Relations between age at occupational exposure to ionising radiation and cancer risk

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Abstract

Objectives—To discover how the age when a given dose of ionising radiation is received (exposure age) affects the subsequent cancer risk, and whether the types of cancer caused by repeated exposure to small doses during adult life differ from naturally occurring cancers at that age.

Method—A nested case-control design with all possible controls in a cohort of nuclear workers, and a Mantel-Haenszel test (requiring only one degree of freedom) to discover whether there was any level of exposure age where the null hypothesis of no effects of radiation was rejected. This analysis was followed by inspection of how different types of cancers were related to the cancer risk.

Results—For radiation received at least 15 years before a cancer death (to allow for cancer latency) evidence of a dose related risk was found which was largely the result of exposures during the last 10 years of working life (between 55 and 65 years of age). The relative frequency of site specific cancers showed no signs of being different for radiogenic and idiopathic cancers, and there was no evidence of the exceptionally strong association between radiation and leukaemia found in atomic bomb data and other high dose situations.

Conclusions—Sensitivity to carcinogenic effects of radiation increases progressively with age during adult life and, provided the dose is too small to produce many cell deaths, the ratio of leukaemias to solid tumours is no different for radiogenic and idiopathic cancers.

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Keywords: nuclear workers; cohort analysis; exposure age

The purpose of the present paper is to show how the cancer risks of nuclear workers are related to the age when each annual dose of radiation is received (exposure age), and to discover which types of cancer are most likely to be caused by these occupational exposures. This choice of objectives was a direct consequence of two, independent analyses of exactly the same data coming to very different conclusions. Thus, according to Gilbert *et al* (whose method of statistical analysis made no

allowance for any cancer modifying effects other than lag period)

“Updated analyses of mortality of workers at the Hanford site provide little evidence of a positive correlation with cumulative occupational radiation dose and mortality from leukaemia and from all cancer except leukaemia. Estimates of the excess relative risk per 10 mSv are consistent both with no risk and with estimates obtained through extrapolation from high-dose data”.¹

But, according to Kneale and Stewart (whose analysis allowed for cancer modifying effects of three factors other than radiation dose)

“by a conservative estimate, about three per cent of the pre 1987 cancer deaths of Hanford workers had occupational exposures to external radiation as the critical (induction) event. These radiogenic cancers were evenly distributed between five diagnostic groups, but as a result of there being greater sensitivity to ‘cancer induction by radiation’ after than before 50 years of age, they were concentrated among the cancers which proved fatal after 70 years of age”.²

In the Gilbert *et al* analysis comparisons between the nuclear workers and national statistics (standardised mortality ratio (SMR) analysis) were followed by an attempt to estimate the excess relative risk with the person-year formulation of the Breslow and Day linear model of relative risk and observing the effect of different lag periods (ERR analysis).³ In the ERR analysis by Kneale and Stewart an alternative formulation of the Breslow and Day model was used—that is, the Cox risk set formulation,⁴ as this allowed modelling for any dependence of the cancer risk on factors such as the age when each annual dose of radiation was received (exposure age), the calendar year of each annual dose (exposure year), and the interval after exposure (cancer latency).

The two discordant analyses of Hanford data have since been followed by an analysis of pooled data from the United States, Canadian, and United Kingdom nuclear facilities.⁵ On this occasion the ERR analysis of Gilbert *et al* was used to show that the excess relative risk of leukaemia and other malignant neoplasms was not significantly different from estimates based on atomic bomb data. There was no attempt to discover how the numerous exposure ages of long term workers influenced the cancer risk, and no mention of any Kneale *et al* analyses of Hanford data.^{2,6} Hence the need for further tests of age related effects of radiation, bearing in mind how little is known about these effects in situations where there

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Table 1 Specifications of 2054 cancer cases

Specifications	Cancer cases			
	A	B	Total	B(%)
Birth dates:				
1875-89	50	14	64	21.9
1890-99	220	43	263	16.3
1900-09	517	60	577	10.4
1910-19	656	54	710	7.6
1920-29	312	15	327	4.6
1930-39	85	5	90	4.4
1940+	23	—	23	
Death dates:				
1944-59	152	3	155	4.9
1960-64	122	11	133	
1965-69	205	17	202	8.4
1970-74	272	34	306	11.1
1975-79	360	42	402	10.4
1980-84	449	56	505	11.1
1985-89*	323	28	351	8.0
Cancers sites (ICD No):				
Digestive (150-159)	484	45	529	8.5
Respiratory (160-163)	581	49	630	7.8
Genitourinary (180-189)	242	54	296	18.2
Neoplasms of the reticuloendothelial system (200-209)	198	20	218	9.2
Other and unspecified	358	23	381	6.0
Total	1863	191	2054	9.3

A = cases where cancer was the underlying cause of death; B = cases where cancer was a contributory cause of a non-cancer death.

*Incomplete identification of death certificate data, mainly affecting deaths outside the State of Washington.

are multiple exposures of the same person, and no question of cell killing effects of the radiation evoking the usual responses to life threatening situations.

Materials and methods

BASIC ASSUMPTIONS AND METHODOLOGY

In accordance with well established radiobiological principals, separate doses of radiation should act independently, and the total effect of several separate doses should equal the sum of each effect. Nevertheless, according to atomic bomb data (which describe the effects of a single exposure to a wide range of radiation doses) observable effects of the radiation were modified both by the age of the recipient (exposure age), and the duration of the period after exposure (cancer latency).⁸ It follows that, in situations where most of the people have repeated exposure to many small doses, the excess relative risk of cancer death at a particular point in time can only be accurately predicted as a weighted sum of the separate doses, with weights depending on the age when each component of a total individual dose is received, and the duration of each period after exposure.

In a cohort study of nuclear workers, this model of excess relative risk requires a statistical model the parameters of which can, in theory, be estimated by a standard statistical

package such as generalised linear models (GLIM). There are, however, many practical problems, including the fact that an individual worker could have 30 annual doses (each with a different exposure age and period after exposure) or 900 combinations of his or her total dose each with a separate weighting in the statistical model. This number could be reduced to 60 by assuming that each pair of exposure age dose weights and latency dose weights is a product of the two factors. But even so, the parameters would have to be further reduced by assuming specific parametric forms for 30 dose weights of age and 30 dose weights of latency.

In the 1993 analysis of Hanford data by Kneale and Stewart the parametric forms were step functions. In other words, for all exposure ages below a critical age (determined by the parameter) the dose weight was zero, and for all higher exposure ages there was a constant weight. The latency factor was treated in exactly the same way and thus was equivalent to the "dose lagging" procedures of Gilbert *et al.*¹ However, the constraints of this model prevented consideration of more than one modifying factor, and the alternative model of Kneale and Stewart had no such constraints and produced both a critical value for minimal latency that was close to 15 years and a critical value for the youngest exposure age with any detectable effects of the radiation that was close to 60 years. Kneale and Stewart also showed that their second modifying factor (exposure age) was the principle reason why they found evidence of a dose related cancer risk—which was robust to a wide range of possible sources of error or confounding—and Gilbert *et al.* failed to do so.²

The Kneale and Stewart findings for exposure age have not gained wide acceptance, possibly because they conflict with official interpretations of atomic bomb data.⁹ Hence, the present attempt to show that, *if there is earlier expectation that the minimum cancer latency is close to 15 years, and that the cancer induction risk is different during early and late phases of adult life*, then a relatively simple analysis of Hanford data would allow one to see the part played by exposure age in the cancer risks of nuclear workers and other people repeatedly exposed to low doses of ionising radiation.

MATERIALS AND STATISTICAL ANALYSIS

The Hanford data have already been described.^{1,2} They include records of 35 868 badge monitored workers (mostly men) whose employment ages ranged from 18 to 65 years, and whose employment periods ranged from less than one to more than 30 years; and for each worker there was a set of annual doses of external penetrating radiation compiled from daily or weekly doses recorded on film badges. The mean annual dose rate was less than 1 mSv, and there were only 18 times when the maximal permissible dose of 50 mSv per annum was exceeded. For the period 1944-78 the total cumulative dose was 831 Sv, and for the period 1944-89 the number of ascertained deaths was 7874. For 1863 of these deaths,

Table 2 Recorded doses of 2045 cancer cases by interval before death

Interval before death (y)	Exposure age (y)	Dose (mSv)	
		Total	Mean
0-14 (lag period)	All ages	223 081	108.6
≥ 15 (excluding lag period):			
< 35		49 960	24.3
35-44		108 650	52.9
45-54		128 115	62.4
≥ 55		834 268	40.5
All ages		369 993	180.1
Total	All ages	593 1074	288.7

Table 3 Cancer cases in 334 informative risk sets

Final years	Cancer cases by death ages (y)											Total
	< 25	< 30	< 35	< 40	< 45	< 50	< 55	< 60	< 65	< 70	≥ 75	
1944	—	—	—	—	—	1	—	—	—	—	—	1
1945	—	1	—	—	—	—	—	1	—	—	—	2
1946	—	—	—	—	—	—	—	—	—	—	—	1
1947	—	1	—	—	—	1	—	1	—	—	—	3
1948	—	1	—	1	1	—	1	1	—	—	—	5
1949	—	1	—	1	1	—	2	2	—	—	—	7
1950	—	—	—	1	—	—	1	3	—	—	—	5
1951	1	1	—	—	1	4	1	1	2	—	—	11
1952	—	1	—	—	1	2	3	1	1	—	—	9
1953	—	1	1	2	3	2	3	3	1	—	—	16
1954	—	—	2	—	1	2	3	1	—	3	—	12
1955	—	2	—	1	1	2	1	4	1	—	—	12
1956	—	—	1	1	2	1	2	1	4	1	—	13
1957	—	—	1	—	2	3	5	2	1	2	—	16
1958	—	1	1	4	3	2	1	4	4	1	1	22
1959	—	—	—	—	5	3	3	4	2	2	1	20
1960	—	—	—	2	1	3	3	4	5	2	2	22
1961	—	—	4	4	1	1	—	4	5	—	3	22
1962	—	1	2	—	4	4	6	1	5	4	2	29
1963	—	—	—	1	1	3	7	10	6	2	1	31
1964	1	—	—	2	5	1	3	7	5	4	1	29
1965	—	—	—	2	2	4	4	6	7	8	2	35
1966	—	—	—	—	1	4	6	3	2	4	6	26
1967	—	1	3	1	—	7	11	6	7	4	2	42
1968	—	—	2	4	2	1	7	11	11	3	2	43
1969*	—	1	2	1	4	3	8	10	12	12	3	56
1970	—	1	—	—	4	10	12	8	10	4	8	57
1971	—	—	—	2	1	8	14	13	9	11	9	67
1972	1	—	—	2	3	4	8	13	10	7	10	58
1973	—	1	1	3	4	7	6	12	12	8	8	62
1974	—	—	—	2	2	10	9	9	7	7	16	62
1975	—	—	2	1	3	4	12	15	13	8	9	67
1976	—	—	—	2	2	7	6	24	9	16	14	80
1977	—	3	—	—	1	9	7	17	9	16	16	78
1978	1	—	1	3	3	6	10	19	16	13	17	89
1979	—	—	2	3	6	4	7	16	17	15	18	88
1980	—	—	—	1	2	7	15	14	21	21	21	102
1981	—	—	1	2	2	3	7	12	29	16	14	86
1982	—	—	1	—	3	2	19	9	22	16	29	101
1983	—	—	—	2	4	3	10	11	34	15	24	103
1984	—	—	—	3	2	4	11	17	25	21	30	113
1985	—	—	—	—	3	2	12	13	21	19	32	102
1986	1	—	—	2	5	6	7	11	11	22	37	102
1987	—	—	—	—	—	3	3	11	9	14	20	60
1988	1	—	—	—	1	2	4	3	8	10	17	46
1989	—	—	1	—	—	2	—	4	10	8	16	41
Total	6	18	28	56	93	157	260	343	383	319	391	2054

*See tables 5 and 6.

All the cancer cases in each final year have birth cohort in common with one another and with the controls in table 4.

cancer was the underlying cause, and for a further 191 deaths, cancer was a contributory cause (table 1). For the combined series of 2054 cancer related deaths the mean dose was 289 mSv, and for radiation received at least 15 years before death (prelag doses) the mean was 180 mSv (table 2).

In the 1993 analysis of these data there were so many controlling factors that the number of informative risk sets (or risk sets containing one or more cancer cases) was only a fraction smaller than the total number of cancer cases, and there were no sets with more than five cases.² By having only the two controlling factors that are essential for any cohort analysis (date of birth and date of death), the number of informative risk sets was reduced to 334, and there were 49 sets with more than a dozen cases (tables 3 and 4).

The number of cases and controls in the 334 informative risk sets ranged from 58 for one of the 10 sets whose final year was 1958 (one case and 57 controls), to 3770 for one of the eight sets whose final year was 1977 (nine cases and 3761 controls), and in four of the 32 sets with cancer related deaths after 74 years of age, there were more than 25 cases.

The much larger number of controls than cases in each risk set was the result of the Cox methodology making it necessary (a) to

include, in each set of each final year, all the workers from a specific birth cohort who were still alive at the beginning of the final year, and (b) to restrict the cases to workers who recorded a cancer related death during this one year.⁴ With Hanford data in this formation we had the equivalent of a case-control study embedded in a cohort study. This meant that the likelihood function formula recommended by Breslow and Day for use in conventional case-control studies could be applied, since each of the 334 informative risk sets now corresponded to a single stratum in a Mantel-Haenszel analysis.

When it came to estimating the excess relative risk, the number and size of the informative risk sets threatened to create a computer storage problem. This was avoided with (as a test of the null hypothesis of no radiation effects) a later modification of the original Mantel-Haenszel procedures.¹⁰ With this Mantel method for testing trends of relative risk with increasing dose there is only one degree of freedom. Therefore, it was no longer necessary to store more than the mean doses of each risk set and their mean squares. This saving of computer space was important as, for each annual dose, we needed five separate components, one for lag period exposures, and four for age specific prelag exposures.

Table 4 Matched controls of the cancer cases in table 3 and in 344 informative risk sets

Final years	Death ages of the cancer cases										
	< 25	< 30	< 35	< 40	< 45	< 50	< 55	< 60	< 65	< 70	≥ 75
1944	—	—	—	—	—	188	—	—	—	—	—
1945	—	1324	—	—	—	—	—	104	—	—	—
1946	—	—	—	—	—	—	—	136	—	—	—
1947	—	1731	—	—	—	593	—	170	—	—	—
1948	—	2030	—	1301	990	—	419	206	—	—	—
1949	—	2107	—	1453	1116	—	476	240	—	—	—
1950	—	—	—	1593	—	—	526	287	—	—	—
1951	2504	2498	—	—	1254	1008	600	330	139	—	—
1952	—	2654	—	—	1463	1050	691	376	165	—	—
1953	—	2781	2656	2283	1596	1171	730	432	196	—	—
1954	—	—	2727	—	1752	1288	801	484	—	78	—
1955	—	3151	—	2644	1947	1244	1049	533	274	—	—
1956	—	—	2977	2822	2127	1432	1071	593	311	128	—
1957	—	—	3061	—	2348	1609	1118	671	341	150	—
1958	—	3019	3164	2945	2500	1747	1238	711	384	176	57
1959	—	—	—	—	2627	1852	1342	787	427	200	79
1960	—	—	—	2981	2734	1986	1265	1022	473	233	93
1961	—	—	3355	3084	2883	2112	—	1020	531	—	122
1962	—	2696	3267	—	2915	2317	1571	1044	600	283	140
1963	—	—	—	3289	2997	2476	1680	1156	610	312	176
1964	1777	—	—	3436	3018	2609	1786	1243	678	348	196
1965	—	—	—	3524	3045	2730	1926	1181	883	379	233
1966	—	—	—	—	3156	2876	2062	1321	877	429	267
1967	—	2169	2966	3443	—	2923	2259	1469	918	463	296
1968	—	—	2793	3385	3386	3015	2417	1585	1017	489	322
1969*	—	2232	2579	3340	3539	3048	2548	1693	1089	551	357
1970	—	2208	—	—	3623	3084	2667	1825	1041	722	408
1971	—	—	—	3206	3625	3211	2818	1937	1156	711	467
1972	1452	—	—	3099	3575	3295	2852	2122	1293	745	510
1973	—	2004	2459	2942	3493	3428	2936	2271	1405	823	529
1974	—	—	—	2823	3479	3613	2986	2416	1505	862	594
1975	—	—	2658	2742	3458	3707	3054	2512	1636	844	760
1976	—	—	—	2772	3475	3732	3216	2652	1749	967	781
1977	—	2697	—	—	3457	3761	3360	2715	1916	1091	825
1978	2740	—	2887	3075	3390	3745	3532	2817	2052	1216	909
1979	—	—	2825	3080	3189	3709	3701	2864	2179	1308	1009
1980	—	—	—	3098	3056	3646	3782	2957	2271	1410	1143
1981	—	—	2846	3000	2999	3571	3763	3109	2423	1502	1254
1982	—	—	2947	—	3013	3472	3713	3228	2483	1637	1403
1983	—	—	—	2868	3042	3341	3638	3371	2578	1761	1554
1984	—	—	—	2801	3049	3144	3606	3526	2634	1877	1686
1985	—	—	—	—	3068	3024	3546	3584	2725	1966	1855
1986	795	—	—	2823	2974	2959	3478	3565	2878	2096	2016
1987	—	—	—	—	—	2966	3379	3534	2983	2168	2221
1988	295	—	—	—	2846	3002	3258	3475	3149	2281	2530
1989	—	—	2656	—	—	3017	—	3473	3306	2400	2840

*See tables 5 and 6.

All the controls in each final year have birth cohort in common with one another and with the cancer cases in table 3.

Results

EXPOSURE AGE EFFECTS

With the cancer related deaths stretching from 1944–89, it was necessary to repeat 46 times simple hand calculations of observed and expected doses for five subdivisions of the total dose for each final year. Tables 5 and 6 only show the workings for one of these years, 1969, with 56 cases and 10 risk sets. But this is sufficient to show each step of a process which allowed for latency effects by having two expo-

sure periods (lag and prelag), and for exposure age effects by having four levels of age specificity for all prelag exposures (< 35; 35–44, 45–54 and > 55 years).

In 1969 there were no cancer deaths before 30 years of age (table 3). This still left 10 sets of total and mean doses for the lag period, and 16 sets of total and mean doses for the prelag period (table 5). For example, in the set which included three cancer deaths after 75 years of age and 357 controls, there were the usual

Table 5 Total and mean doses (mSv) for 10 informative risk sets (1969 cancer deaths)

Interval before death (y)	Exposure age (y)	Death age (y)	Death age (y)									
			< 30	< 35	< 40	< 45	< 50	< 55	< 60	< 65	< 70	≥ 75
< 15 y (lag period)	Total	a	40 317	53 441	84 095	82 984	72 553	70 932	42 357	18 958	2566	207
		b	18.1	20.7	25.2	23.4	23.8	27.8	24.9	77.2	4.6	0.6
> 15 y (excluding the lag period):	< 35	30–59	61	2461	11 746	16 670	10 134	4027	—	—	—	—
		a	0.0	1.0	3.5	4.7	3.3	1.6	—	—	—	—
	35–44	50–69	—	—	—	—	6402	11 541	6114	1488	—	—
		a	—	—	—	—	2.1	4.5	3.6	1.4	—	—
	45–54	60+	—	—	—	—	—	—	3438	4528	1860	436
		a	—	—	—	—	—	—	2.0	4.1	3.3	1.2
	55+	70+	—	—	—	—	—	—	—	—	894	1047
		a	—	—	—	—	—	—	—	—	1.6	2.9
		b	—	—	—	—	—	—	—	—	4.9	4.7
	Total	a	61	2461	11 746	16 670	16 536	15 568	9553	6016	2754	1484
		b	0.0	1.0	3.5	4.7	5.4	6.7	5.6	5.5	4.9	4.7
All intervals:	Total	a	40 378	55 902	95 841	99 654	89 089	86 500	51 909	24 974	5320	1691
		b	18.7	21.7	28.7	28.1	29.2	33.8	30.5	22.7	9.4	4.7
Cancer cases (n)			1	2	1	4	3	8	10	12	12	3
Matched controls (n)			2232	2579	3340	3539	3048	2548	1693	1089	551	357

a = Dose for all members of each informative risk set; b = mean worker dose.

Table 6 Observed and expected doses (mSv) for 10 informative risk sets (1969 cancer deaths)

Interval before death (y)	Exposure age (y)	Death age (y)	Death age (y)										Total dose	Ratio O:E	
			< 30	< 35	< 40	< 45	< 50	< 55	< 60	< 65	< 70	≥ 75			
< 15 y (lag period): Total			O	21	61	9	83	20	157	370	176	27	0	924	0.94
		E	18.1	41.4	25.2	93.6	71.4	222.4	249.0	206.4	55.2	1.8	984.5		
> 15 y (excluding the lag period):															
< 35	30-59	O	—	—	3	40	3	7	—	—	—	—	53	1.13	
		E	0.0	2.0	3.5	18.8	9.9	12.8	—	—	—	—	47.0		
35-44	50-69	O	—	—	—	—	1	41	25	13	—	—	80	0.84	
		E	—	—	—	—	6.3	36.0	36.0	16.8	—	—	95.1		
45-54	60+	O	—	—	—	—	—	—	28	35	86	1	150	1.33	
		E	—	—	—	—	—	—	20.0	49.2	39.6	3.6	112.4		
≥ 55	70+	O	—	—	—	—	—	—	—	—	27	10	37	1.33	
		E	—	—	—	—	—	—	—	—	19.2	8.7	27.9		
Total			O	0	0	3	40	4	48	53	48	113	11	320	1.13
		E	0.0	2.0	3.5	18.8	16.2	48.8	56.0	66.0	58.8	12.3	282.4		
All Intervals:															
Total		O	21	61	12	123	24	205	423	224	140	11	1244	0.98	
		E	18.1	43.4	28.7	112.4	87.6	270.4	305.0	272.4	112.8	14.1	1264.9		
Cancer cases (n)				1	2	1	4	3	8	10	12	12	3	56	

O = Observed doses for all cancers in each informative risk set; E = expected dose or mean worker dose times the number of cancer cases.

(four) choices of age for any prelag exposures, but there were no such exposures before 45 years. For the next 10 years of age (45-54) the total dose was 436 mSv and the mean 0.8 mSv, and for all later exposures the total dose was 1047 mSv and the mean 2.9 mSv. Both for the 10 groups of lag period exposures, and for the 16 groups of prelag exposures we have (table 6) observed and expected doses for the cases, the expected being based on the relevant mean dose in table 5. Thus, for the three cases over 74 years of age the observed doses were: zero for the lag period, 1 mSv for prelag exposures before 55 years, and 10 mSv for later prelag exposures, and the expected doses were 1.8, 3.6, and 8.7 mSv.

Table 6 also shows the O:E ratios for the 56 cases under three headings: (a) all lag period and prelag exposures with a total dose of 1244 mSv and an expected dose of 1264.9 mSv (ratio 0.98); (b) lag period exposures only, with a total dose of 924 mSv and an expected dose of 984.5 mSv (ratio 0.94), and (c) prelag exposures only, with a total dose of 320 mSv and an expected dose of 282.4 mSv (ratio 1.13). Finally, for the four groups of age specific prelag doses the O:E ratios were 1.13 (< 35 years); 0.84 (35-44 years); and 1.33 (45-54 and > 55 years).

For the complete series of 2054 cancer cases (with 334 risk sets distributed between 46 final years) the O:E ratios were 1.01 for all exposures (total dose of 59 292 mSv), 0.78 for the lag period exposures (total dose of 22 362 mSv), and 1.22 for the remaining, prelag exposures (total dose of 36 930 mSv, table 7). For four groups of age specific prelag doses the ratios were 1.06 (< 35 years); 1.15 (35-45 years); 1.11 (45-54 years), and 1.78 (> 55 years).

Table 7 also shows how the findings for the total follow up period (1944-89) compare with two shorter periods, 1944-75 with 796 cancer cases in 235 risk sets, and 1944-84 with 1703 cases in 298 risk sets. For each follow up period the O:E ratio was higher for prelag than lag period doses, and higher for prelag exposures after 55 years of age than for earlier exposures. But it was not until the follow up period exceeded 40 years that all O:E ratios for prelag exposures were greater than 1.0. For prelag exposures with the highest O:E ratio (1.78) the observed and expected dose were 8321 and 4666 mSv. According to the χ^2 test of Mantel¹⁰ this is a highly significant difference ($P < 0.0001$). Therefore, despite the need for separate consideration of five components of each total dose, a remarkably simple analysis has provided strong support for an earlier conclusion of Kneale and Stewart, namely, that the cancer risk after exposure to radiation is much greater for exposures after than before 50 years of age. But also note that with the Gilbert *et al* model (which only incorporates lag or latency effects) we would have been left with 36 930 mSv as the observed dose and 30 303 for the expected dose, and an O:E ratio of 1.22, which was only of doubtful significance.

TWO TYPES OF RADIOGENIC CANCER

Although there has never been any suggestion of a special relation between leukaemia and radiation either in the Hanford data or in studies of carcinogenic effects of prenatal x ray films,¹¹ uniform ERRs for several types of adult cancer are relatively recent findings.² Therefore, in table 8, the cancer cases whose prelag doses for exposures after 55 years of age were

Table 7 Observed and expected doses for ascertained cancers in three follow up periods

Follow up period (ascertained cancers)	Exposure period	Exposure age (y)	Dose (mSv)		Ratio O:E
			O	E	
1944-74 (796)	All	all ages	13 975	14 921	0.94
	Lag	all ages	10 234	11 602	0.88
		< 35	642	696	0.92
	Prelag	35-44	1477	1221	1.21
		45-54	1121	1028	1.09
1944-84 (1703)	All	all ages	40 441	47 223	0.86
	Lag	all ages	19 631	26 546	0.74
		< 35	2929	3305	0.89
	Prelag	35-44	6694	6581	1.02
		45-54	6917	7875	0.88
1944-89 (2054)	All	all ages	59 292	58 816	1.01
	Lag	all ages	22 362	28 513	0.78
		< 35	4996	4709	1.06
	Prelag	35-44	10 803	9409	1.15
		45-54	12 810	11 519	1.11
Prelag exposures all ages	1944-89	≥ 55	8321	4666	1.78
			374	3319	1.13
			20 810	20 677	1.01
			36 930	30 303	1.22

Abbreviations as in table 6.

Table 8 Comparisons between all cancer cases and the high risk cases in five diagnostic groups

Types of cancer	High risk cancers*			Other cancers		
	All cases n	B series† n	(%)	All cases n	B series† n	(%)
Digestive	32	7	21.9	497	38	7.6
Respiratory	50	8	16.0	580	41	7.1
Prostate	24	9	37.5	146	29	19.9
Other genitourinary	12	2	16.7	114	14	12.3
Neoplasms of the reticuloendothelial system	16	2	12.5	202	18	8.9
Other and unspecified	29	5	34.5	352	18	5.1
Total	163	33	20.2	1891	158	8.4

*Cancers with doses from prelag exposures after 55 years of age that exceeded the expected dose; †see footnote to table 1.

greater than the expected dose (163 high risk cases) are compared with the remaining 1891 cases, after division of each group into six diagnostic categories and separate identification of the cancers that were only contributory causes of death (B series, as in table 1).

In the high risk group 100% of the deaths occurred after 75 years of age, and in the comparison group the corresponding proportion was only 12%. In both series the dominant disease was lung cancer (31%) but in the high risk subset there was better representation of cancers with exceptionally late death ages (prostate tumours) than in the comparison group, and in the B series of high risk cancers almost a quarter of the cases were prostate tumours. In short, apart from a tendency for cancers with late death ages to concentrate in a series which was, by definition, restricted to deaths after 70 years of age, there were no detectable differences between these elderly cases and the remaining 1891 deaths related to cancer. And the proportion of leukaemias and other reticuloendothelial system neoplasms was certainly no higher for the high risk cases (10%) than the other cases (11%).

Discussion

People who are approaching the end of the life span are exceptionally sensitive to all causes of death. Therefore, the idea that old people are less sensitive to carcinogenic effects of radiation than young adults is totally out of line with normal experience. This common assumption is the result of the Radiation Effects Research Foundation (RERF) both finding a lower excess relative risk for atomic bomb survivors who were over 50 years of age in 1945 than for younger people,⁹ and insisting that "the survivors, apart from their radiation, are representative human beings".¹² From atomic bomb data has also come the idea that radiation is more likely to cause leukaemia than other cancers, and the idea that there were no lasting effects of the tissue damage caused by cell deaths from radiation.^{13 14}

Numerous tests of the RERF assumptions have satisfied radiation protection committees.⁸ However, an independent analysis of atomic bomb data recently found both evidence of selection effects of deaths before 1950¹⁵ and evidence of late effects of marrow damage.¹⁶ Furthermore, according to Stewart—who has long suspected that the

exceptionally high death rate for aplastic anaemia in the life span study cohort was the result of irreversible damage to the reticuloendothelial system¹⁷—the special association between leukaemia and radiation in atomic bomb data could easily be the result of a life saving leucocytosis leaving survivors at high risk of an early death from leukaemia caused by excessive numbers of mutant myelocytes and cancer promoter effects of damage to the reticuloendothelial system.⁷

Even without this last conjecture there are strong grounds for thinking that any holocaust would leave an indelible mark on a closed population of survivors, such as the life span study cohort, and that there are no exceptions to the rule that sensitivity to all causes of death relentlessly increases with age during adult life. Therefore, although the present findings of a relation between radiation effects and exposure age are at variance with official interpretations of atomic bomb data, this should not be regarded as a reason for doubting that middle aged and elderly workers are far more sensitive to effects of radiation in the induction of cancer than young recruits. Nor is it unreasonable to suggest that cell killing as well as mutational effects of the atomic bomb radiation contributed to the high death rate from myeloid leukaemia in the life span study cohort.

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