with the all-worker dose and the number of cases in each diagnostic category is compared with an expected number which shows how the same diseases were distributed among the 1960 cancer deaths of U.S. white males (Bu71). For 8 neoplasms, the radiation dose was higher than the level for all certified deaths (107 centirads) and for 9 the dose was below this level. For the group with above average doses, the observed and expected numbers were 397 and 318 (ratio 1.25), and for the other group they were 273 and 352 (ratio 0.78).

Controlled analyses

The preliminary findings were compatible with a causal association between the radiation exposures and some of the cancer deaths. Therefore comparisons between the two main groups of certified deaths (cancers and non-cancers) were continued in analyses which controlled separately for five possible sources of false impressions, namely:

(1) Calendar year of the exposures.
(2) Employment year of the exposures.
(3) Pre-death year of the exposures.
(4) Exposure age or age at the end of each badge-reading year.
(5) Death age.

Calendar years (Table 5 and Fig. 1)

The calendar year classification showed that: (i) the proportion of exposed workers was higher during the first half of the study period than the second half, but the opposite was true of the annual radiation doses of exposed workers (AREW doses in centirads) and (ii) only during the high dose period were differences between cancers and non-cancers at all pronounced.

Each year the proportion of exposed workers remained a fraction higher for cancers than non-cancers (Fig. 1). However, from

Table 4. Observed and expected numbers of specific neoplasms listed according to mean cumulative dose of external radiation

No. Neoplasms*	Mean cumulative radiation dose (centirads)	No. of deaths† Observed	Expected	Ratio Obs:Exp
1. Myelomas	775‡	11	7.6	1.45
2. Pancreas	253‡	49	37.3	1.31
3. Brain	220‡	18	17.3	1.04
4. Kidney	187‡	21	15.0	1.40
5. Lung	169‡	192	144.4	1.33
6. Large intestine	135‡	61	63.1	0.97
7. Myeloid leukemia	122‡	11	5.8	1.90
8. Lymphomas	119‡	34	27.7	1.23
9. Rectum	99	19	29.6	0.64
10. Mouth & pharynx	89	24	21.9	1.10
11. Other genito-urinary	82	15	30.9	0.49
12. Stomach	60	38	58.7	0.65
13. Prostate	42	43	67.5	0.64
14. Other intestinal	32	18	18.0	1.00
15. Liver & gall bladder	31	18	12.5	1.44
16. Lymphatic leukemia	19	3	9.4	0.32
17. Other RES neoplasms	12	5	20.3	0.25
18. Other solid	81	90	83.0	0.59
Nos. 1.8	188‡	397	318.2	1.25
9–18	65	273	351.8	0.78
All cancers	138‡	670	670.0	1.00

*See Table 3.
†Observed see Table 3; expected see 1960 cancer deaths of white U.S. males in NCI Monograph 33.
‡ = Above the mean value for all certified deaths (107), see Table 2.

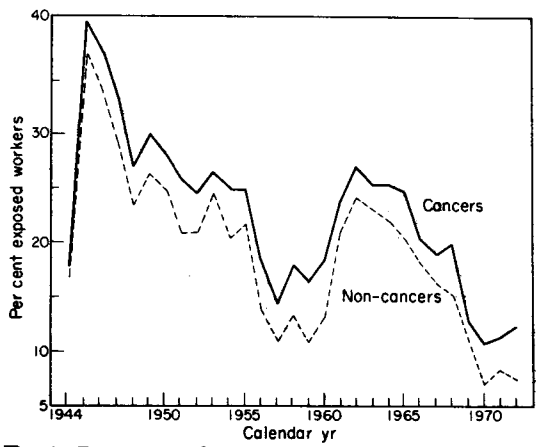

FIG. 1. Per cent of exposed workers by calendar years cancer and non-cancer deaths of males.

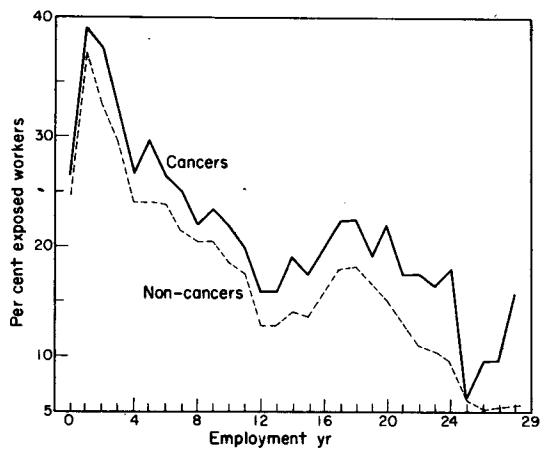

FIG. 2. Per cent of exposed workers by employment years cancer and non-cancer deaths of males.

1944 to 1957 (when AREW doses averaged 14.9 for cancers and 18.7 for non-cancers), there were equal numbers of years with above average doses for the two causes of death (high risk years); and from 1958 to 1972 (when AREW doses averaged 51.3 for cancers and 47.7 for non-cancers), there were more high risk years for cancers (11) than non-cancers (4) (Table 5).

Employment years (Table 6 and Fig. 2)

The employment year classification showed that: (i) the proportion of exposed workers decreased with progressive lengthening of the interval between hire and exposure but the trend for AREW doses was in the opposite direction, and (ii) only during the high dose period were differences between cancers and non-cancers at all pronounced.

Each year the proportion of exposed workers remained a fraction higher for cancers than non-cancers (Fig. 2). However, when intervals from hire to exposure were shorter than 10 yr (and AREW doses averaged 21.5 for cancers and 21.1 for non-cancers), there

Table 5. Mean annual radiation doses for exposed workers (cancer and non-cancers) (calendar years)

Calendar years	Exposed workers*		Radiation doses†		High risk years‡	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
1944–45	237	901	26.5	26.0	2	—
1946–47	333	1268	11.9	13.2	—	2
1948–49	325	1169	12.6	8.4	1	1
1950–51	311	1101	12.4	12.8	—	2
1952–53	302	1119	22.2	20.2	2	—
1954–55	288	1007	28.4	23.1	2	—
1956–57	185	568	40.8	41.6	—	2
1958–59	183	524	53.6	51.7	2	—
1960–61	203	661	53.0	47.8	2	—
1962–63	227	789	47.4	43.2	2	—
1964–65	184	599	63.1	59.6	1	1
1966–67	120	390	44.1	46.6	1	1
1968–69	75	213	39.0	43.1	1	1
1970–72	32	76	42.8	19.4	2	1
Total	3005	10,385	30.6	27.8	18	11
1944–57	1981	7133	19.9	18.7	7	7
1958–72	1024	3252	51.3	47.7	11	4

*Number of workers with positive badge readings in each year.
†Mean annual radiation doses of exposed workers in centirads (AREW doses).
‡Number of years with higher doses for cancers than non-cancers or vice versa.
Note there are small differences in the totals for Tables 5–8 which are due to the time units being measured to the nearest whole year.

Table 6. Mean annual radiation doses for exposed workers (cancers and non-cancers) (employment years)

Employed years	Exposed workers*		Radiation doses*		High risk years*	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
0–1	463	1786	21.8	23.1	—	2
2–3	475	1747	15.6	16.8	—	2
4–5	368	1294	18.3	17.2	2	—
6–7	321	1162	24.5	22.7	1	1
8–9	273	985	34.4	28.3	2	—
10–11	232	811	41.9	33.1	2	—
12–13	164	528	47.5	44.4	1	1
14–15	171	521	54.9	47.8	2	—
16–17	171	541	47.2	45.6	1	1
18–19	144	461	46.5	43.1	1	1
20–21	103	294	53.3	52.4	1	1
22–23	73	160	40.3	32.0	2	—
24–25	35	74	27.0	21.7	2	—
26–29	14	22	14.4	16.1	1	2
Total	3007	10,386	30.1	27.8	18	11
Under 10 yr	1900	6974	21.5	21.1	5	5
Over 10 yr	1107	3412	46.3	41.7	13	6

*See footnotes to Table 5.

were equal numbers of high risk years for the two causes of death. When intervals from hire to exposure were longer than 10 yr (and AREW doses averaged 46.3 for cancers and 41.7 for non-cancers), there were twice as many high risk years for cancers (13) as non-cancers (6).

Pre-death years (Table 7 and Fig. 3)

The pre-death year classification showed that: (i) the proportion of exposed workers decreased with progressive shortening of the pre-death period, but the trend for AREW doses was in the opposite direction and (ii) in the middle of the time scale, the radiation doses were consistently higher for cancers than non-cancers but towards the beginning and end of the range, the radiation doses were frequently lower for cancers than non-cancers.

Each year the proportion of exposed workers remained a fraction higher for cancers than non-cancers (Fig. 3). However, when the interval between exposure and death was less than 8 or more than 20 yr (and AREW doses averaged 30.1 for cancers and 30.6 for non-cancers), there were over twice as many high risk years for non-cancers (12) as cancers (5). Between these extremes (when AREW doses averaged 31.0 for cancers and 25.1 for non-cancers), there was an unbroken series of high risk years for cancers (Table 7).

Exposure age (Table 8 and Fig. 4)

The exposure age analysis, which was restricted to men between 20 and 65 yr and to

Table 7. Mean annual radiation doses for exposed workers (cancers and non-cancers)

Pre-death years†	Exposed workers*		Radiation doses*		High risk years*	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
0–1	156	675	29.6	28.8	1	1
2–3	241	854	41.8	35.4	2	—
4–5	273	974	39.8	42.4	1	1
6–7	305	1015	37.1	39.1	—	2
8–9	310	1022	36.8	32.7	2	—
10–11	283	933	33.4	28.2	2	—
12–13	242	868	35.1	25.4	2	—
14–15	257	863	29.0	22.2	2	—
16–17	239	861	27.3	21.3	2	—
18–19	210	724	21.4	18.2	2	—
20–21	186	592	12.9	14.2	—	2
22–23	143	481	14.9	15.4	—	2
24–25	111	353	18.2	16.9	1	1
26–28	56	172	15.7	23.5	—	3
Total	3012	10,388	30.6	27.8	17	12
8–19 yr	1541	5271	31.0	25.1	12	—
Other yr	1471	5117	30.1	30.6	5	12

*See footnotes to Table 5.
†Interval between exposure and death (in yr).

Table 8. Mean annual radiation doses for exposed workers (cancers and non-cancers)

Exposure age in years†	Exposed workers*		Radiation doses*		High risk years*	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
20–22	11	22	25.2	13.8	2	1
23–25	21	99	11.4	21.4	1	2
26–28	55	172	25.9	25.9	1	2
29–31	93	272	22.3	30.0	—	3
32–34	111	419	14.4	30.9	—	3
35–37	150	536	19.7	23.8	1	2
38–40	160	609	20.9	21.3	2	1
41–43	224	665	25.8	24.9	2	1
44–46	233	744	28.9	26.4	2	1
47–49	253	777	37.6	31.9	3	—
50–52	281	876	33.7	30.7	3	—
53–55	265	930	34.3	26.0	3	—
56–58	235	863	30.7	25.3	2	1
59–61	196	708	28.4	24.5	3	—
62–64	160	527	34.5	24.2	3	—
Total	2448	8219	28.9	26.5	28	17
Under 35 yr	291	984	18.4	28.4	4	11
35–55 yr	1566	5137	30.0	26.8	16	5
Over 55 yr	591	2098	31.0	24.3	8	1

*See footnotes to Table 5.
†Excluding exposures before 20 yr of age, or after 65 yr, or within 5 yr of death.

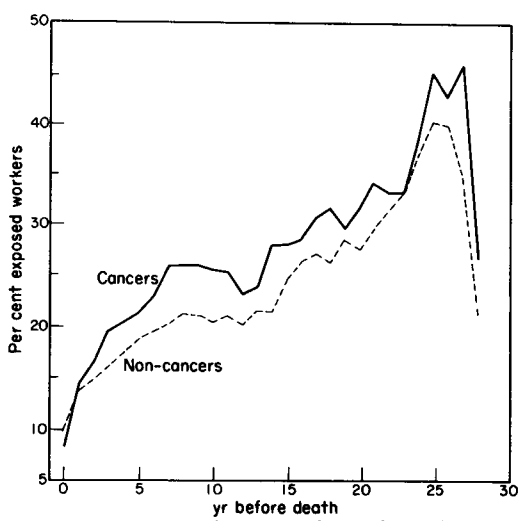

FIG. 3. Per cent of exposed workers by years before death cancer and non-cancers deaths of males.

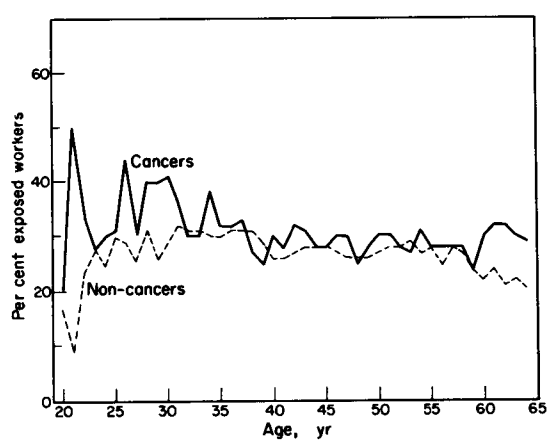

FIG. 4. Per cent of exposed workers by exposure age (excluding exposures within 5 yr of death).

exposures more than 5 yr before death, showed that: (i) the proportion of exposed workers was virtually independent of age (Fig. 4) and (ii) only after 40 yr were the radiation doses noticeably higher for cancers than non-cancers.

From 20 to 35 yr of age, there were more than twice as many high risk years for non-cancers (11) as cancers (4) and AREW doses were also higher for non-cancers (28.4) than cancers (18.4). However, for the group with initially high radiation doses there was a decrease with age (non-cancers) and for the group with initially low doses there was an increase with age (cancers). Therefore, by 40 yr the men who eventually developed fatal cancers were recording higher doses than the men with other causes of death. Thus, from 35 to 55 yr there were 16 high risk years for cancers and 5 for non-cancers, and from 56 to 65 yr the corresponding numbers were 8 and 1. In the younger of these two age groups the AREW doses were 30.0 for cancers and 26.8 for non-cancers, and in the older age group they were 31.0 and 24.3.

Age at death

With recurrent events as controlling factors (e.g. exposure years and exposure ages), there was no way whereby men who remained in the monitored population for short periods of time could contribute as much to the final results as men who remained for long periods and no way whereby the findings for each subgroup could be totally independent. However, with age at death as the controlling factor, there was no difficulty in obtaining strictly independent findings for any number of subgroups. Therefore, the analysis proceeded along new lines and was directed towards obtaining a stringent test of the null hypothesis of no correlation between the radiation dose and the proportion of cancer deaths after controlling for age at death (see Spearman's rank correlation coefficients in Table 11).

The basic data for this test were: (i) age at death for subgroups defined by cause of death (Table 9); (ii) radiation doses for subgroups defined by age and cause of death (Table 10); and (iii) cancers as a proportion of all certified deaths in groups defined by age at death and radiation dose (Table 11). Thus Table 9 shows that: (i) although accidents were often causes of early death, men who eventually developed malignant diseases did not have appreciably longer life spans than men with other causes of death and (ii) between two thirds and three quarters of all the deaths occurred between 50 and 80 yr of age.

Table 9. Age distributions of cancer and non-cancer deaths: stated causes of death (and I.C.D. Nos.)

Age at death in years	Cardiovascular (390–458) %	Respiratory; digestive (460–577) %	Accidents (800–999) %	Other non-malignant %	All non-cancers %	Cancers (140–209) %	All causes %
Under 40	2.6	5.1	30.0	12.6	8.0	3.7	7.2
40–49	11.9	12.3	27.3	11.7	14.4	12.8	14.1
50–59	25.3	20.7	21.6	27.0	24.4	27.9	25.0
60–69	29.0	32.5	16.2	23.9	26.9	35.7	28.6
70–79	23.4	24.9	4.2	17.8	20.1	17.3	19.6
80+	7.8	4.5	0.7	7.0	6.2	2.5	5.5
Totals:							
Nos.	1837	333	450	230	2850	670	3520
%	52.2	9.5	12.8	6.5	81.0	19.0	100.0

Table 10. Mean cumulative radiation doses for stated causes of death and stated age at death

	Mean cumulative doses (R) in centirads									
Age at death in years	Cardiovascular (390–458)	Accidents (800–999)	Other non-cancers	Solid tumors (140–199)	RES neoplasms (200–209)	All cancers (140–209)	All non-cancers (001–136; 210–999)	All deaths (001–999)	Radiation dose Ratios* Ca: Non-Ca	RES: Solid
Under 40	59	47	76	55	40	52	56	55	0.93	0.73
40–49	95	114	104	100	57	93	102	100	0.91	0.57
50–59	157	133	64	187	329	201	136	150	1.48	2.19
60–69	132	116	125	145	82	140	129	132	1.09	0.62
70–79	46	24	72	60	787	103	51	60	2.02	13.12
80+	39	6	13	17	97	22	34	33	0.65	2.94
All ages	105	94	88	130	219	138	99	107	1.39	2.05

*Ca = Cancers; Non-Ca = Non-cancers; RES = RES Neoplasms; Solid = Solid tumors.

Table 11. Test for correlation between the percentage of cancer deaths and the cumulative radiation dose after standardization for age at death

Age at death in years	Mean cumulative radiation dose for all workers (in centirads)											
	Zero		1–19		20–99		100–499		500+		Total	
	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers
Under 40	108	*9.3*	55	*10.9*	58	*8.6*	24	*8.3*	9	*22.2*	254	*9.8*
40–49	185	*13.0*	82	*15.9*	137	*21.9*	74	*23.0*	17	*11.8*	495	*17.3*
50–59	331	*19.3*	137	*16.1*	200	*24.5*	155	*21.9*	58	*31.0*	881	*21.2*
60–69	360	*22.2*	162	*21.6*	248	*26.6*	184	*25.0*	53	*22.6*	1007	*23.7*
70+	352	*13.6*	189	*11.6*	251	*17.5*	74	*18.9*	17	*29.4*	883	*15.1*
Total	1336	*16.9*	625	*15.7*	894	*21.7*	511	*22.0*	154	*25.3*	3520	*19.0*

	Ranking Nos. for cancer proportions					Value of† rho
Under 40	3	4	2	1	5	0.1
40–49	2	3	4	5	1	0.0
50–59	2	1	4	3	5	0.8
60–69	2	1	5	4	3	0.5
70+	2	1	3	4	5	0.9
Means	2.2	2.0	3.6	3.4	3.8	0.46 ± 0.22*

*This value is statistically significant at the 5% level.
†Value of Spearman's rank correlation coefficient between the percentage of cancer deaths and the radiation dose level.

Table 10 shows that division of men who lived for more than 50 and less than 80 yr into three age groups still left each subgroup of cancers with a higher radiation dose than the corresponding group of non-cancers and still left each subgroup of RES neoplasms with a higher dose than the corresponding group of solid tumors.

Finally, Table 11 includes the results of the correlation test and shows that division of the certified deaths into 5 age groups and 5 dose levels still left the highest radiation dose groups (over 500 centirads) with the highest proportion of cancer deaths. As a result of this consistent trend, there was a firm rejection of the null hypothesis by the statistical test. Thus in three age groups Spearman's rank correlation coefficient (between the proportion of cancer deaths and the radiation dose level) had a value equal to or greater than 0.5 and the mean coefficient over age had a value of 0.46 ± 0.22. This is a statistically significant result since the coefficient for (n) observations has a variance of $(1/n - 1)$. Therefore, for a mean coefficient from 5 age groups, each with 5 dose levels, the variance is (1/20) implying a standard error of 0.22.

SPECIAL TESTS OF THE RADIATION ASSOCIATIONS

The impression of a causal association between the exposures to external radiation and the cancer deaths was strengthened rather than weakened by the controlled analyses. Therefore it only remained to test the safety threshold hypothesis (i.e. the theory that below the maximal permissible dose radiation has no carcinogenic properties) against the only logical alternative, namely, that with any exposure to ionizing radiation there is a cancer hazard which is proportional to the dose.

The choice of statistical test was influenced by the following assumptions: first, the most plausible alternative to the safety threshold hypothesis is a dose–response relationship that is either linear or at least monotonically increasing. Secondly, in Hanford data the stimulus or radiation dose, is continuously variable and the response or development of a fatal cancer, is a binary one (or an all-or-nothing response). Therefore, the most appropriate statistical model was the logistic or log-linear one which states that the logarithm of the odds-ratio of a response is linearly related to the stimulus over a suitable range of intensity (Co70).

Under the assumptions of this model the most powerful test of the null hypothesis was the permutation test of the difference between the mean cumulative radiation dose for men developing fatal cancers and the mean for all certified deaths. Therefore the test could be carried out in three stages:

(1) *Test for cancers with definite radiation associations*

Let N = size of whole population;
n = size of subpopulation of cancer deaths;

R = average value of radiation dose for the whole population;
r = average value of radiation dose for the subpopulation cancer deaths;
S = average value of the squared dose for the whole population.

Then, the estimate of variance in whole population $(V) = (N/(N-1))(S-R^2)$ and $t = [(r-R)/\sqrt{V[(1/n)-(1/N)]}]$ where this statistic is approximately distributed as a t statistic with $(N-1)$ degrees of freedom for testing the null hypothesis (see Appendix).

(2) *Quantitative estimates of radiation sensitivity (doubling dose)*

Should the null hypothesis of no associations between the radiation doses and the cancer deaths be rejected by the first test (as a result of t exceeding a critical value of approx +2.0), a quantiative estimate of radiation sensitivity would be required and could be obtained in the following way:

Let D = the radiation dose which is just sufficient to double the normal risk of a cancer death (doubling dose). Then r will have an expected value of $(R + S/D)/(1 + R/D)$ (see Appendix).

Therefore, by solving this equation with observed values of r, one could obtain for any cancer with definite radiation associations an estimate of the doubling dose (D).

(3) *Quantitative estimates of radiosensitivity in relation to pre-death years and ages*

There is no reason why the above formulas should not be used in relation to radiation doses for stated time periods or ages; and there are strong grounds for believing that: (i) tissue specific cancers have characteristic, albeit long, intervals between initiation and death, and (ii) sensitivity to the cancer-induction effects of any mutagen is strongly age dependent. Therefore, in Hanford data, the search for radiosensitive cancers can be directed towards discovering which of several pre-death years or ages (in relation to tissue specific cancers) are associated with statistically significant differences between observed and expected radiation doses (or t values equal to or greater than 2.0).

By taking this approach the identification of cancers with definite radiation associations (radiosensitive cancers) can be combined with estimates of: (i) the relative sensitivity of different tissues (as measured by doubling doses for the relevant cancers); (ii) characteristic intervals between initiation dates and death (or the pre-death years showing the maximum contrast between observed and expected radiation doses); and (iii) the ages of maximal and minimal sensitivity to the cancer-induction effects of ionizing radiation (or the ages showing maximum and minimum differences between observed and expected doses). Therefore, the search for radiosensitive cancers (and other diseases with radiation associations) was pursued, first in relation to pre-death periods (Tables 12–15), then in relation to age (Table 16).

Table 12. Cumulative radiation doses for stated pre-death periods

	Non-cancers			
	Mean cumulative radiation doses in centirads			
Pre-death years*	All non-cancer† deaths	Cardiovascular diseases	Accidents	Other non-cancers
28	3.2	3.4	0.0	3.2
26	15.8	15.3	7.1	19.2
24	19.4	17.4	10.9	28.2
22	22.4	20.6	18.3	29.4
20	24.1	22.7	20.0	30.7
18	29.0	27.9	23.5	35.1
16	35.2	24.8	32.3	38.1
14	41.3	41.3	37.1	43.2
12	48.2	48.9	44.3	47.9
10	56.6	57.2	54.8	55.5
8	67.3	68.0	64.4	66.6
6	80.0	81.6	76.4	76.7
4	92.6	94.6	91.0	86.6
2	100.9	104.0	100.5	90.7
0	106.0	110.9	101.4	93.2
Number of deaths	2850	1837	450	563

*See footnote to Table 7.
†Standard values, see later tables.

Table 13. Cumulative radiation doses for stated pre-death periods

	Cancers		
Pre-death years§	All cancers	RES neoplasms	Solid tumors
28	1.9	0.7	2.2
26	12.5	24.6	11.5
24	18.9	14.3	19.3
22	22.7	23.1	22.7
20	25.2	33.0	24.5
18	34.0	*52.2**	32.3
16	44.3	*83.0*†	40.6
14	*54.3**	*105.2*†	49.1
12	*65.0**	*126.0*†	58.8
10	*76.7**	*154.0*†	69.1
8	*90.4**	*175.4*†	81.7
6	104.2	*194.5**	95.0
4	116.6	*200.9**	107.7
2	129.0	*216.2**	119.6
0	134.4	*223.1**	125.0
Number of deaths	670	64	606

Figures in italics significantly differ from the standard values in Table 12.
Levels of significance:
*$P < 0.05$.
†$P < 0.01$.
‡$P < 0.001$.
§See footnote to Table 7.

Table 14. Cumulative radiation doses for stated pre-death periods

Pre-death years*	Mean cumulative radiative radiation doses in centirads† Bone marrow (203; 205)	Other sites (200–2; 204; 206–9)
28	1.0	0.0
26	3.0	57.0
24	4.2	26.4
22	19.0	26.7
20	37.6	29.1
18	53.1	51.1
16	*121.6*‡	50.5
14	*180.5*‡	54.0
12	*231.1*‡	60.7
10	*310.2*†	63.4
8	*401.4*‡	62.3
6	*446.9*‡	65.0
4	*438.5*‡	72.9
2	*468.1*‡	90.3
0	*469.2*‡	100.1
Number of deaths	22	42

*See footnote to Table 7.
†See footnotes to Tables 12 and 13.
‡See significance levels in Table 13.

Table 15. Cumulative radiation doses for stated pre-death periods

Pre-death years*	Solid tumors Mean cumulative radiation doses in centirads† Large intestine (153)	Pancreas (157)	Lung (162)	Kidney (189)	Brain (191)	Other solid tumors
28	0.0	12.0	4.0	1.0	0.0	0.0
26	8.7	12.0	15.0	2.0	40.0	6.3
24	19.1	25.6	18.4	1.3	39.2	17.8
22	27.9	33.6	23.3	2.6	36.5	18.9
20	25.7	35.9	25.0	3.0	46.9	21.2
18	45.2	35.9	35.3	13.7	59.3	25.8
16	54.7	48.2	45.7	24.9	70.7	30.9
14	63.1	65.5	*61.8*‡	35.9	70.8	32.2
12	74.3	90.1	*72.1*‡	74.8	93.7	35.3
10	92.3	*119.9*‡	86.9	88.9	98.1	37.7
8	106.5	*142.7*‡	103.4	98.1	124.8	43.9
6	125.1	*173.9*‡	117.1	123.6	158.4	49.4
4	129.6	*214.5*‡	132.6	159.9	193.9	54.1
2	137.0	*247.0*‡	147.5	172.7	226.8	59.1
0	141.8	*269.0*‡	153.4	171.3	233.4	62.6
Number of deaths	61	49	192	21	18	265

*See footnote to Table 7.
†See footnotes to Tables 12 and 13.
‡See significance levels in Table 13.

radiation was 48.2 centirads for all non-cancer deaths (standard or control group). For cardiovascular deaths, the corresponding dose was 48.9 (case: control ratio 1.01), for fatal accidents 44.3 (ratio 0.92) and other non-cancer deaths 47.9 (ratio 0.99). There were, however, positive findings for all cancers and for some of the neoplasms with exceptionally high radiation doses.

Thus for all cancers (ICD Nos. 140–209), there were positive findings (i.e. significant differences between observed and expected doses of external radiation) over a period of nearly 10 yr, namely, 7–15 yr before death; and for RES neoplasms there were positive findings over a period of nearly 20 yr, namely, from 0 to 18 yr before death (Table 13). For bone marrow cancers there were exceptionally strongly positive findings for the period 0–17 yr before death (Table 14), and for 2 of the 5 solid tumors with high radiation doses some of the differences between observed and expected doses were statistically significant. Thus, for pancreatic tumors, there were positive findings for the period 0–11 yr before death, and for lung cancers there were similar findings for the period 11–14 yr before death (Table 15).

For all cancers the critical interval between exposure and death—or the period of maximum case:control contrast as indicated by the t value—was 12 yr (case:control ratio 1.35 and $t+2.4$). For RES neoplasms the corresponding period was 11 yr (ratio 2.71 and $t+3.7$), and for bone marrow cancers 9 yr (ratio 5.86 and $t+6.1$). For lung cancers the critical interval was 14 yr (case: control ratio 1.50 and $t+2.0$), and for pancreatic tumors under 1 yr (ratio 1.50 and $t+3.0$).

For other cancers with high radiation doses, there was less certain evidence of a

*Table 16. Estimated doubling doses for critical pre-death years**

Radio-sensitive cancers	Critical pre-death periods Years before death	Estimated doubling dose in rads	Proportion of all deaths Observed %	Expected† %
Bone marrow	9	0.8	0.62	0.30
Pancreas	0	7.4	1.39	0.85
Lung	14	6.1	5.45	3.26
All RES neoplasms	11	2.5	1.82	1.15
All cancers	13	12.2	19.02	15.15

*The years before death which showed the maximum contrast compared with the standard group of all non-cancer deaths (see Tables 13–15).
†See U.S. Vital Statistics for deaths of white males (1960).

RADIOSENSITIVITY AND CRITICAL PRE-DEATH PERIODS

Division of the non-cancer deaths into several subgroups failed to produce any evidence of radiation associations in either the pre-death period or the age analysis (Table 12). For example, 12 yr before death the mean cumulative radiation dose for external

causal association. However, for brain tumors there was a period of 3 yr when observed doses were twice as high as expected doses and t values were greater than +1.5 (i.e. 17–19 yr before death), and for cancers of the large intestine the observed dose 18 yr before death was 58% above the expected dose ($t + 1.3$). Finally, there were two findings which suggested that, given a longer period of records, there might have been a wider range of radiosensitive cancers. As a result of the study being restricted to men who died before 1973, there were very few records of radiation exposures 26 yr before the final (death) year. However, in this rare group 3 cases of brain tumors recorded a radiation dose which was almost 3 times as high as the expected dose ($t + 1.3$), and 2 cases of lymphosarcomas recorded a radiation dose nearly 4 times as high as the expected dose ($t + 1.8$).

DOUBLING DOSES FOR RADIOSENSITIVE CANCERS

From the records for critical pre-death periods, estimates were made of the amount of radiation which would be needed to double the normal risk of developing any of the cancers with definite radiation associations (see doubling doses in Table 16). According to these estimates, 12.2 rads would be needed to double the normal risk of dying from any form of cancer. For cancers of pancreas or lung, the doses would be somewhat lower (7.4 or 6.1 rads) and for RES neoplasms or bone marrow cancers, they would be even lower (2.5 or 0.8 rads).

These suggested doses are so much lower than the estimates based on atom bomb survivors (Co70) that they are unlikely to go unchallenged. Therefore, we have included in Table 16 the proportions of certified deaths caused by the cancers with definite radiation associations, and the proportions of these cancers expected on the basis of all certified deaths of U.S. white males in 1960 (VSUS60). From these observed and expected proportions, standardized mortality ratios (SMRs) were obtained in the usual way and compared with the results of solving the following equation with observed values of D and R:

$$\mathrm{EMR} = 100 \times \left(1 + \frac{R}{D}\right)$$

where EMR = excess mortality from a radiosensitive cancer relative to a standard risk of 100 for all certified deaths.

According to the SMRs, the risks for Hanford workers were increased by 26% for all cancers, by 58% for RES neoplasms, and by 107% for bone marrow cancers (Table 17) and, according to the EMRs, the risks were increased by 4% for all cancers, by 21% for RES neoplasms, and by 79% for bone marrow cancers. Since the more conservative estimates were based on the doubling doses in Table 16, we are faced with two alternatives: either the actual doubling doses were even smaller than the estimates in this table; or, more likely, external radiation was not the only source of trouble for Hanford workers. In other words our analysis of the records relating to external radiation has shown the need for a similar analysis of the records relating to internal radiation.

Table 17. Excess cancer mortality of Hanford workers: Comparisons between conventional SMRs and estimates based on radiation doubling doses (EMRs)

Cancers with definite Radiation associations	SMRs*	EMRs†
Bone marrow	207	179
Pancreas	163	114
Lung	167	107
All RES neoplasms	158	121
All cancers	126	104

*See Table 16. (Standard = 100).
†See text.

INTERNAL RADIATION

The data relating to depositions of radioactive substances are not yet in a form suitable for testing the null hypothesis of no trouble from this potential source of radiation-induced cancers. It is, however, possible to distinguish between Hanford workers with and without positive urine analyses and thus discover whether the positive findings in Tables 13–15 were due solely to workers in high risk or doubly monitored occupations or partly to men in low risk occupations or ones which were only monitored for external radiation.

Division of the certified deaths into two

groups (with and without records of internal radiation) showed that: (i) the proportion of cancer deaths was higher in the positive group (22%) than in the negative group (18%) (Table 18) and (ii) the all-worker dose for external radiation was much higher in the positive group (357 centirads) than in the negative group (23). However, even in the low dose group the external radiation dose was higher for cancers (29) than non-cancers (21), and in both groups a pre-death period analysis produced positive findings in relation to RES neoplasms (Tables 18 and 19).

In the high dose group there were 17 RES neoplasms and 7 bone marrow cancers, and in the low dose group there were 47 RES neoplasms and 15 bone marrow cancers. In the first of these two groups there were positive findings in relation to these neoplasms for 8 of the 29 pre-death years (Table 18), and in the second group there were positive findings for 5 of these years (Table 19). Also, for the period associated with positive findings in both high and low dose groups (i.e. 12 yr before death), the estimated doubling doses were not significantly different for the two occupational groups.

Table 18. External radiation doses of workers with positive and negative records of internal radiation

Internal radiation*	Diagnostic categories	Cases Nos.	Cases %	External radiation in centirads Total	External radiation in centirads Mean
Positive	Cancers	194	21.9	79,004	407
	Non-cancers	691	78.1	236,940	343
	Total	885	100.0	315,944	357
Negative	Cancers	476	18.1	13,653	29
	Non-cancers	2159	81.9	46,021	21
	Total	2635	100.0	59,674	23
Both	Cancers	670	19.0	92,651	138
	Non-cancers	2850	81.0	282,961	99
	Total	3520	100.0	375,618	107

*One or more depositions of radioactive substance.

Table 19. Cumulative doses of external radiation for stated pre-death years

Pre-death years	Men with positive urine analyses Non-cancers	RES neoplasms	Lung and pancreas	Other solid tumors
28	13.7	—	27.6	4.9
26	21.5	57.0	35.5	13.8
24	28.4	26.2	29.2	26.2
22	36.7	53.2	49.1	31.5
20	47.2	89.2	59.9	37.0
18	59.4	159.1*	78.6	52.3
16	76.1	201.2*	114.4	73.7
14	99.9	243.3*	130.2	96.3
12	127.6	257.1*	172.3	135.0
10	158.4	300.1	224.8	174.4
8	198.2	312.5	269.3	212.1
6	245.2	376.8	323.8	260.7
4	292.1	396.2	379.1	302.5
2	324.6	407.6	409.5	335.9
0	380.3	418.7	460.4	381.1
Number of deaths	691	17	86	91

*See significance levels in Table 13.

Table 20. Cumulative doses of external radiation for stated pre-death years

Pre-death years	Men with no record of internal radiation Non-cancers	RES neoplasms	Lung and pancreas	Other solid tumors
28	7.8	0.5	20.5	24.5
26	12.5	1.7	14.5	19.8
24	14.1	14.4	19.0	19.5
22	16.0	12.3	16.4	18.2
20	16.0	15.3	15.4	18.6
18	17.5	24.7	18.0	20.6
16	18.6	27.2	17.3	22.1
14	19.1	29.8	19.7	22.5
12	19.9	36.0*	22.2	25.2
10	22.0	42.0*	24.5	25.5
8	24.5	46.6*	29.2	27.2
6	27.1	46.3	30.9	28.2
4	29.3	46.4	34.6	30.1
2	31.8	49.9	34.7	32.5
0	40.1	51.7	36.2	39.7
Number of deaths	2159	47	155	274

*See significance levels in Table 13.

AGE AND SENSITIVITY TO THE CANCER-INDUCTION EFFECTS OF RADIATION

The search for sensitive age groups utilized a single set of controls (all non-cancer deaths) and two sets of cases, viz RES neoplasms and solid tumors with high radiation doses (see pancreas, lung, brain, kidney and large intestine in Table 3).

Towards the beginning and end of the age range of external radiation records (which covered the period between 21 and 78 yr), there was virtually no data for the smaller case group (RES neoplasms), but between 30 and 70 yr of age the records for this group were strongly suggestive of an exponential increase in cancer sensitivity with advancing age. Thus, between 30 and 40 yr of age the observed doses were consistently lower than the expected doses. However, by 45 yr the observed doses were 15% higher than the standard dose; and by 50 yr they were 50% higher. These differences were not statistically significant, but by 55 yr there was a threefold difference between the observed and expected doses ($t + 2.5$), and by 70 yr a 14-fold difference ($t + 9.2$).

For the larger case group, there were positive findings at both ends of the age scale and a lull period between 25 and 40 yr. Thus, in

*Table 21. Mean cumulative doses of external radiation by stated ages: Non-cancers, RES neoplasms and other selected cancers**

Age in years	Non-cancers R†	RES neoplasms R	RES neoplasms t‡	Other cancers* R	Other cancers* t	Nos. of observations Non-cancers	Nos. of observations RES Neoplasms	Nos. of observations Other cancers
21	8	—	—	39	*2.3*	43	1	6
22	7	2	—	39	*3.1*	87	2	7
23	9	7	—	47	*3.2*	118	3	7
24	13	11	—	40	*2.1*	145	3	9
25	19	11	—	34	—	177	3	12
30	38	37	—	40	—	353	13	43
35	51	39	—	42	—	623	22	85
40	56	35	—	48	—	870	30	126
45	59	68	—	66	—	1093	34	175
50	73	116	—	105	*2.0*	1302	33	205
55	83	230	*2.5*	154	*3.2*	1397	30	213
60	80	211	*2.0*	130	*2.1*	1326	25	169
65	76	458	*5.3*	132	*2.0*	1072	15	112
70	48	701	*9.2*	80	—	716	8	59
71	43	701	*9.9*	89	—	645	8	52
72	43	34	—	98	*2.7*	587	5	40
73	38	34	—	100	*3.5*	521	5	29
74	37	35	—	98	*3.1*	454	4	25
75	36	45	—	98	*2.8*	386	3	22
76	35	45	—	115	*3.3*	338	3	16
77	35	45	—	112	*3.0*	278	3	15
78	37	68	—	119	*2.5*	231	2	10

*Cancers of the pancreas, lung, brain, kidney, and large intestine (see Table 3).
†R = Mean cumulative dose of external radiation.
‡*t*-values greater than the critical value of 2.0.

the youngest age group (21 yr with 6 cases and 43 controls), the observed and expected radiation doses were 39 and 8 ($t + 2.3$). In the next three age groups (22–24 yr), differences between observed and expected doses remained statistically significant, but from 25 to 45 yr there was nothing to choose between the observed and expected doses. Thereafter there was a steady increase in the cancer: non-cancer contrasts and by 60 yr the observed dose was 63% higher than the expected dose ($t + 2.1$). Finally, by 72 yr there was a twofold difference between the observed and expected doses ($t + 2.7$), and by 78 yr a threefold difference ($t + 2.5$).

*Table 22. Estimated doubling dose for stated ages: RES neoplasms and other selected cancers**

Age in years	Estimated doubling doses in rads: RES neoplasms	Estimated doubling doses in rads: Other selected cancers†
21	—	0.2
22	—	0.1
23	—	0.2
24	—	0.4
25	—	1.5
30	∞	49.2
35	∞	∞
40	∞	∞
45	30.0	70.4
50	13.0	17.9
55	6.2	14.6
60	6.8	18.3
65	1.2	14.8
70	0.1	16.0
71	0.1	8.7
72	—	2.5
73	—	1.1
74	—	1.1
75	—	1.2
76	—	0.8
77	—	0.9
78	—	0.9

*See Table 21 for the number of cases for each estimate.
†Cancers of the pancreas, lung, brain, kidney, and large intestine.

These findings were suggestive of greater sensitivity to the cancer-induction effects of radiation in early and late adult life than during the intervening period and this impression was re-enforced by doubling dose estimates for various ages (Table 22). These estimates were also based on RES neoplasms and solid tumors with high radiation doses, and they showed that (i) for men between 25 and 40 yr of age the exposures to external radiation probably had no delayed effects; (ii) for older men the doubling doses decreased rapidly with age; and (iii) for younger men the trend was probably in the opposite direction.

Females

Certified deaths of female workers totalled 412 and included 126 or 31% of cancers. The proportion of these workers with records of external radiation was small compared with the men and equally small for 127 women whose deaths were ascribed to cancers and 285 women with other causes of death (30%). Nevertheless, within the group of exposed workers the mean cumulative radiation dose was twice as high for cancers (133) as non-cancers (68).

Division of the cancer and non-cancer deaths of females into 4 age groups (Table 23)

Table 23. Cancer and non-cancer deaths of females by age and radiation dose

Age at death	Radiation dose levels (centirads)	No. of deaths (N)	(C)	%*	Cancers Rank	rho†	Radiation doses in centirads Totals (N)	(C)	Means for exposed workers (N)	(C)
20–49	0	71	35	33.0	(2)					
	1–	24	11	31.4	(1)					
	50–	4	3	42.9	(4)					
	100+	2	1	33.3	(3)					
	Σ	101	50	33.1		0.6	1071	564	33	38
50–59	0	31	30	49.2	(3)					
	1–	10	5	33.3	(2)					
	50–	6	2	25.0	(1)					
	100+	3	4	57.1	(4)					
	Σ	50	41	45.1		0.2	1190	2172	63	197
60–69	0	46	13	22.0	(2)					
	1–	9	1	10.0	(1)					
	50–	5	2	28.6	(3)					
	100+	6	3	33.3	(4)					
	Σ	66	19	22.4		0.8	2451	1372	123	229
70+	0	52	11	17.5	(2)					
	1–	11	—	0.0	(1)					
	50–	4	4	50.0	(3)					
	100+	1	2	66.7	(4)					
	Σ	68	17	20.0		0.8	1085	927	68	155
All ages	0	200	89	30.8	(2.25)					
	1–	54	17	23.9	(1.25)					
	50–	19	11	36.7	(2.75)					
	100+	12	10	45.5	(3.75)					
	Σ	285	127	30.8		0.60‡ ±0.29	5797	5035	68	133

*% of all certified deaths.
†See Table 11.
N = Non-cancers
C = Cancers
‡This is a significant finding at the 5% level.

showed that: (i) radiation dose levels were always higher for cancers than non-cancers; (ii) cancer: non-cancer contrasts were greater for deaths after 50 yr of age than for earlier deaths; and (iii) in three age groups the proportion of cancer deaths was highest for the top level of radiation dose (over 100 centirads).

Finally, despite the small numbers of female workers with records of external radiation, the null hypothesis of no correlation between the radiation dose and the proportion of cancer deaths after controlling for age was rejected by a correlation test. According to this test, 3 of 4 Spearman's rank correlation coefficients (between proportions of cancer deaths and radiation dose levels) were equal to or greater than 0.6 and the mean coefficient over age had a value of 0.60 ± 0.29 (which is significant at the 5% level).

Estimates of the number of cancer deaths attributable to external radiation

In the final stages of the analysis, the best estimates of risk were used to discover how many of the cancers with records of external radiation (442 cases) were attributable to these exposures (Table 24). For 14 bone marrow cancers, the estimated number of radiation-induced cases was 9.3, and for 161 cancers of the pancreas or lungs, the estimate was 18.6. The estimate for all cancers (25.8) was a fraction smaller than the sum of the estimates for the three cancers with definite radiation associations (27.9), and the estimate for all RES neoplasms (11.1) was a fraction larger than the estimate for bone marrow cancers (9.3). Therefore, the proportion of radiation-induced cancers among the exposed cases probably lay between 6 and 7%, and the corresponding proportion for all certified deaths probably lay between 1% and 2%.

*Table 24. Estimated frequency of radiation-induced cancers among certified deaths of Hanford workers**

Certified causes of death	Exposed workers Nos.	Radiation-induced cancers Nos.	%
Bone marrow	14	9.3	69.3
Pancreas	31	6.0	19.4
Lung	130	12.6	9.7
RES neoplasms	47	11.1	23.6
All cancers	442	25.8	5.8
All certified deaths	2184	25.8	1.2

*Provisional estimates for deaths during the period 1944–72.

DISCUSSION

A preliminary analysis of the records relating to external radiation has shown that there is sufficient data in the Hanford study to: (i) identify some of the more radiosensitive cancers; (ii) quantify the radiosensitivity of these neoplasms; (iii) obtain estimates of characteristic intervals between initiation and death; and (iv) recognize the ages of maximum and minimum sensitivity to the cancer induction effects of radiation.

Further analyses will be needed to rule out the now remote possibility that the positive findings were merely the result of the radiation exposures having associations with other cancer-related factors. These analyses will proceed in two directions. First, there will be joint standardization for all the factors with known or suspected radiation or cancer associations (e.g. exposure age, interval between hire and exposure, intervals between exposure and death, and depositions of radioactive substances). Secondly, there will be an extension of these analyses from non-survivors with certified causes of death to other members of the monitored population, or workers who are still alive at the time of follow-up.

Meanwhile cursory inspection of the records relating to men who were still alive in 1973 (Table 1) has shown that one of the reasons why the doses of external radiation have always been higher for survivors than non-survivors (Ma74) is because the survivors include a disproportionately large number of men with positive urine analysis (Table 25). This bias is due to an association between high risk occupations and young recruits, which has caused the proportion of young recruits to be different for: (i) singly and doubly monitored occupations; (ii) men with positive and negative urine analyses and (iii) survivors and non-survivors.

Since workers with positive urine analyses were more often and more intensively exposed to external radiation than other workers (Table 18), it is essential, when comparing survivors with non-survivors, to include internal radiation among the controlling factors. This necessity is clearly seen in Table 26 where 5 sets of standardized radiation doses are shown for 3 groups in Table 1 (survivors, non-cancers and cancers). For instance even controlling for two factors simultaneously (i.e. exposure year and cohort), still left the survivors with a higher dose (127) than the non-cancers (79) or the cancers (94), but when internal radiation was added to the other controlling factors, the standardized dose was not only lower for non-cancers (84) than cancers (112) but also lower for the survivors (101) than cancers.

Nevertheless, the absolute doses were higher for the men who were still alive in 1973 than for the non-survivors included in the present investigation, and for Hanford workers as a whole, the trend of radiation doses (and proportions of exposed workers) is in an upward direction. Therefore we should be prepared for future analyses of Hanford data to show both a wider range of cancers with definite radiation associations (due to better representation of cancers with long latent periods) and a higher proportion of radiation-induced cancers among the exposed workers.

Table 25. Age distributions of men monitored for internal and external radiation

Age at hire in years	Doubly monitored* (A) %	(B) %	Singly monitored* %	Survivors† %	Certified deaths %
Under 30	54.8	49.1	41.1	55.8	13.1
30–39	28.1	26.4	28.4	28.6	24.5
40–49	3.2	12.4	17.7	11.7	31.0
50–59	3.7	10.8	10.2	3.6	25.4
60+	0.2	1.3	2.6	0.3	6.0
Σ Nos.	12,095	3716	9128	21,206	3520
%	48.5	14.9	36.6	85.0	14.1

*Doubly Monitored = Monitored for internal and external radiation.
A = Positive urine analyses.
B = Negative urine analyses.
Singly monitored = Only monitored for external radiation.
†See Table 1.

Table 26. Standardized radiation doses of survivors and non-survivors in relation to various controlling factors

Controlling factors	Standardized radiation doses* (1)	(2)	(3)
Nil	156	63	81
Exposure year (E)	142	71	87
Cohort or year of hire (C)	138	72	90
E + C	127	79	94
E + C + internal radiation	101	84	112

*Standard (100) = External radiation doses recorded by the 1973 Survivors and certified deaths in Table 1.
(1) = 1973 Survivors.
(2) = Non-cancer deaths.
(3) = Cancer deaths.

Acknowledgements—The Hanford study is supported by the Division of Biology and Medicine, and Division of Occupational Safety of the former Atomic Energy Commission, AEC Contract No. (AT(30-1)-3394 and No. CH-AT(11-1)-3428, and ERDA Contract No. E(11-1)-3428.

The data were processed by Dr. Barkev Sanders, Dr. Allen Brodsky, Mr. Albert Becher, Viola Frost and Marceille Rice; and computer assistance was provided by the Union Carbide Nuclear Division and by the University of Pittsburgh.

Finally, we are indebted to the Hanford Environmental Health Foundation, the former Atomic Energy Commission and The Social Security Administration for continuous cooperation and assistance.

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APPENDIX
PROOFS OF STATISTICAL FORMULAE

(I) *Optimality of tests of mean doses in a linear logistic model* [after Cox (Co70)]

The assumed model is given by:

$$\ln\left(\frac{p_i}{1-p_i}\right) = \alpha + \beta x_i$$

where:

p_i = probability of individual i developing cancer;
x_i = dose of individual i; and
α and β are parameters (β for the effect of dose).
Then the log-likelihood is given by:

$$L = \sum_i z_i(\alpha + \beta x_i) - \sum_i \ln(1 + e^{\alpha+\beta x_i})$$

where:

$z_i = 1$ if individual i develops cancer, 0 otherwise, so $L = n\alpha + nr\beta - \sum_i \ln(1 + e^{\alpha+\beta x_i})$ in terms of n and r (defined in text). Since the only random variables occurring in this equation are n and (nr), they are jointly (and in fact individually) sufficient for α and β. Therefore by the principle of conditional test construction known to be optimal in such exponential type distributions, the best test of $\beta = 0$ is based on the distribution of (nr) given n and the set of values x_i. Evidently this is the permutation distribution of the mean of a sample of n from a population of size N, and this reduces by standard arguments to the t-test described in the text if N is sufficiently large and the distribution of the set x_i is suitably regular.

(II) *Estimation of the doubling dose in a linear model*

The assumed model is given by:

$$P\{\text{cancer}|\text{dose } x\} = A(1 + x/D)$$

where A = spontaneous cancer rate and D is defined as in the text. Let $P\{\text{dose } x \text{ in whole population}\} = f(x)$.

So that R (defined in text) $= \int_0^\infty xf(x)\,dx$.

Then, by Bayes theorem:

$$P\{\text{dose } x|\text{cancer}\} = \frac{A(1 + x/D)f(x)}{\int_0^\infty A(1 + x/D)f(x)\,dx}.$$

Evaluating r (the mean dose given cancer) from this formula, and simplifying, one arrives at the formula quoted in the text, since:

$$r = E\{x|\text{cancer}\} = \int_0^\infty xP\{\text{dose } x|\text{cancer}\}\,dx.$$

(III) *Validity of normal theory approximation for the t-value distributions*

The question whether the radiation dose distributions were sufficiently regular for the standard

t-test to apply) was answered by estimating the empirical distributions of the t-values by Monte Carlo simulations. In 1000 simulated random samples of size $n = 22$ (corresponding to bone marrow neoplasms) from the distribution of doses of $N = 3520$ certified deaths, only 6 random samples had t-values equal to or greater than 4.48 (or the actual t-value for the sample of bone marrow neoplasms). Thus the empirical probability is $P < 0.060$ compared with a theoretical value (based on a normal theory approximation) of $P < 10^{-4}$. A similar experiment with $n = 48$ (corresponding to pancreatic tumours) gave an empirical probability (to the t-value of 2.99 for pancreatic tumours) of $P < 0.010$ compared with a theoretical value of $P < 10^{-3}$. Thus in neither case is the probability increased so much as to give a false conclusion at the 1% level of confidence.