Childhood leukaemia and non-Hodgkin's lymphoma near large rural construction sites, with a comparison with Sellafield nuclear site

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Abstract

***Objective*—To determine whether population mixing produced by large, non-nuclear construction projects in rural areas is associated with an increase in childhood leukaemia and non-Hodgkin's lymhoma.**

***Design*—A study of the incidence of leukaemia and non-Hodgkin's lymphoma among children living near large construction projects in Britain since 1945, situated more than 20 km from a population centre, involving a workforce of more than 1000, and built over three or more calendar years. For periods before 1962 mortality was studied.**

***Setting*—Areas within 10 km of relevant sites, and the highland counties of Scotland with many hydroelectric schemes.**

***Subjects*—Children aged under 15.**

***Results*—A 37% excess of leukaemia and non-Hodgkin's lymphoma at 0-14 years of age was recorded during construction and the following calendar year. The excesses were greater at times when construction workers and operating staff overlapped (72%), particularly in areas of relatively high social class. For several sites the excesses were similar to or greater than that near the nuclear site of Sellafield (67%), which is distinctive in its large workforce with many construction workers. Seascale, near Sellafield, with a ninefold increase had an unusually high proportion of residents in social class I. The only study parish of comparable social class also showed a significant excess, with a confidence interval that included the Seascale excess.**

***Conclusion*—The findings support the infection hypothesis and reinforce the view that the excess of childhood leukaemia and non-Hodgkin's lymphoma near Sellafield has a similar explanation.**

Introduction

Large scale mixing of rural and urban groups of people has been associated with increases of childhood leukaemia and non-Hodgkin's lymphoma. An infective basis is strongly suggested, as such situations[1-9] would increase contacts between susceptible and infected individuals. Large construction projects in rural districts produce unaccustomed mixing of people, as the limited local resources of labour require recruitment of workers from outside. Studies of such projects within the North Sea oil industry have already indicated the relevance of construction workers to population mixing and childhood leukaemia.[6] We examined the incidence of childhood leukaemia and non-Hodgkin's lymphoma near other (non-nuclear) construction projects in rural Britain over the past 50 years.

Methods

RURAL INDUSTRIAL SITES

The following criteria were used to select for study rural non-nuclear projects outside the North Sea oil industry: (*a*) situated in a (pre-1974) local authority rural district; (*b*) over 20 km (as in a previous study[6]) from a large town (population over 70 000; an arbitrary definition that embraced most of the former county boroughs); (*c*) built over at least three successive calendar years; (*d*) involving a peak workforce of more than 1000. In the absence of any single source of relevant information details of rural projects over the past 50 years were compiled with the help of the annual official handbook on Britain[10] (section on large construction projects), the managers of the major fossil fuel power stations in rural Britain, senior members of the construction industry, and a limited search of civil and mechanical engineering publications. Though we tried to be comprehensive, one or two projects may have been overlooked or inappropriately excluded because of incorrect information on, say, the peak workforce. The projects (table I) were mainly power stations, hydroelectric schemes, and oil refineries. Most required work camps, reflecting the need for outside labour. Some were very large, such as Longannet and Drax, successively the largest fossil fuel power stations in Western Europe, and Dinorwig, the world's largest (hydroelectric) pumped storage scheme.

The extensive postwar hydroelectric work in Scotland concerned some of the remotest parts of Europe. By 1965, apart from the laying of thousands of miles of electric cable in the highlands, this included 56 power stations and 54 major dams.[11] Individually most of these projects were carried out with workforces of less than 1000, though the Loch Sloy scheme in Dunbartonshire was an exception.[12] Collectively, however, several thousand men were involved in the construction at any one time over a wide period. These projects fulfilled conditions (*a*) and (*b*) individually, but conditions (*c*) and (*d*) only collectively. They were therefore treated collectively in this study, on a county basis.

Several otherwise suitable construction projects such as the Channel tunnel were not eligible for inclusion because they were within 20 km of a large town. However, the Fawley oil refinery in New Forest Rural District, built in 1949-51 by a workforce of over 5000, seemed to warrant inclusion though within 20 km of Southampton; an unbridged inlet of the sea (Southampton Water) prevents direct access and the journey by road exceeds 20 km.

STUDY AREAS AND STUDY PERIODS

In England and Wales the study areas comprised those parishes largely within 10 km of each site, whereas in Scotland the (smaller) local authority areas were used before 1974 and afterwards postcode sectors. The 10 km distance was arbitrary but, given the minimum 20 km separation from a large town, seemed reasonable. In the case of Scottish hydroelectric schemes the local population was usually very

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TABLE I—*Details of large non-nuclear construction projects in rural Britain 1945-93*

Site	County	Local authority rural district	Type of project	Construction project	Other population mixing activities
Specific projects:					
Drax Phase 1	Yorkshire	Selby RD	Power station	1965-74	Other fossil fuel power stations nearby
Drax Phase 2	West Riding		Power station Flue gas desulphurisation project	1979-86 1988-94	
West Burton	Nottinghamshire	East Retford RD	Power station	1961-67	Other fossil fuel power stations nearby
Longannet	Fife	Dunfermline DC	Power station	1964-72	Cumbernauld New Town (designated 1965); Stirling University (built late 1960s)
Invergordon	Ross and Cromarty	Invergordon DC	Aluminium smelter	1968-71	Platform construction yard 9 km away
Pembroke and Milford Haven area	Pembrokeshire	Pembroke RD Haverfordwest RD Haverfordwest RD	Refineries (two)* Power station Refinery	1957-82 1966-72 1977-82	
Peterhead (Boddam)	Aberdeenshire	Deer DC	Power station	1972-82	Oil industry activity nearby
Dinorwig	Gwynedd	Arfon CD	Power station (pumped storage scheme)	1976-83	
Holyhead	Anglesey	Valley RD	Aluminium smelter	1969-71	Adjacent to major route to Ireland
Fawley	Hampshire	New Forest RD	Refinery Power station	1949-51 1962-71	Chemical works on site
Hydroelectric schemes, collectively considered by county:					
	Ross and Cromarty		Over 50 power stations and over 50 dams	1946-61	Growth of tourism in highlands
	Dunbartonshire			1945-59	
	Sutherland			1955-60	
	Inverness-shire			1947-62	
	Perthshire			1947-62	

RD=Rural district. DC=District of county. CD=County district. *And catalytic cracking complex.

TABLE II—*Observed (O) and expected (E) numbers of cases of childhood leukaemia and non-Hodgkin's lymphoma in areas near large rural construction sites*

	Period	Age 0-4 years O	E	Age 5-14 years O	E	Age 0-14 years O	E
Specific projects:							
Drax Phase 1	1965-75	5	3·04	4	3·25	9	6·29
Drax Phase 2	1979-93	7	3·92	6	4·07	13	7·99
Longannet	1964-73	13	9·08	12	9·69	25	18·77
West Burton	1961-68	3	1·83	1	2·13	4	3·96
Pembrokeshire First refinery	1957-61	2	0·80	0	1·07	2	1·87
Pembrokeshire Later projects	1966-83	1	3·09	6	4·28	7	7·37
Invergordon	1968-73	3	0·53*	0	0·48	3	1·01
Peterhead	1972-83	3	1·79	1	1·82	4	3·61
Dinorwig	1976-84	0	0·73	4	1·10	4	1·83
Holyhead	1969-72	0	0·44	1	0·48	1	0·92
Fawley Refinery	1949-52	1	0·20	0	0·18	1	0·38
Fawley Power station	1962-72	3	1·74	3	1·81	6	3·55
Total		41	27·19**	38	30·36	79	57·55**
[O:E (95% confidence interval)]		[1·51 (1·15 to 1·63)]		[1·25 (0·89 to 1·72)]		[1·37 (1·10 to 1·73)]	
Hydroelectric schemes (whole counties)†:							
Ross and Cromarty	1946-62	6	4·03	11	4·24**	17	8·27**
Dunbartonshire	1945-60	7	4·61	6	4·45	13	9·06
Inverness-shire	1947-63	4	3·68	2	4·08	6	7·76
Sutherland	1955-61	1	0·40	0	0·45	1	0·85
Perthshire	1947-63	4	5·34	10	5·97	14	11·31
Total		22	18·06	29	19·19*	51	37·25*
[O:E (95% confidence interval)]		[1·22 (0·76 to 1·84)]		[1·51 (1·01 to 2·17)]		[1·37 (1·02 to 1·80)]	
Grand total		63	45·25**	67	49·55*	130	94·80***
[O:E (95% confidence interval)]		[1·39 (1·07 to 1·78)]		[1·35 (1·05 to 1·72)]		[1·37 (1·15 to 1·63)]	

†Excluding large burghs and detached portion of Dunbartonshire. *P<0·05. **P<0·01. ***P<0·001.

small. In view of this and the fact that the hydroelectric board as policy employed a high proportion of men from the highlands,[11 12] the whole of the relevant counties (apart from any large burgh) were included so as to cover (as in a previous study[6]) the home areas of those local workers. Inevitably this crude approach included many unaffected communities. (Argyll was not included because of the fewer men employed in this work in this very large county (of over 800 000 hectares).)[11]

Three periods were chosen for study: (*a*) from the calendar year in which construction began to the year after its completion, with different construction phases on the same site separated by two or more years being examined separately; (*b*) parts of the above that overlapped with the operation of the plants; and (*c*) the five year periods that preceded and followed (*a*).

LEUKAEMIA AND NON-HODGKIN'S LYMPHOMA

The incidence of leukaemia and non-Hodgkin's lymphoma below age 15 in study areas was examined by using registration data (available from 1962) from the national registry maintained by the Childhood Cancer Research Group. Before 1962 mortality was our measure of incidence, the diseases being then almost invariably rapidly fatal, and we used leukaemia death certificates for 1945 and later years, assembled many years previously for certain Medical Research Council studies.[13 14] Corresponding details for non-Hodgkin's lymphoma deaths were available for 1953-62 from the Childhood Cancer Research Group.

ANALYSES

In each study area observed numbers of cases were compared with expected numbers calculated by applying the relevant national rates at ages 0-4, 5-9, and 10-14 years to the corresponding local populations. Local population details were taken from the (partly unpublished) small area statistics of the relevant censuses, supplemented in intercensal years by estimates obtained by linear interpolation.

Observed and expected numbers of cases were examined in terms of the proportions of social classes I and II combined (approximated as in a previous study[15]) among economically active men. These were derived from parish data from a 10% sample of the decennial censuses (1961, 1971, 1981) made available by the Office of Population Censuses and Surveys. Social class details for Scotland were also available from the censuses. The constituent parts (mainly parishes) of all the study areas were first ranked on the basis of these proportions in 1971, the census year in which more areas were under study than any other. In this order their childhood populations (0-14 years) were accumulated and then divided into two similar sized groups of respectively "lower" and "higher" social classes. It was then convenient to apply the 1971 cut point (15·3% of social classes I and II) to similarly ranked data from the other censuses when there were much smaller numbers of areas to consider. This procedure was not intended to correspond to any independent measure of social class but simply to provide a basis for deriving two groups of contrasting social class in a way that was independent of the leukaemia findings. Finally, comparisons of the incidence of these malignancies were made between the study areas and a similar area around Sellafield in Cumbria, where an excess of leukaemia and non-Hodgkin's lymphoma has aroused much concern.

Results

Table II gives details of the observed and expected numbers of leukaemia and non-Hodgkin's lymphoma

cases at ages 0-4, 5-14, and 0-14 years in the vicinity of the different sites during their construction together with the single following year. To simplify presentation findings in the overlapping areas around five large Pembrokeshire sites[16] are combined. The specific sites considered together showed a significant excess ($P<0.01$) at both ages 0-4 and 0-14 years. The Scottish hydroelectric counties also showed a significant excess ($P<0.05$) at 0-14 years and in addition at ages 5-14. In the study overall there was a 35% or greater excess in each of the three age groups, highly significant at ages 0-14 ($P<0.001$), though also significant at 0-4 ($P<0.01$) and 5-14 years ($P<0.05$) (table II). Above age 4 the excess was more pronounced at ages 10-14 (32 cases observed, 22·15 expected; $P=0.054$) than at 5-9 (35 *v* 27·40). These excesses were mainly in (pre-1974) rural districts; urban districts separately analysed showed no significant excess (33 cases observed, 28·89 expected).

The excesses were more pronounced in each age group in periods when the operation of the plants overlapped with construction (observed to expected ratio 1·72 at 0-14 years; $P<0.001$ (table III)). They were also pronounced in areas of higher social class; this was particularly so within the overlap periods, the observed to expected ratios being 2·3 at ages 0-4 years ($P<0.001$), 2·2 at 5-14 ($P<0.05$), and 2·2 at 0-14 ($P<0.001$). The findings of the above analyses are summarised in table IV for leukaemia and non-Hodgkin's lymphoma combined, as well as for leukaemia separately. The overlap analyses did not include the Scottish hydroelectric counties, because those schemes required few or no operating staff; nor did the social class analyses, because of our ignorance of the precise home areas of the construction workers. Observed and expected numbers of cases of leukaemia and non-Hodgkin's lymphoma in the five year periods before and after the construction periods (as defined above) showed no excess (see table V).

TABLE III—*Observed (O) and expected (E) numbers of cases of childhood leukaemia and non-Hodgkin's lymphoma in overlapping construction and operational phases*

	Period	Age 0-4 years O	E	Age 5-14 years O	E	Age 0-14 years O	E
Specific projects							
Drax Phase 1	1970-75	3	1·84	1	1·84	4	3·68
Drax Phase 2	1979-93	7	3·92	6	4·07	13	7·99
Longannet	1968-73	10	5·66	10	5·74	20	11·40*
West Burton	1966-68	1	0·69	1	0·80	2	1·49
Pembrokeshire First refinery	1960-61	1	0·34	0	0·43	1	0·77
Pembrokeshire Later projects	1968-83	1	1·77	5	2·19	6	3·96
Invergordon	1970-73	3	0·35***	0	0·32	3	0·67*
Peterhead	1979-83	2	0·77	1	0·69	3	1·46
Dinorwig	1981-84	0	0·32	3	0·49	3	0·81
Holyhead	1970-72	0	0·33	1	0·36	1	0·69
Fawley Refinery	1951-52	1	0·10	0	0·09	1	0·19
Fawley Power station	1962-72	3	1·74	3	1·81	6	3·55
Total		32	17·83**	31	18·83	63	36·66***
[O:E (95% confidence interval)]		[1·80 (1·23 to 2·54)]		[1·65 (1·12 to 2·34)]		[1·72 (1·32 to 2·21)]	

*P<0·05. **P<0·01. ***P<0·001.

TABLE IV—*Summary of findings of childhood leukaemia and non-Hodgkin's lymphoma near large rural construction sites. Results expressed as: observed to expected ratio [observed number of cases] (95% confidence interval) in study overall and in certain subgroups*

		Age 0-4 years	Age 5-14 years	Age 0-14 years
		Leukaemia and non-Hodgkin's lymphoma		
All study areas		1·39 [63] (1·07 to 1·78)	1·35 [67] (1·05 to 1·72)	1·37 [130] (1·15 to 1·63)
All specific sites		1·51 [41] (1·11 to 2·08)	1·25 [38] (0·89 to 1·72)	1·37 [79] (1·10 to 1·73)
Overlap of construction and operation	Yes	1·80 [32] (1·23 to 2·54)	1·65 [31] (1·12 to 2·34)	1·72 [63] (1·32 to 2·21)
	No	1·07 [9] (0·51 to 1·97)	0·61 [7] (0·25 to 1·26)	0·82 [16] (0·48 to 1·31)
Higher social class	Yes	1·83 [24] (1·17 to 2·72)	1·42 [21] (0·88 to 2·17)	1·61 [45] (1·17 to 2·15)
	No	1·29 [17] (0·76 to 2·04)	1·10 [17] (0·64 to 1·77)	1·19 [34] (0·83 to 1·66)
Higher social class in overlap periods	Yes	2·25 [18] (1·36 to 3·52)	2·21 [19] (1·33 to 3·45)	2·23 [38] (1·58 to 3·06)
	No	1·39 [14] (0·74 to 2·38)	1·18 [12] (0·61 to 2·06)	1·28 [25] (0·83 to 1·89)
		Leukaemia only		
All study areas		1·54 (1·18 to 1·97)	1·43 (1·09 to 1·85)	1·48 (1·23 to 1·77)
All specific sites		1·67 (1·20 to 2·27)	1·33 (0·91 to 1·87)	1·50 (1·18 to 1·89)
Overlap of construction and overlap	Yes	1·99 (1·36 to 2·81)	1·75 (1·15 to 2·57)	1·88 (1·43 to 2·43)
	No	1·06 (0·49 to 2·01)	0·65 (0·24 to 1·41)	0·84 (0·47 to 1·39)
Higher social class	Yes	2·16 (1·39 to 3·22)	1·73 (1·04 to 2·70)	1·95 (1·41 to 2·62)
	No	1·27 (0·74 to 2·03)	0·99 (0·53 to 1·70)	1·13 (0·76 to 1·61)
Higher social class in overlap periods	Yes	2·37 (1·40 to 3·74)	2·44 (1·43 to 3·91)	2·40 (1·67 to 3·34)
	No	1·66 (0·91 to 2·78)	1·15 (0·52 to 2·17)	1·41 (0·90 to 2·12)

TABLE V—*Observed (O) and expected (E) numbers of cases of childhood leukaemia and non-Hodgkin's lymphoma in areas near large rural construction sites in five years before start and five years after completion of construction phase (and associated following year)*

	Before construction O	E	After completion O	E
Specific sites:				
Drax	3	2·45	1	1·65
Longannet	9	8·50	9	10·15
West Burton	1	1·94	1	2·75
Pembrokeshire	1	1·54	0	1·96
Invergordon	2	0·83	0	1·24
Peterhead	0	1·31	1	1·67
Dinorwig	2	1·45	3	0·95
Holyhead	1	1·07	0	1·21
Fawley	0	0·38	2	3·18
Total	19	19·47	17	24·76
Main "hydroelectric" counties:				
Ross and Cromarty	1	1·27	4	2·59
Dunbartonshire	4	1·76	5	3·30
Inverness-shire	2	1·18	0	2·32
Sutherland	2	0·48	0	0·58
Perthshire	2	1·72	3	3·30
Total	11	6·41	12	12·09
Grand total	30	25·88	29	36·85

In all cases preceding periods extended to year immediately before earliest calendar year in table I; all were five years long except in Fawley, which related to 1945-8. Following periods began in calendar year immediately after latest calendar year in table II, and all were five years long except in the case of Drax, for which only available years were 1976-8 (before restart of construction).

Discussion

This study found a significantly increased incidence of leukaemia and non-Hodgkin's lymphoma in children living near large rural industrial sites, or in Scottish hydroelectric counties, while construction was under way. By concentrating on such periods and only a single following year we aimed at minimising confusion with any effects of the operations of the plants, though these were also investigated (table V). As in a previous study of construction workers,[6] the excess of cases was greater in areas of higher social class, where the prevalence of people susceptible to infective agents is likely to be higher than average. These excesses were not typical of the areas in question as they were not present in preceding periods (table V), nor were they typical of rural areas more generally at the times of construction (unpublished data).

The excess was more pronounced in periods of overlap on the sites between (outside) construction workers and locally resident operating staff. This may reflect the additional opportunities for contacts, both direct and indirect, between outside construction workers and local residents. However, it is possible that the findings in these periods also reflected the increased activity (and therefore additional population mixing) that tends to occur as construction work nears completion. At such times workforce numbers are often maximal and a succession of new workers arrive to perform specialised jobs as others leave. Certain aspects of the lifestyle of construction workers may have particular relevance for the transmission of infection. Thus many live an itinerant life far from home with much time spent, both at work and in leisure, in crowded conditions in which hygiene is not a priority.

Of all the study areas, the excess of leukaemia and non-Hodgkin's lymphoma was most pronounced (<0.01) in Ross and Cromarty during the construction of hydroelectric schemes. Two factors may have contributed. Firstly, the isolation of the area: with the

exception of Sutherland (with few schemes) it was the remotest of all study areas. Secondly, the extent of "exposure" of its residents to construction workers was probably high. Beyond the stated policy of the hydroelectric board of employing local men, no details could be traced about the composition of any of these workforces. However, it seems not improbable that the workforce in Ross and Cromarty contained a particularly high proportion of men from that county because of the large scale of unemployment there. In the nearest previous period with available data (1937) it had the highest level of unemployment among all the counties of Britain (40% of insured workers).[17]

Near certain study areas there were other examples of population mixing (see table I), though there was no means of knowing if they contributed to the findings. An exception was the excess near the Invergordon aluminium smelter, which preceded work at the nearby (oil industry) platform construction yard at Nigg. There was no excess of leukaemia and non-Hodgkin's lymphoma among children in the vicinity of sites that immediately adjoined a town, such as those next to Pembroke, Holyhead, and Peterhead, each with a population of about 10 000 (see table II). Possibly the greater local resources of labour there than in the more rural areas in this study resulted in less population mixing of the relevant type. Again the major route to Ireland through Holyhead may have exposed that area to some urban mixing so that the proportion of susceptible people was fairly low. In addition, the lack of an appreciable excess in urban districts within 10 km of study sites was similar to the findings in other studies.[26] Had we considered these possibilities in advance our criteria might have excluded such areas, with consequent increases in the excesses recorded in remaining areas.

COMPARISON WITH SELLAFIELD AREA

The population mixing hypothesis was partly suggested by the excess of childhood leukaemia and non-Hodgkin's lymphoma near the nuclear site at Sellafield.[1] The relevance of construction workers to this hypothesis was suggested by observations in a study of the North Sea oil industry,[6] implying a similar role at Sellafield.[6,18] Despite support for the present hypothesis[1-9] and the finding that an alternative hypothesis[19] about paternal preconceptional irradiation was incorrect,[20] the magnitude of the excess in Seascale, near Sellafield, and possibly also the obvious source of radiation nearby have weighed in the minds of some against population mixing as the explanation for this particular increase. However, two considerations tend to be overlooked. The first is that the well known excess in Seascale tends to restrict interest to this parish taken in isolation from the entire area close to Sellafield. A geographical study prompted by concern about Sellafield would initially be directed to the area surrounding the plant rather than to a single part or segment of this (see below). When the area within 10 km of Sellafield was considered as a whole (table VI) the excess of leukaemia and non-Hodgkin's lymphoma (observed to expected ratio 1·67) was similar to that in the study areas in the overlap periods (1·72, table III).

However, the increase of these diseases near Sellafield was concentrated in Seascale, where eight cases in children below age 15 occurred in the period 1947-93 compared with about 0·9 expected (observed to expected ratio 8·9, table VII). Comparisons of the magnitude of this excess with those in the study parishes are influenced by the fact that, as emphasised recently,[21] it was the Seascale cases themselves (specifically those before the report by the Black committee in 1984) that drew attention to this parish, thereby making conventional statistical tests inappropriate. Somewhat comparable would be for us to single out one parish near the Drax power station simply because of the five cases in a prolonged overlap period (7·9-fold increase). In Seascale only the cases after 1983 are amenable to hypothesis testing, since appreciable opportunities exist for chance to inflate the excess among the earlier cases, a group that was in effect stumbled on.[21]

The second consideration is the highly unusual demography of Seascale, which greatly limits testing

TABLE VI—*Observed to expected (O:E) ratios and observed numbers of cases (O) of leukaemia and non-Hodgkin's lymphoma in children, together with details of study areas and of Sellafield area*

Site	Overlap periods		Construction periods		Maximum No in workforce		Years of overlap with construction workers	Distance from population centre (km)	% Of population resident in family with:			
	O:E	O	O:E	O	Construction workers	Employees			≥40% in social class I	≥20% in social class I	≥50% in social classes I, II	≥25% in social classes I, II
Drax	1·5	1	1·5	22	3500	1100	20	28	0	0·2	3	32
Longannet	1·7	20	1·3	25	>2000	700	5	34	0	0	0	3
West Burton	1·3	2	1·0	4	>2000	700	3	22	0·4	0·4	1	12
Pembroke sites	0·9	4	1·0	9	>2000	>1000	8	76	0	0	3	17
Invergordon	4·5	3	3·0	3	>2000	1500	3	90	0	0	5	7
Peterhead	2·1	3	1·1	4	1600	200	4	40	0	0	0	0
Dinorwig	3·7	3	2·2	4	2700	130	4	75	0	0	0	43
Holyhead	1·4	1	1·1	1	1500	1300	3	110	0	0	0	22
Fawley (refinery, power station)	1·9	7	1·8	7	5000	>3000	13	12	0	0	0	3
Sellafield†	1·7	18	1·6	18	7800	9200	44	60	10	16	12	26

†Entire period 1947-93 was regarded as being "exposed" to construction workers; overlap period = 1950-93.

TABLE VII—*Observed to expected ratios (O:E) and observed numbers of cases (O) of childhood leukaemia and non-Hodgkin's lymphoma: comparisons of Sellafield area and sites in present study, distinguishing between post hoc observations and hypothesis testing investigations*

Sellafield site					Non-nuclear (specific) sites				
Type of area (parish or within 10 km of site)	Whether test of hypothesis	O:E	O	95% Confidence interval	Type of area	Whether test of hypothesis	O:E	O	95% Confidence interval
Seascale before 1984	No (source of hypothesis)	8·8	7†	3·5 to 18·0	Parish§	No‖	7·9	5	2·6 to 18·5
Within 10 km before 1984	No‡	1·5	13	0·8 to 2·6	Within 10 km¶	No‖	4·5	3	0·9 to 13·1
Within 10 km from 1984	Yes	1·9	5	0·6 to 4·4	Within 10 km of all sites	Yes	1·4	79	1·1 to 1·7
Seascale from 1984	Yes	10·0	1	0·3 to 55·7	Parish with percentage of social class I as in Seascale††	Yes	58·8	1	1·4 to 327·6
Seascale with another high social class I parish, from 1984	Yes	19·2	2	2·4 to 72·3					

†Eight cases are shown in reference 26 but in one pre-1962 case diagnosed in Seascale death occurred outside.
‡Except cases outside Seascale.
§Near power station A.
‖That is, not as selected post hoc; but in combination with other study areas they are hypothesis testing.
¶Near aluminium smelter.
††Near power station B.

any hypothesis at the parish level, comparable places being so rare. Situated more than 60 km from a population centre, it is additionally secluded by being away from a main road and, with the sea beyond, it is effectively a cul de sac. It is also distinctive in being the Cumbrian parish with the highest proportion of residents working at Sellafield; it also has an 18-fold higher proportion of Sellafield workers born outside Cumbria than among such workers in the rest of West Cumbria.[22] The nuclear authority was largely responsible for the building programme that resulted in it growing threefold between 1948 and 1961, and the houses were originally allocated to staff mainly on the basis of grade. As a result Seascale has an exceptionally high proportion of people in social class I: in 1961 this was 43% compared with 4% nationally, and in 1971 it was 46% compared with 7% nationally.[23] These proportions were responsible for the high social class structure of the whole Sellafield area shown in table VI.

Among the 124 constituent units in this study, only one resembled Seascale in having 41% of men in social class I (the next highest having only 20% and 22%). Interestingly, a case of leukaemia occurred in this small parish (with less than a tenth of Seascale's population), which is a significant excess (expected 0·017; observed to expected ratio 58·8) for it represents a test (the only one possible in this study) of the importance of Seascale's high social class structure. The confidence interval around the 58-fold increase easily encompasses both the unbiased 10-fold excess in Seascale since 1984 (also based on one case under 15 years) and the potentially biased ninefold increase before 1984 (see table VII).

A remarkable aspect of the excess of leukaemia and non-Hodgkin's lymphoma in the Sellafield area is its duration, for it has been present from the 1950s. This might seem to argue against an infective explanation, as most infective epidemics are self limiting, ending when the number of susceptible people has declined below some critical level. However, two facts are relevant. Firstly, the level of movement among the administrative and scientific staff there both to other parts of the nuclear industry in Britain and also from Seascale to more traditional villages in Cumbria is high; the large numbers of new arrivals who replace them include susceptible children[23] (and perhaps some adults). The presence of these new arrivals combined with the effects of hygiene (high social class) and geography (isolation) would ensure a continuing high level of susceptible people, a potent factor in promoting and maintaining an epidemic.[24]

Secondly, the other requirement for a prolonged epidemic—namely, a source of infection—is adequately provided by the large numbers of construction workers continuously over a long period at Sellafield, an aspect that distinguishes it from other rural industrial sites in Britain. Quite independently of the large nuclear workforce (up to more than 9000), a large contractors' workforce (reaching a peak of 7800 in 1991) has also been present on the site in most of its 45 years of operation. Only one site in our study (Drax) has had a prolonged period of construction work after its operational start, and it alone has shown an excess of childhood leukaemia and non-Hodgkin's lymphoma over an extended period (see tables II, III, and VI).

In a recent study[25] of the distribution of cases of childhood leukaemia and non-Hodgkin's lymphoma children within 25 km of the 29 nuclear installations in England and Wales only Sellafield showed a noticeable distance effect, entirely due to the Seascale cases. However, in contrast with the present study all but one site was studied after completion of construction; few of the 29 had a later construction phase, and these were not examined separately. The findings therefore do not conflict with those of this study.

Key messages

- Large scale unaccustomed mixing of rural and urban people promotes increases of childhood leukaemia and non-Hodgkin's lymphoma, consistent with an underlying infective basis
- Large construction projects in rural areas entail such mixing because the workforces are drawn from a wide area
- A significant excess of leukaemia and non-Hodgkin's lymphoma combined has been found in areas near large, non-nuclear construction projects in rural Britain over the past 50 years, similar to that near Sellafield
- The high incidence of these diseases in Seascale children appears to be due to the high proportion of susceptible subjects consequent on the unusually high social class and the regular addition of new children to the parish
- The findings are further evidence that the excess of leukaemia and non-Hodgkin's lymphoma near Sellafield is due to an infective process; probably the excesses found in the present study would have been noticed earlier had there been a local source of radiation

CONCLUSIONS

Overall these findings provide further support for the hypothesis that prompted the study—that rural population mixing is conducive to the transmission of the underlying infective agent(s) among susceptible people so as to increase the incidence of childhood leukaemia and non-Hodgkin's lymphoma. These excesses had not been noticed before because no one had looked for them. No doubt if any of the situations had included a source of radiation the excesses would have attracted attention sooner. The study also finds that the increased incidence near Sellafield (the source of the hypothesis) is not very different from that near large non-nuclear rural construction sites, particularly when (as at Sellafield) operating staff and construction workers are present on the same site. The findings also predict that in a parish like Seascale the excess would be particularly noticeable as a result of its high social class make up and relative isolation—and also prolonged because of the continual influx of new susceptible people.

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1 Kinlen LJ. Evidence for an infective cause of childhood leukaemia: comparison of a Scottish new town with nuclear reprocessing sites in Britain. *Lancet* 1988;ii:1323-7.
2 Kinlen LJ. Evidence from population mixing in British new towns 1946-85 of an infective basis for childhood leukaemia. *Lancet* 1990;336:577-82.
3 Kinlen LJ, Hudson C. Childhood leukaemia and poliomyelitis in relation to military encampments in England and Wales in the period of national military service 1950-63. *BMJ* 1991;303:1357-62.
4 Kinlen LJ, Hudson C, Stiller C. Contacts between adults as evidence for an infective origin of childhood leukaemia: an explanation for the excess near nuclear establishments in west Berkshire? *Br J Cancer* 1991;64:549-54.
5 Kinlen LJ, Stiller C. Population mixing and excess of childhood leukaemia. *BMJ* 1993;306:930.
6 Kinlen LJ, O'Brien F, Clark K, Balkwill A. Rural population mixing and childhood leukaemia: effects of the North Sea oil industry in Scotland—including the area near the Dounreay nuclear site. *BMJ* 1993;306:743-8.
7 Kinlen LJ, John SM. Wartime evacuation and mortality from childhood leukaemia in England and Wales in 1945-9. *BMJ* 1994;309:1197-202.
8 Langford I. Childhood leukaemia mortality and population change in England and Wales 1969-73. *Soc Sci Med* 1991;33:435-40.

9 Kinlen LJ. Epidemiological evidence for an infective basis in childhood leukaemia. *Br J Cancer* 1995;71:1-5.
10 *Britain. An official handbook (years 1954-90).* London: HMSO, 1954-90.
11 Payne PL. *The hydro.* Aberdeen: Aberdeen University Press, 1988.
12 Fulton AA. Civil engineering aspects of hydro-electric development in Scotland. *Proceedings of the Institution of Civil Engineers* 1952;1(part I): 248-77.
13 Court Brown WM, Doll R. *Leukaemia and aplastic anaemia in patients irradiated for ankylosing spondylitis.* London: HMSO, 1957.
14 Court Brown WM, Doll R, Hill AB. Incidence of leukaemia after exposure to diagnostic radiation in utero. *BMJ* 1960;ii:1539-45.
15 Cook-Mozaffari PJ, Darby SC, Doll R, Forman D, Hermon C, Pike MC, *et al.* Geographical variation in mortality from leukaemia and other cancer in England and Wales in relation to proximity to nuclear installations, 1969-78. *Br J Cancer* 1989;59:476-85.
16 McKay K. *A vision of greatness: the history of Milford 1790-1990.* Haverfordwest: Brace Harvatt, 1989.
17 Fogarty MP. *The prospects of the industrial areas of Great Britain.* London: Methuen, 1945.
18 Kinlen LJ. Childhood leukaemia and non-Hodgkin's lymphoma in young people living close to nuclear reprocessing sites. *Biomed Pharmacother* 1993;47:429-34.
19 Gardner MJ, Snee MP, Hall AJ, Powell CA, Downes S, Terrell JD. Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in west Cumbria. *BMJ* 1990;300:423-9.
20 Doll R, Evans HJ, Darby S. Paternal exposure not to blame. *Nature* 1994;367:678-80.
21 Draper G, Stiller CA, Cartwright RA, Craft AW, Vincent TJ. Cancer in Cumbria and in the vicinity of the Sellafield nuclear installation, 1963-90. *BMJ* 1993;306:89-94.
22 Health and Safety Executive. *Health and Safety Executive investigation of leukaemia and other cancers in the children of male workers at Sellafield.* London: HMSO, 1993.
23 Gardner MJ, Hall AJ, Downes S, Terrell JD. Follow up study of children born to mothers resident in Seascale, west Cumbria (birth cohort). *BMJ* 1987;295:822-7.
24 Anderson RM, May RM. *Infectious diseases of humans. Dynamics and control.* Oxford: Oxford University Press, 1992.
25 Bithell JF, Dutton SJ, Draper GJ, Neary NM. Distribution of childhood leukaemia and non-Hodgkin's lymphomas near nuclear installations in England and Wales. *BMJ* 1994;309:501-5.
26 Kinlen LJ. Can paternal preconceptional radiation account for the increase of leukaemia and non-Hodgkin's lymphoma in Seascale? *BMJ* 1993;306: 1718-21.

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Weight growth in infants born to mothers who smoked during pregnancy

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Abstract

***Objective*—To determine whether maternal smoking during pregnancy causes impairment in growth after birth.**

***Design*—Longitudinal study.**

***Setting*—Six medical university centres of six towns of north, central, and south Italy.**

***Subjects*—12 987 babies (10 238 born from non-smoking mothers, 2276 from mothers smoking one to nine cigarettes a day, and 473 from mothers smoking ⩾10 cigarettes a day) entered the study.**

***Main outcome measures*—Difference in weight gain between children born to smoking mothers and those born to non-smoking mothers. Weight was measured at birth and at 3 and 6 months of age. Maternal smoking habit was derived from interview on third or fourth day after delivery.**

***Results*—Compared with children born to mothers who did not smoke during pregnancy, the birth weights of children born to mothers who smoked up to nine cigarettes a day were 88 g (girls) and 107 g (boys) lower; in children born to mothers who smoked ⩾10 cigarettes a day weights were 168 g and 247 g lower. At six months of age for the first group the mean weight for girls was 9 g (95% confidence interval −47 g to 65 g) higher and for boys 64 g (−118 g to −10 g) lower than that of children born to mothers who did not smoke. The corresponding figures for the second group were 28 g (−141 g to 85 g) lower for girls and 24 g (−136 g to 88 g) lower for boys.**

***Conclusions*—The deficits of weight at birth in children born to mothers who smoked during pregnancy are overcome by 6 months of age. These deficits are probably not permanent when smoking habit during pregnancy is not associated with other unfavourable variables (such as lower socioeconomic class).**

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Introduction

A causal relation between smoking in pregnancy and birth weight is generally accepted. Mothers who smoke during pregnancy generally deliver infants weighing from 100 g to 300 g less than children born to non-smoking mothers.[1,2] A dose-effect relation between number of cigarettes smoked by a pregnant woman and her infant's weight has been shown, whereas there are no differences in weight between babies born to women who never smoked during their lives and those who quit smoking only during pregnancy.[1,3-5] Limited data on the follow up of children born to mothers who smoke suggest that the deficits at birth may remain in childhood and possibly even into adulthood.[3,6,7] Almost all these data, however, were collected on small samples in the early 1970s in the United States and the United Kingdom, where smoking habit was often associated with poor social class and lower educational level. Furthermore this long term effect has not been found by other authors.[8,9] The issue of maternal smoking during pregnancy and child development thus remains controversial.

We evaluated weight gain in the first six months of life of babies born to mothers who smoked during pregnancy.

Subjects and methods

SUBJECTS

Data reported here were obtained from a large nationwide multicentre obstetric-paediatric survey carried out in Italy between 1973 and 1981 supported by the Consiglio Nazionale delle Ricerche (CNR).[10-12] The survey consisted of a cross sectional part at birth and a longitudinal part up to the third birthday. Babies were born in six university medical centres of six towns of north, central, and south Italy. Some of these centres were referring centres for pregnancies at risk, and high risk infants were therefore systematically oversampled. The longitudinal survey collected data on about 60% of children whose mothers turned up for at least one visit among the eight planned. Information on smoking and sociodemographic characteristics of the mothers was obtained by interview on the third or fourth day after delivery.

In this study only singleton babies without congenital malformations for whom information on maternal smoking habit and weight growth was available were considered. Babies born to mothers who quit smoking during pregnancy (2464) were excluded from this study. Birth weight and weight growth in these babies were the same as those of babies born from non-smoking mothers. In total, 12 972 babies (6193 girls and 6779 boys) who were followed up at 3 and 6 months and 15 (11 girls and four boys) who had only birth weight (two) or birth weight and weight at 6 months