Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria

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Abstract

Objective—To examine whether the observed excess of childhood leukaemia and lymphoma near the Sellafield nuclear plant is associated with established risk factors or with factors related to the plant.

Design—A case-control study.

Setting—West Cumbria health district.

Subjects—52 Cases of leukaemia, 22 of non-Hodgkin's lymphoma, and 23 of Hodgkin's disease occurring in people born in the area and diagnosed there in 1950-85 under the age of 25 and 1001 controls matched for sex and date of birth taken from the same birth registers as the cases.

Main outcome measures—Antenatal abdominal *x* ray examinations, viral infections, habit factors, proximity to and employment characteristics of parents at Sellafield.

Results—Expected associations with prenatal exposure to *x* rays were found, but little information was available on viral illnesses. Relative risks for leukaemia and non-Hodgkin's lymphoma were higher in children born near Sellafield and in children of fathers employed at the plant, particularly those with high radiation dose recordings before their child's conception. For example, the relative risks compared with area controls were 0·17 (95% confidence interval 0·05 to 0·53) for being born further than 5 km from Sellafield 2·44 (1·04 to 5·71) for children of fathers employed at Sellafield at their conception, and 6·42 (1·57 to 26·3) for children of fathers receiving a total preconceptual ionising radiation dose of 100 mSv or more. Other factors, including exposure to *x* rays, maternal age, employment elsewhere, eating seafood, and playing on the beach did not explain these relationships. Focusing on Seascale, where the excess incidence has predominantly been reported, showed for the four out of five cases of leukaemia and one case of non-Hodgkin's lymphoma whose fathers were employed at Sellafield and for whom dose information was obtained that the fathers of each case had higher radiation doses before their child's conception than all their matched control fathers; the father of the other Seascale case (non-Hodgkin's lymphoma) was not employed at the plant. These results seem to explain statistically the geographical association. For Hodgkin's disease neither geographical nor employment associations with Sellafield were found.

Conclusions—The raised incidence of leukaemia, particularly, and non-Hodgkin's lymphoma among children near Sellafield was associated with paternal employment and recorded external dose of whole body penetrating radiation during work at the plant before conception. The association can explain statistically the observed geographical excess. This result suggests an effect of ionising radiation on fathers that may be leukaemogenic in their offspring, though other, less likely, explanations are possible. There are important potential implications for radiobiology and for protection of radiation workers and their children.

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Introduction

There has been concern about levels of childhood cancer around nuclear installations in the United Kingdom since 1983, when a Yorkshire Television programme (*Windscale: the Nuclear Laundry*) suggested that there was an excess of leukaemia near Sellafield. Several studies have been carried out since,[1] and the one reported here was a direct consequence of a recommendation of the Black committee (of which MJG was a member).[2] This investigation was a case-control study of leukaemia and lymphoma among young people in West Cumbria specifically asking whether known causes or factors associated with the nuclear site might have been responsible for the observed excess.

Methods

The design of the study, methods of data collection, and basic information are described in detail in the accompanying paper (p 429).[3] Essentially all identified cases of leukaemia and lymphoma among people born in West Cumbria and diagnosed there at ages under 25 during 1950-85 were compared with controls matched by sex and date of birth selected—both unmatched (area controls) and matched (local controls) for civil parish of residence—from the same birth register into which the case's birth was entered. For both types of control up to eight controls were included in the analysis for each case, some of whom were both area and local controls. Comparisons were carried out using data from birth and medical records, from questionnaires to parents of cases and controls, and from employment and radiation records held by British Nuclear Fuels.

The analysis was carried out within the sets of cases and area or local controls, and findings are presented as relative risks with confidence intervals. The results were calculated using conditional logistic regression analysis,[4] which produces estimates of odds ratios that approximate closely to relative risks, with the computer program EGRET.[5] Unless otherwise stated the relative risks are for presence compared with absence of each factor; where specifically mentioned in tables relative risks are for the first compared with the second grouping, except in ionising radiation dose categories, where the risks are relative to the unexposed group.

Results and comment

Findings are shown for leukaemia alone and for leukaemia and non-Hodgkin's lymphoma combined (see accompanying paper) for area and local controls

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separately. Because some controls, who were entered closely adjacent to a case in the birth register, were both area and local controls these two analyses by control type were not completely independent statistically—for example, for the 52 leukaemia cases there were 217 area only controls, 207 local only controls, and 140 who were both (see table III of accompanying paper[3]). Results for non-Hodgkin's lymphoma are presented here only in combination with leukaemia for the reasons given in the accompanying paper and because the numbers were smaller. Numbers of individuals included in the analyses for different factors varied with the availability of data, and the number of case-control sets is given by the total number of cases. Results for Hodgkin's disease are not given in detail as they did not show any important associations with analysed factors in the same way as leukaemia and non-Hodgkin's lymphoma.

ANTE-NATAL X RAYS

Table I shows relative risks for leukaemia and non-Hodgkin's lymphoma associated with maternal abdominal radiographic examinations according to whether the information was obtained from obstetric records or questionnaire responses. The relative risks ranged from about 1·2 to 1·7, comparable to levels reported in earlier studies. This study was too small for meaningful analysis by number of films or trimester of exposure.

For cases of Hodgkin's disease a report of an abdominal *x* ray examination was made for none of the six mothers for whom we located obstetric records and by two of the 12 parents who responded on the questionnaire.

TABLE I—*Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by maternal exposure to abdominal x rays in pregnancy according to medical records and questionnaires*

Source of *x* ray information	Type of control	Cases		Controls		Relative risk	95% Confidence interval
		Total	No exposed to *x* rays	Total	No exposed to *x* rays		
		Leukaemia					
Medical records	Area	20	3	116	15	1·15	0·31 to 4·28
	Local	20	3	109	13	1·21	0·31 to 4·66
Questionnaire	Area	35	4	116	9	1·74	0·44 to 6·82
	Local	34	4	104	11	1·19	0·33 to 4·31
		Leukaemia and non-Hodgkin's lymphoma					
Medical records	Area	28	5	167	25	1·19	0·43 to 3·32
	Local	28	5	153	20	1·34	0·46 to 3·88
Questionnaire	Area	47	5	152	14	1·32	0·43 to 4·08
	Local	45	5	143	15	1·14	0·37 to 3·53

TABLE II—*Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by some suspected risk factors*

Suspected risk factor	Type of control	Cases		Controls		Relative risk	95% Confidence interval
		Total	Positive	Total	Positive		
		Leukaemia					
Maternal viral infection in pregnancy	Area	35	2	119	7	1·12	0·22 to 5·67
	Local	35	2	103	6	1·23	0·22 to 7·04
Caesarean delivery	Area	20	2	116	8	1·38	0·27 to 6·99
	Local	20	2	109	9	1·17	0·24 to 5·81
Social class* (birth certificate)	Area	44	9	293	54	1·14	0·50 to 2·60
	Local	44	9	287	75	0·61	0·25 to 1·47
Social class* (questionnaire)	Area	20	5	51	16	0·90	0·24 to 3·34
	Local	19	5	54	21	0·60	0·17 to 2·10
Mother's age (≥25 *v* <25 years)	Area	52	32	351	220	0·94	0·51 to 1·72
	Local	52	32	344	213	0·96	0·52 to 1·78
Mother's age (≥40 *v* <25 years)	Area	52	4	351	6	4·94	1·11 to 21·85
	Local	52	4	344	8	3·38	0·88 to 13·03
Father's age (≥25 *v* <25 years)	Area	46	38	287	220	1·42	0·63 to 3·18
	Local	46	38	276	213	1·43	0·61 to 3·33
Father's age (≥40 *v* <25 years)	Area	46	6	287	26	1·87	0·59 to 5·91
	Local	46	6	276	24	2·27	0·66 to 7·76
Birth weight (≥3·5 *v* <3·5 kg)	Area	18	7	99	42	0·88	0·32 to 2·42
	Local	18	7	94	41	0·84	0·29 to 2·42
		Leukaemia and non-Hodgkin's lymphoma					
Maternal viral infection in pregnancy	Area	47	2	156	12	0·69	0·15 to 3·24
	Local	46	2	144	8	0·94	0·18 to 4·87
Caesarean delivery	Area	28	2	167	15	0·75	0·16 to 3·56
	Local	28	2	153	11	0·95	0·20 to 4·50
Social class* (birth certificate)	Area	64	14	418	75	1·33	0·68 to 2·59
	Local	64	14	408	100	0·70	0·33 to 1·49
Social class* (questionnaire)	Area	26	7	70	20	1·11	0·34 to 3·64
	Local	25	7	75	30	0·61	0·21 to 1·79
Mother's age (≥25 *v* <25 years)	Area	74	47	492	311	0·99	0·60 to 1·65
	Local	74	47	484	305	0·99	0·59 to 1·66
Mother's age (≥40 *v* <25 years)	Area	74	7	492	10	5·08	1·66 to 15·53
	Local	74	7	484	12	4·03	1·41 to 11·52
Father's age (≥25 *v* <25 years)	Area	66	52	403	318	0·95	0·50 to 1·79
	Local	66	52	389	304	1·00	0·51 to 1·93
Father's age (≥40 *v* <25 years)	Area	66	9	403	34	1·51	0·60 to 3·78
	Local	66	9	389	34	1·58	0·60 to 4·16
Birth weight (≥3·5 *v* <3·5 kg)	Area	26	11	149	62	1·01	0·44 to 2·34
	Local	26	11	137	64	0·86	0·37 to 2·01

*Social class of father at child's birth: I, II, III non-manual *v* III manual, IV, V.

VIRAL INFECTIONS AND OTHER SUSPECTED RISK FACTORS

Only one episode of viral infectious illness during pregnancy was recorded in the hospital records examined, so analysis was restricted to data from the questionnaires. Results for any episode of chickenpox, shingles, influenza, measles, or rubella are given in table II, with no strong finding. Also shown are relative risks, again based on small numbers, for delivery by caesarean section based on information from obstetric records.

Findings are given for social class based on occupation at birth as recorded on each of birth certificates and questionnaires, and the similar results reflect the high level of agreement between the data sources. The table shows relative risks around unity for a broad higher social class category in relation to area controls but lower values for local controls. More detailed analysis did not identify any strong trends by social class.

Relative risks around unity were also found for maternal age at birth of 25 or older compared with under 25 years. For mothers of 40 or older, however, when examined in a comparison of all age groups—that is, <25, 25-29, 30-34, 35-39, and ≥40 years—relative risks were about 4. The latter finding was much less strong for fathers. Birth weight, from obstetric records, showed no particular relation in either the broad categories listed or smaller groups.

For Hodgkin's disease there were no important relationships with any of the above factors including parental ages.

QUESTIONNAIRE HABIT FACTORS

Table III shows findings based on the behavioural data obtained by questionnaire. The factors included, particularly those for which there were data on substantial numbers of cases, did not show any important relations with leukaemia and non-Hodgkin's lymphoma. Results for playing on the beach are shown in the table with all cases for whom information was available. Children aged under 5 years at diagnosis were less likely because of their illness to have played in the sand, and excluding these cases and their controls made little difference, with the relative risks against area controls for leukaemia alone and combined with non-Hodgkin's lymphoma becoming 0·83 and 1·04 respectively. The relative risks for play on the fells were particularly low.

Analysis by fish eating habits did not indicate any associated risk. For shellfish eating the relative risks were raised compared with area controls but not compared with local controls; the raised relative risks were, however, based on only two exposed cases (both diagnosed before 1980). Restriction of these analyses to cases born during periods when discharges from Sellafield were highest did not show any important differential relative risks. Finally, there was no evidence of any increased risk in conjunction with families growing their own vegetables or using seaweed as a fertiliser.

There were no important relationships of Hodgkin's disease with these factors.

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TABLE III—*Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by family habit factors from parental questionnaire*

Habit factor	Type of control	Cases		Controls		Relative risk	95% Confidence interval
		Total	Positive	Total	Positive		
		Leukaemia					
Play on beach (more v less often than monthly)	Area	28	13	94	47	0·89	0·37 to 2·17
	Local	28	13	92	57	0·62	0·24 to 1·59
Play on fells (more v less often than monthly)	Area	27	3	77	23	0·29	0·06 to 1·39
	Local	24	3	71	18	0·53	0·14 to 2·07
Eating fish (more v less often than weekly)	Area	29	16	97	49	1·26	0·50 to 3·21
	Local	28	16	93	49	1·16	0·45 to 3·00
Eating shellfish (more v less often than weekly)	Area	15	2	36	1	7·03	0·61 to 80·43
	Local	15	2	29	3	1·11	0·15 to 7·91
Grow own vegetables	Area	35	15	123	54	0·98	0·45 to 2·13
	Local	35	15	112	45	1·07	0·46 to 2·48
Seaweed as fertiliser	Area	11	1	25	1	1·73	0·10 to 30·76
	Local	13	1	25	1	2·00	0·13 to 31·98
		Leukaemia and non-Hodgkin's lymphoma					
Play on beach (more v less often than monthly)	Area	40	18	131	61	0·95	0·45 to 2·00
	Local	39	18	131	78	0·66	0·31 to 1·40
Play on fells (more v less often than monthly)	Area	36	4	103	28	0·33	0·09 to 1·21
	Local	32	4	98	31	0·36	0·11 to 1·17
Eating fish (more v less often than weekly)	Area	39	20	126	62	1·03	0·45 to 2·37
	Local	36	19	127	67	0·86	0·38 to 1·98
Eating shellfish (more v less often than weekly)	Area	19	2	44	2	2·99	0·40 to 22·11
	Local	18	2	39	5	0·82	0·14 to 5·01
Grow own vegetables	Area	47	20	161	71	0·99	0·52 to 1·93
	Local	46	20	154	72	0·87	0·42 to 1·81
Seaweed as fertiliser	Area	15	1	30	1	1·73	0·10 to 30·76
	Local	17	1	36	1	2·00	0·13 to 31·98

TABLE IV—*Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by distance from Sellafield of residence at birth for area controls*

Distance (km)	Leukaemia				Leukaemia and non-Hodgkin's lymphoma			
	Cases (n=51)	Area controls (n=350)	Relative risk	95% Confidence interval	Cases (n=73)	Area controls (n=491)	Relative risk	95% Confidence interval
≤4	5	14	1		8	16	1	
5-9	5	31	0·35	0·08 to 1·62	6	43	0·21	0·06 to 0·78
10-14	14	117	0·21	0·05 to 0·92	22	160	0·17	0·05 to 0·56
15-19	5	35	0·22	0·04 to 1·22	8	50	0·16	0·04 to 0·67
20-24	9	52	0·22	0·03 to 1·59	11	84	0·07	0·01 to 0·38
25-29	8	66	0·14	0·02 to 0·91	12	100	0·06	0·01 to 0·31
≥30	5	35	0·17	0·02 to 1·88	6	38	0·11	0·02 to 0·80

GEOGRAPHY OF CASES AND CONTROLS RELATIVE TO SELLAFIELD

Distances of addresses of cases and controls from Sellafield were calculated by taking the grid reference of the plant to be NY 027 039 as used by the National Radiological Protection Board in its analysis of atmospheric discharges (J Stather, personal communication). The results given here are for area controls using addresses at birth. Table IV shows findings in circles of increasing 5 km radiuses moving away from Sellafield, and risks are given relative to the inner circle (which completely contains Seascale and some other smaller villages). All five cases of leukaemia and two of the three cases of non-Hodgkin's lymphoma in the inner circle occurred in children born to parents resident in Seascale. There was a large fall in relative risk in moving to outside the inner circle to levels of about one third and smaller, with some suggestion also of a decreasing risk with further distance. For leukaemia and non-Hodgkin's lymphoma combined the relative risks away from the inner circle were lower than for leukaemia alone. The relative risk of leukaemia for all children born outside the inner circle was 0·26 (95% confidence interval 0·07 to 1·01) and for leukaemia and non-Hodgkin's lymphoma together it was 0·17 (95% confidence interval 0·05 to 0·53). These latter results also applied when analysis was limited to cases born in the birth registration district containing Sellafield rather than all West Cumbria. None of the 23 cases of Hodgkin's disease in the study had an address at birth within the 5 km radius inner circle. Of the 95 total cases with complete information 79 (83%) remained in the same 5 km sector from birth to diagnosis.

FATHER'S OCCUPATION AND EMPLOYMENT AT SELLAFIELD

Three separate sources of parental occupational information were used: birth certificates, questionnaires, and the computer file of past and present workers at Sellafield. Maternal occupation is generally recorded on a birth certificate only in the absence of paternal occupation, questionnaire data were available for only about half the study members, and relatively few women have worked at Sellafield, so results given here are restricted to father's employment.

Table V shows the relative risks for leukaemia and non-Hodgkin's lymphoma associated with various paternal employment categories. These data were taken from birth certificates rather than questionnaires because of the greater completeness of information—for example, data for the 74 fathers of children with leukaemia and non-Hodgkin's lymphoma were available from 64 (86%) birth certificates but only 32 (43%) questionnaires. Results are given for the main industrial groups in West Cumbria which employed more than 5% of control fathers. Raised relative risks were associated with fathers working at Sellafield and in iron and steel, farming, and chemicals, with children of coal miners having low relative risks but based on small numbers. Similar results were found using the questionnaire data and when examining employment on the questionnaire at conception rather than birth, although then relative risks were somewhat higher in relation to Sellafield and farming than those shown in table V.

For Hodgkin's disease the relative risks associated with fathers working at Sellafield according to data from birth certificates were low—for example, for local controls the relative risk was 0·71 (95% confidence interval 0·08 to 6·03). This result was based on only one positive case, since, although we had records that four fathers altogether were Sellafield workers, for three this employment occurred after the birth of their children.

RADIATION DOSIMETRY AT SELLAFIELD

Table VI shows relative risks for leukaemia and non-Hodgkin's lymphoma in children associated with

TABLE V—*Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by paternal occupation and industry recorded on birth certificates*

Father's occupation/ industry	Type of control	Cases	Controls	Relative risk	95% Confidence interval
		Leukaemia			
Total	Area	46	286		
	Local	46	277		
Sellafield	Area	9	29	2·82	1·07 to 7·40
	Local	9	41	2·03	0·69 to 5·93
Coal mining	Area	2	33	0·37	0·09 to 1·61
	Local	2	31	0·35	0·08 to 1·60
Iron and steel	Area	5	18	1·84	0·60 to 5·60
	Local	5	16	2·36	0·71 to 7·78
Farming	Area	5	19	1·98	0·66 to 5·96
	Local	5	11	2·63	0·77 to 8·95
Chemicals	Area	5	25	1·39	0·49 to 3·97
	Local	5	23	1·58	0·52 to 4·84
		Leukaemia and non-Hodgkin's lymphoma			
Total	Area	64	393		
	Local	64	383		
Sellafield	Area	10	38	2·02	0·87 to 4·67
	Local	10	54	1·32	0·51 to 3·43
Coal mining	Area	5	53	0·51	0·19 to 1·39
	Local	5	53	0·46	0·16 to 1·30
Iron and steel	Area	9	31	2·06	0·88 to 4·82
	Local	9	25	3·20	1·23 to 8·28
Farming	Area	6	27	1·54	0·57 to 4·11
	Local	6	16	2·15	0·71 to 6·51
Chemicals	Area	7	27	1·90	0·75 to 4·78
	Local	7	25	2·15	0·80 to 5·77

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TABLE VI—*Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by timing of paternal employment and external ionising radiation dosimetry at Sellafield*

Father's employment/ radiation group	Type of control	Cases	Controls	Relative risk	95% Confidence interval
		Leukaemia			
Total	Area	46	288		
	Local	46	276		
Employed:					
Before conception	Area	9	36	1·97	0·82 to 4·78
	Local	9	45	1·39	0·53 to 3·65
At conception	Area	8	25	2·79	1·04 to 7·52
	Local	8	32	2·07	0·69 to 6·14
At birth	Area	8	27	2·51	0·95 to 6·67
	Local	8	33	1·92	0·66 to 5·56
Before diagnosis	Area	9	53	1·17	0·49 to 2·76
	Local	9	58	0·89	0·36 to 2·18
Ever	Area	12	65	1·35	0·61 to 2·96
	Local	12	65	1·22	0·54 to 2·74
Dose record:					
Before conception	Area	8	35	1·71	0·68 to 4·26
	Local	8	40	1·40	0·50 to 3·94
At conception	Area	8	24	3·07	1·09 to 8·65
	Local	8	30	2·43	0·80 to 7·41
Before diagnosis	Area	8	48	1·11	0·45 to 2·72
	Local	8	54	0·81	0·31 to 2·10
Total dose before conception:					
1-49 mSv	Area	3	19	1·12	0·31 to 4·05
	Local	3	26	0·77	0·20 to 3·00
50-99 mSv	Area	1	11	0·69	0·08 to 5·73
	Local	1	11	0·78	0·08 to 7·73
≥100 mSv	Area	4	5	6·24	1·51 to 25·76
	Local	4	3	8·38	1·35 to 51·99
Dose during 6 months before conception:					
1-4 mSv	Area	3	18	1·30	0·32 to 5·34
	Local	3	24	1·10	0·25 to 4·91
5-9 mSv	Area	1	3	3·54	0·32 to 38·88
	Local	1	3	3·04	0·28 to 32·61
≥10 mSv	Area	4	5	7·17	1·69 to 30·44
	Local	4	3	8·21	1·62 to 41·73
		Leukaemia and non-Hodgkin's lymphoma			
Total	Area	66	404		
	Local	66	389		
Employed:					
Before conception	Area	11	47	1·77	0·82 to 3·85
	Local	11	62	1·08	0·47 to 2·52
At conception	Area	10	34	2·44	1·04 to 5·71
	Local	10	46	1·48	0·59 to 3·75
At birth	Area	10	37	2·14	0·93 to 4·92
	Local	10	50	1·26	0·48 to 3·28
Before diagnosis	Area	11	72	0·97	0·46 to 2·03
	Local	11	83	0·64	0·28 to 1·45
Ever	Area	14	88	1·01	0·51 to 2·02
	Local	14	93	0·81	0·39 to 1·69
Dose record:	Area	10	45	1·63	0·73 to 3·64
Before conception	Local	10	58	1·00	0·40 to 2·51
	Area	10	32	2·71	1·12 to 6·60
At conception	Local	10	45	1·58	0·60 to 4·18
	Area	10	66	0·95	0·44 to 2·05
Before diagnosis	Local	10	78	0·60	0·25 to 1·41
Total dose before conception:					
1-49 mSv	Area	4	27	1·06	0·35 to 3·21
	Local	4	41	0·53	0·16 to 1·78
50-99 mSv	Area	2	13	1·16	0·24 to 5·46
	Local	2	14	0·95	0·17 to 5·28
≥100 mSv	Area	4	5	6·42	1·57 to 26·32
	Local	4	3	8·30	1·36 to 50·56
Dose during 6 months before conception:					
1-4 mSv	Area	5	22	1·80	0·59 to 5·53
	Local	5	33	0·97	0·28 to 3·41
5-9 mSv	Area	1	4	2·41	0·25 to 23·43
	Local	1	7	1·12	0·13 to 9·93
≥10 mSv	Area	4	8	4·33	1·16 to 16·12
	Local	4	5	5·01	1·13 to 22·24

their fathers' employment and exposure to ionising radiation obtained through linkage with the Sellafield workforce file. As well as analysing the total radiation dose recorded before conception (taken as nine months before birth) we looked at that during the immediately preceding six months, since it has been suggested that this is the most sensitive period for the induction of transmissible genetic damage.[6] The six monthly doses were estimated proportionally from the recorded annual doses of the father and the date of birth of his child.

For paternal employment at the plant relative risks were higher for leukaemia alone than for leukaemia and non-Hodgkin's lymphoma combined and were higher for employment at conception than at any other time. Relative risks for leukaemia and non-Hodgkin's lymphoma were higher for fathers with a radiation dose record at conception than for those with a radiation dose record at any time before conception or diagnosis. The highest relative risks—of the order of sixfold—were for fathers with total radiation doses of 100 mSv or greater before the date of their child's conception or doses of 10 mSv or greater during the six months before conception. Figures for all the control fathers in this study indicated that about 9% of the workforce had had accumulated preconceptual doses over 100 mSv and about 13% had had doses over 10 mSv during the six months before conception.

The results shown in the table relate to all fathers in the study for whom we could make a definite positive or negative linkage to the Sellafield file. The same analysis limited to fathers positively linked to the Sellafield file showed similar relations to ionising radiation dose but with larger relative risks in the highest categories. For example, there was a relative risk of 17·2 for leukaemia compared with area controls in children of fathers with total radiation doses before conception of 100 mSv or more with a 95% confidence interval of 1·1 to 278, the wide interval reflecting that the analysis was based on a total of 11 case-control sets rather than 46 as in the table.

For cases of Hodgkin's disease none of the four fathers employed at Sellafield had a record of occupational radiation exposure before their child's conception.

SEASCALE

Earlier studies have concentrated on the geographical excess of childhood leukaemia in the neighbourhood of the Sellafield plant. This excess was found in Seascale particularly and was based on around five cases compared with fewer than one expected, depending on which age group and calendar period were reported. A pertinent question is to what degree this excess may be explained statistically by the demonstrated relationship with paternal radiation dose during employment.

Three of the five Seascale cases in this study were among the four cases of leukaemia with fathers in the highest total radiation dose group (table VI), with doses of 102 mSv (over about 7 years' employment), 162 mSv (about 6 years), and 188 mSv (about 7 years). The one case in the intermediate group was also from Seascale, with a paternal total dose of 97 mSv (over about 13 years). The fifth Seascale leukaemia case was not, however, linked with the Sellafield computer file owing to our being unable to trace a date of birth for his father, although we know that the father worked at Sellafield from the child's birth certificate and the mother's questionnaire. Thus, we know that three of the five Seascale cases had fathers whose accumulated preconceptual radiation dose was in the group with an estimated sixfold to eightfold relative risk of leukaemia and the father of the fourth was in the group just below the cut off value used. These five Seascale leukaemia cases were precisely those in the inner circle of table IV, where the risk was highest.

If the exposure of the father to ionising radiation was the cause of leukaemia in the children then the reported geographical excess could effectively be explained on this basis. If, alternatively, the fact of living in Seascale itself were responsible for the excess then it would not be expected that three of the four fathers linked to the Sellafield workforce file would have a total radiation dose before conception in the highest category, whereas 16 out of 20 fathers of the local controls for these four cases (also born to mothers resident in Seascale) had a radiation record with only one in the highest category (the other four had not been employed at Sellafield). Moreover, in no father of the 20 local controls was their total preconception dose as high as in the father of their related case. For fathers of the area

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controls the corresponding figures were 9 out of 27 with a radiation record but none in the highest category (17 of the other 18 had not been employed at Sellafield), and all the total preconception doses of the fathers of the 27 area controls were lower than those of the father of their related case. These comparisons are shown in table VII and graphically in the figure, where case 1 was in the intermediate dose category of table VI and cases 2, 3, and 4 in the highest category. Similar results were found for radiation dose during the six months before conception, except that two of the 18 fathers of the total of 43 controls with a radiation record during this period had higher doses than the father of their associated case. Two mothers of the five leukaemia cases had been employed at Sellafield; neither worked there at the time of conception of their child, but one had experienced previous exposure to radiation (of 26 mSv) at the plant.

None of the 23 cases of Hodgkin's disease had an address at birth in Seascale.

TABLE VII—*Numbers of Seascale leukaemia cases and their controls by paternal employment and total external ionising radiation dose at Sellafield before their child's conception**

Paternal employment/ preconceptual radiation dose at Sellafield	Cases	Controls	
		Local	Area
Not employed	0	4	17
No dose record	0	0	1
1-49 mSv	0	8	6
50-99 mSv	1	7	3
≥100 mSv	3	1	0
Total	4	20	27

*One Seascale case (and associated controls) is omitted from this table owing to lack of information on the father (see text). The 20 local controls, as the four cases, were all born to mothers resident in Seascale but only four of the 27 area controls

Discussion

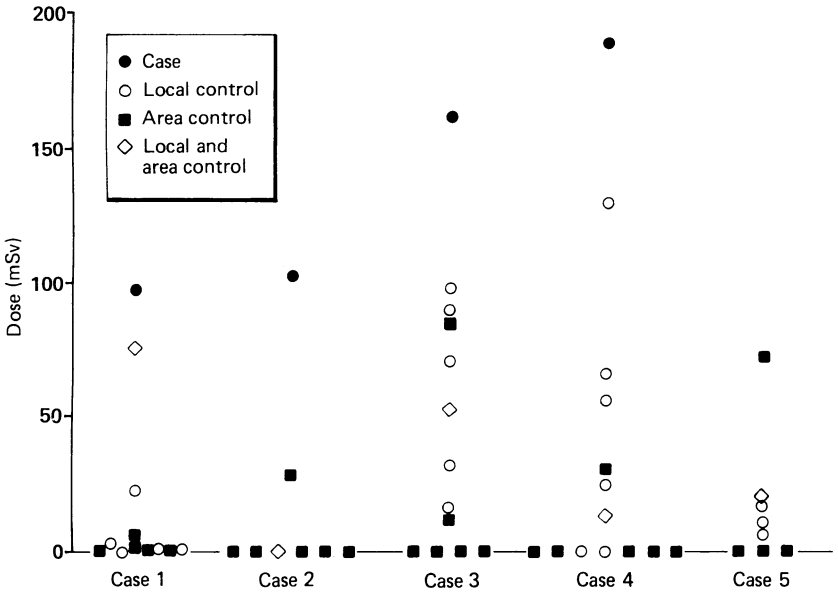
The main finding of this study is that the recorded external dose of whole body ionising radiation to fathers during their employment at Sellafield is associated with the development of leukaemia among their children. Since radiation badge recording will reflect gonadal dose we interpret this finding to suggest an effect of the radiation exposure on germ cells producing a mutation in sperm that may be leukaemogenic in subsequent offspring. Other explanations may be possible, such as exposure to internally incorporated radionuclides or other concomitant exposures in the workplace: it has not been possible to examine the first of these so far, and the second seems unlikely (see below). Additionally, contamination of the home with radioactive or other material through occupational exposure may be relevant, although there is no evidence to support this.

The results suggest highest risks in those with the highest accumulated ionising radiation doses before conception, either over their total duration of exposure or during the preceding six months. For both periods of exposure the same four cases of leukaemia were in the highest groups, three of them in children born in Seascale, and none were lymphomas. We have not yet examined any other duration of exposure period. Comparison of the relative size of various calculated risks associated with fathers' being employed or having a radiation record at Sellafield either at any time or before the diagnosis of their children's illness supports the relevance of preconceptual exposure.

Other factors that we examined indicated smaller relations with leukaemia. Some of those were expected, such as antenatal exposure to *x* rays, but the high relative risk in mothers aged over 40 was at least twice that previously reported.[7] This was not due to an excess of Down's syndrome as none of the cases in our study born to mothers in this age group had trisomy 21. The question arises whether any of these other factors explain the relation with paternal radiation dose. The one well established cause of childhood leukaemia, exposure in utero to *x* rays, is considered to have a relative risk of around 1·5 and be responsible alone for some 5% of cases. This level of increase is not sufficient to explain the observed relative risks for the highest occupational radiation doses. Moreover, each mother of the four cases in the highest exposure category reported on her questionnaire that she had not had an abdominal *x* ray examination during pregnancy, although we could trace the hospital record of only one mother to verify this information. The high risk found in mothers aged over 40 was also not an explanation since only one of the four cases in the highest radiation dose group was born to a mother of this age, as was one of three in the lowest group. Neither of these two cases born to mothers aged 40 or over with paternal radiation exposure at Sellafield was born in Seascale.

Of the four cases of leukaemia in the highest radiation dose group three were acute lymphatic leukaemia. The father of the non-Seascale case in this group had a total preconceptual dose of 370 mSv (over about 10 years). On their children's birth certificates two of the fathers were described as process workers, one as an analytical chemist, and the other as a fitter's mate. Although we have not yet examined jobs in detail, these various occupations do not suggest common non-radiation exposures that might be relevant to these findings. We are limited in the identification of individual cases that we can give both from our own ethical considerations and also from our undertakings to the British Medical Association ethical committee and British Nuclear Fuels.

The results for non-Hodgkin's lymphoma, for which the number of cases was much smaller, were less suggestive than for leukaemia. However, one of the two Seascale cases in this study had a father with a total preconceptual radiation dose of 97 mSv (during about 15 years' employment), higher than all 11 related control fathers, of whom six had a radiation record before their child's conception. The father of the other case was not employed at Sellafield. There were no cases of Hodgkin's disease with paternal ionising



Total external ionising radiation dose during employment at Sellafield before the child's conception in fathers of Seascale leukaemia cases and in fathers of their controls (case 5 not linked to Sellafield workforce file). The different numbers of controls for each case are due to loss from the study of original controls who had moved from Seascale before their case's diagnosis and varying success in identifying fathers and obtaining information to attempt their linkage to the Sellafield file (see accompanying paper[4]). The local and local and area controls were born to mothers resident in Seascale at the time (as were the five cases); the area controls were born outside Seascale but resident in the same birth registration district

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radiation dose records at Sellafield before their conception nor among Seascale children; this lack of association with radiation exposure is as could be expected (see accompanying paper) and strengthens the findings in this paper.

One of the weaknesses of this study might be considered to be the relatively low quality information on potential confounding factors such as antenatal exposure to *x* rays and infectious illnesses in the mother during pregnancy. Nevertheless, the strength of the observed finding, together with the mothers of the relevant cases not reporting having had an abdominal *x* ray examination, would suggest that the imperfections in measuring confounders of lower and uncertain risk are not detrimental. Additionally the potential for low quality data on children playing on the beach and families' seafood eating habits, for example, is acknowledged, but this would be a more serious criticism if there had been a trend for positive answers by parents of cases. We recognise also the possibility of bias from the absence of information on some factors for a number of cases and controls, but this is due to the unavailability of old records and our failure to trace parents as well as to parents' failures to respond to the questionnaire. Also this absence of data did not greatly affect what seems to be the important risk variable.

These findings support the hypothesis, incorporated as part of this study, that exposure of fathers to ionising radiation before conception is related to the development of leukaemia in their offspring. The observed finding (the first of its kind with human data), however, is stronger than could have been expected from past knowledge, although relevant studies have largely not been undertaken. In a study of the offspring of 7387 men irradiated to an estimated mean dose of 492 mSv as a result of exposure to atomic bombs in Japan there was no excess of leukaemia (5 cases observed, 5·2 expected).[8] Nevertheless, the radiation doses in Hiroshima and Nagasaki were instantaneous compared with accumulated over years in the Sellafield workers; the different dose rates may be important. Studies of high doses (360-5040 mSv) in mice have, none the less, indicated that paternal (as well as maternal) exposure to *x* rays induces heritable tumours in their first and second generation progeny, the tumours mainly being in the lung (papillary adenomas) but including lymphocytic leukaemia as well as leading to an increase in anomalies.[9] It was suggested that this effect might operate through germ line mutations, and the finding lends biological plausibility to the pathway suggested here.

Further data relevant to the results shown here are expected from two other British case-control studies currently in progress. These are in areas around other nuclear installations where excesses of childhood leukaemia in particular, but also of other childhood cancers in one instance, have been reported —Dounreay in Caithness and Aldermaston and Burghfield in Berkshire.[10,11] In the latter report the raised incidence in the neighbourhood was much less than around Sellafield or Dounreay (as it has also been much less around other nuclear plants[1]), but this would be expected if the results reported here are applicable since there is no dominant settlement of workers equivalent to Seascale or Thurso. The occupational radiation doses, however, have been somewhat less at these two establishments than at Sellafield. Consideration is currently being given to setting up cohort studies to examine the incidence of cancer among the offspring of nuclear plant workers, as well as other radiation workers, and these are also relevant to provide support or otherwise for the findings shown in this paper.[10,11]

The results here are of interest in relation to those in the cohort studies of Seascale children.[12,13] These showed increased rates of leukaemia and total cancer among children born in Seascale (6 observed cases compared with 0·6 expected and 12 compared with 2·8 respectively) but not among children moving in after birth and attending the local schools (0 compared with 0·6 and 4 compared with 4·0 respectively). If there is a causal role for radiation operating through paternal occupational exposure these very different findings among children born in Seascale and those attending school there are as would be expected, apart possibly from the fact that some at least of the Seascale immigrants came from other nuclear establishments. It seems important now not only to extend the cohort studies in time forward from 1983 and backwards before 1950, which is currently being done, but also to carry out for all parents of children born in Seascale a similar linkage exercise as in this study with the Sellafield workforce file and radiation dose records. Additionally, we are planning to examine recent cases diagnosed in the Seascale area in the same manner as in this study. Furthermore, data on internally incorporated radionuclides will be analysed when these become available. Possibly men with high external doses also have high internal exposure. Certainly some degree of correlation between cumulative radiation dose and monitoring for possible internal contamination by specific radionuclides, including plutonium and tritium, was found among workers at United Kingdom Atomic Energy Authority establishments and the Atomic Weapons Establishment.[14,15]

One of the considerations made at the time of the Black inquiry was that the levels of radioactive discharges from Sellafield to atmosphere and sea were too low to account for the number of excess cases of leukaemia being observed in the Seascale area.[2] This was based on the relatively small additional contribution from Sellafield to total radiation exposure from natural background, medical, and other sources. This conclusion would be supported by the results in this study for playing on the beach and eating seafood. The findings here in relation to occupational radiation exposure of the father suggest a totally different pathway and do not conflict with that reasoning. These results also make other alternative hypotheses that have been proposed unlikely to be the explanations—for example, that epidemics of common infections produce a leukaemic response by mixing of populations[16] and that areas chosen as nuclear sites, existing or potential, share unrecognised risk factors.[17]

The range of total preconceptual external radiation doses of fathers in this study was from 0 to 383 mSv, the worker with the highest dose being employed over seven years. The range of estimated radiation doses during the six months before conception was 0 to 31 mSv. An annual dose limit of 50 mSv for radiation workers was recommended in 1965 by the International Commission on Radiological Protection,[18] and this figure still operates in the United Kingdom, although in 1987 the National Radiological Protection Board recommended a reduction to 15 mSv per year.[19] During 1987 in the United Kingdom some 1100 workers received annual doses above 15 mSv from artificial sources; most of these worked in nuclear fuel processing, with fewer than 10 being, for example, health professionals.[20]

If the associations reported in this paper are causal they need to be explored further to help determine which period of exposure may be most relevant. Although the two measures we have examined this far are highly correlated and show similar relations, there is a more convincing trend of increasing relative risks of leukaemia for paternal radiation dose during the six months preceding conception than for total exposure (table VI). The findings here contrast with those in the mortality follow up of Sellafield radiation workers

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themselves, among whom there were no excess deaths from leukaemia and only a limited suggestion of an association of death from leukaemia with dose of ionising radiation when considering a lag period of 15 years.[21] However, if these results have causal significance then they are of much importance to radiological protection of potential parents and their children.

We thank the registration division of the Office of Population Censuses and Surveys, the West Cumbria Health Authority, the Cumbrian Family Practitioner Committee, and other sources mentioned in the text for their cooperation in identifying records on subjects included in the study; the National Health Service central register for providing follow up and tracing details and, with the generous collaboration of local general practitioners, for forwarding questionnaires to parents; the parents for completing them; the Ordnance Survey and British Nuclear Fuels for making relevant information available to us; and many staff of the Medical Research Council Environmental Epidemiology Unit for their help, particularly Mick Merwood, Carol Wickham, and Paul Winter for computer analyses and Gill Strange for preparing the manuscript. Professor Geoffrey Rose kindly commented on an earlier version of the paper, and Professor Peter Smith and Allison Douglas helped with a sample check of the radiation dosimetry data. The study was approved by the British Medical Association ethical committee and the West Cumbria ethics of research committee and was supported partially by a grant from the Department of Health.

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Methods and basic data of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria

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Abstract

***Objective*—To examine whether the observed excess of childhood leukaemia and lymphoma near the Sellafield nuclear plant is associated with established risk factors or with factors related to the plant.**

***Design*—A case-control study.**

***Setting*—West Cumbria health district.**

***Subjects*—52 Cases of leukaemia, 22 of non-Hodgkin's lymphoma, and 23 of Hodgkin's disease occurring in people born in the area and diagnosed there in 1950-85 under the age of 25 and 1001 controls matched for sex and date of birth taken from the same birth registers as the cases.**

***Main outcome measures*—Antenatal abdominal x ray examinations, viral infections, habit factors, proximity to and employment characteristics of parents at Sellafield.**

***Results*—Ascertainment of cases through multiple sources was as complete as possible, and the diagnosis was established for nearly all cases from hospital records and by independent pathological review when suitable material (60% (58) of cases) was available. Identification and tracing of the parents of cases and controls enabled questionnaires to be forwarded to 730 (66%), and 467 (64%) of the questionnaires were returned completed. Obstetric records were located for 481 (44%) of the relevant births, more frequently in recent years. Linkage of study subjects to the Sellafield workforce file enabled dates of employment and records on external doses of whole body ionising radiation to be obtained. Concordance of information from duplicate sources (when available) was reasonably high with no indications of bias.**

***Conclusion*—Overall the collected data were sufficiently reliable for detailed analysis and careful interpretation.**

Introduction

In November 1983 a Yorkshire Television programme (*Windscale: the Nuclear Laundry*) suggested that there was an excess incidence of childhood leukaemia and other cancers in the village of Seascale and some neighbouring areas close to the Sellafield nuclear site on the coast of Cumbria. The Black committee (of which MJG was a member) was set up to investigate this suggestion and made recommendations for four epidemiological studies related to childhood cancer in West Cumbria.[1] Three of these, two reporting the occurrence of cancer among children born or attending

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