

# Incidence and occupational pattern of leukaemias, lymphomas, and testicular tumours in Western Ireland over an 11 year period

Cecily Kelleher, John Newell, Collette MacDonagh-White, Emer MacHale, Ernest Egan, Eugene Connolly, Helen Gough, Bettie Delaney, Eithne Shryane

## Abstract

**Study objective**—To determine incidence of the following malignancies, testicular tumours, all leukaemias and all lymphomas in the West of Ireland in an 11 year period. Secondly, to examine the relation between disease patterns and available occupational data in male subjects of working age.

**Design**—A census survey of all cases occurring in the three counties in the Western Health Board (WHB) area, Galway, Mayo and Roscommon, for the 11 year period 1980 to 1990 inclusive. Average annual age standardised incidence rates for the period were calculated using the 1986 census data. Rates for the area are compared with rates from the southern region of Ireland, which had a tumour registry. Trends over the time period are evaluated. All male subjects for whom occupational data were available were categorised using the Irish socioeconomic group classification and incidence rates by occupation were compared using the standardised incidence ratio method. In one of the counties, Galway, a detailed occupational history of selected cases and an age matched control group was also elicited through patients' general practitioners.

**Setting**—All available case records in the West of Ireland.

**Results**—There are no national incidence records for the period. Compared with data from the Southern Tumour Registry, the number of cases of women with myeloid leukaemias was significantly lower. Male leukaemia rates were significantly lower as a group (SIR 84 (95%CI 74, 95) but not when considered as individual categories. Regression analysis revealed an increasing trend in the number of new cases of non-Hodgkin's lymphoma among both men ( $r=0.47$ ,  $p=0.02$ ) and women ( $r=0.90$ ,  $p=0.0001$ ) and of chronic lymphocytic leukaemia in men ( $r=0.77$ ,  $p=0.005$ ) and women ( $r=0.68$ ,  $p=0.02$ ) in the WHB region over the last decade. Four hundred and fifty six male cases over the age of 15 years were identified and adequate occupational information was available for 74% of these. Standardised incidence ratios of testicular tumours were significantly increased for semi-skilled manual workers (SIR 367 95%CI

100, 938) and agriworkers other than farmers (SIR 377, 95%CI 103, 967). There were also significantly increased incidence ratios for both non-Hodgkin's lymphoma (SIR 169, 95%CI 124, 266) and three categories of leukaemias among farmers. Hodgkin's disease and acute myeloid leukaemias were significantly increased among semi-skilled people. Interview data with 90 cases and 54 controls of both sexes revealed that among farmers, cases ( $n=31$ ) were significantly less likely than controls ( $n=20$ ) to use tractor mounted spraying techniques (OR = 0.19 (95%CI 0.04, 0.80)) and less likely to wear protective masks (OR 0.22 (95%CI 0.05, 0.84)).

**Conclusions**—Trends of increase in non-Hodgkin's lymphoma and some leukaemias are consistent with studies elsewhere. The study provides further evidence of the relation between agricultural work and certain lymphoproliferative cancers. The possible carcinogenic role of chemicals used in agricultural industries must be considered as an explanation.

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The importance of morbidity surveillance in relation to malignant disease is undoubted in identifying disease aetiology. The assessment of environmental risk factors for malignant diseases can be particularly problematic because of the long potential interval between exposure and development of disease and the difficulty of adequate biological monitoring of hazards. It is especially so in the case of the working environment where a detailed and comprehensive employment history over a number of years is required and where frequent change of employment can occur, particularly in the case of unskilled and semi-skilled workers. Furthermore, new industries are appearing all the time that involve the management of potentially hazardous substances whose safety track record in relation to human exposure is not yet known in epidemiological terms. There is evidence that some cancers may be increasing in incidence.<sup>1</sup> In Ireland, farming and agriculture are particularly important, as there are a relatively large proportion of the population employed in this sector at 14%.<sup>2</sup> There is increasing emphasis on the development of industries associated with agricultural production and processing and one of these, fish farming, has expanded considerably in the past 10 years. Data on morbidity are difficult to

## Departments of Health Promotion and

C Kelleher  
J Newell  
C MacDonagh-White  
H Gough  
B Delaney  
E Shryane

## Haematology and Pathology

E Egan  
E Connolly

## National University of Ireland, Galway

Galway Community Care Area, Western Health Board, Galway  
E MacHale

Correspondence to:  
Professor C Kelleher,  
Department of Health Promotion, Clinical Sciences Institute, National University of Ireland, Galway.

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ascertain as legislation in relation to health and safety practices was only extended comprehensively to the farming sector in Ireland in 1989. Likewise data about occupation are not always systematically recorded in medical case notes and there may be under-reporting of such information.

This report is the third to examine demographic patterns of malignancy in the West of Ireland.<sup>3,4</sup> Incidence and death rates for selected lymphoproliferative disorders are examined but also on this occasion testicular tumours. The findings over the 11 year period of this study are compared with Southern Tumour Registry data and with the results of the previous study. This study was instigated originally because of an anecdotal clinical observation that there appeared to be an undue number of cases with testicular tumours or leukaemia in workers associated with fish farming industry, an issue that needed to be more systematically investigated. All such cases first had to be identified by a census survey of the three counties constituting the Western Health Board area. The incidence over an 11 year period of the candidate neoplasms and their relation with occupation is reported.

### Methods

This study was a census of all available data in the three counties, Galway, Mayo, and Roscommon for the 11 consecutive years 1980 to 1990 inclusive. The total population of the area at the midpoint of the period was 348 328, 51% of whom were men. At the time this study was undertaken the National Tumour Registry had not yet been established, so that no national morbidity data were available for that period apart from the data described here and those collected in the former Southern Tumour Registry, comprising counties Cork and Kerry.<sup>5</sup> The work was overseen by a project steering committee representing the departments of Health Promotion, Haematology and Pathology at University College Galway and the community care area of the Western Health Board. Actual data collection was undertaken by a researcher (HG) with the assistance of two registered nurses (BD and ES).

Detailed checking of all known cases of testicular tumours and of leukaemias and lymphomas was undertaken. Permission to proceed was sought from the university hospital ethical committee and from both medical and administrative personnel in each institution. Data sources identified in advance were (a) hospital records, which included University College Hospital, Galway and all other hospitals in the area, (b) death registers for each district, and (c) records of all general practitioners in the WHB area.

Firstly, all medical personnel dealing with such cases were contacted and asked to complete a comprehensive questionnaire giving details of cases known to them. These were then cross checked by the researchers to identify any duplication of information. The researchers also examined each individual laboratory record and confirmed demographic information by checking hospital charts. Original

records for all cases were histologically re-confirmed by either the consultant haematologist or pathologist dealing with the case to confirm the diagnosis as assigned before entry to the database.

In each case, the following variables were recorded, if available: name, current age, current postal address, sex, occupation, specific malignancy type, date of diagnosis, and date of death, if the patient was now deceased. In addition address at time of diagnosis was recorded. As far as possible the present whereabouts of every patient was established and death, if it had occurred, was documented. All general practitioners registered with the Western Health Board were contacted to establish what they knew of long term outcome of individual patients, particularly where data appeared inadequate from the hospital notes. It was recognised that patients ordinarily resident in the West of Ireland might possibly be referred outside the area for treatment so that general practitioners were asked to provide data on such referrals, if any. Access to a testicular tumour registry supported by the Irish Cancer Society was also afforded and all those records were cross checked by a researcher (HG) against our own records. Likewise referral from neighbouring health board counties into the area might occur and if such cases were identified they were excluded. The research nurses then further cross checked all information recorded from these several sources to assemble the database. In effect, however, negligible additional case information not already available through the primary sources listed above was identified.

The data from the 1986 census for the three counties were used to provide denominator data, for three reasons.<sup>6</sup> Firstly, although preliminary results from the 1991 census were available at the time of analysis these were not sufficiently detailed for our purposes. Secondly, 1986 is a convenient mid time point for the decade as a whole. Finally, detailed sociodemographic breakdown by district electoral division was possible using data specifically provided for the purpose by the Central

Table 1 Average annual crude (CR) and age standardised (ASR) incidence rates/100 000 population during the period 1980-90 for the Western Health Board (WHB) region and the Southern Tumour Registry (STR) and standardised incidence ratios (SIR) with 95% confidence intervals

	STR		WHB			
	CR	ASR	CR	ASR	SIR	95% CI
Testicular tumours	2.9	2.9	2.4	2.4	86	(22,206)
Hodgkin's disease						
Male	4.2	4.1	2.1	1.9	51	(10,149)
Female	2.3	1.9	0.9	1.0	40	(3,162)
Non-Hodgkin's lymphoma						
Male	8.5	7.3	6.2	4.8	62	(31,110)
Female	7.6	5.9	3.8	2.8	48	(18,101)
Acute and chronic lymphocytic leukaemia						
Male	6.0	4.8	6.8	5.1	101	(54,173)
Female	3.9	2.8	4.2	2.9	103	(43,207)
Acute myeloid leukaemia						
Male	4.3	3.6	1.9	1.4	37	(8,102)
Female	3.7	3.1	0.9	0.7	22	(2,80)
Other leukaemia						
Male	0.0	0.0	0.5	0.5	—	—
Female	0.2	0.1	0.2	0.1	75	(1,113)

Table 2 Crude\* and age specific incidence rates for the specific categories of malignancy for both men and women. Number of cases in parentheses

Age groups	Population at risk		Testicular tumours		Hodgkin's disease		Non-Hodgkin's lymphoma		Acute lymphocytic leukaemia		Chronic lymphocytic leukaemia		Acute myeloid leukaemia		Hairy cell leukaemia		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
0-4	16 337	15 411	0.6 (1)	(0)	0.6 (1)	0.6 (1)	0.6 (1)	1.2 (2)	6.7 (12)	(0)	(0)	(0)	0.6 (1)	(0)	(0)	(0)	
5-9	17 433	16 589	0.0 (0)	(0)	3.1 (6)	(0)	1.0 (2)	1.6 (3)	5.2 (10)	(0)	(0)	(0)	(0)	0.5 (1)	(0)	(0)	
10-14	17 344	16 811	0.0 (0)	(0)	1.0 (2)	(0)	(0)	1.1 (2)	1.6 (3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
15-19	16 153	15 369	2.3 (4)	(0)	2.3 (4)	1.2 (2)	0.6 (1)	0.8 (1)	2.3 (4)	0.6 (1)	(0)	(0)	(0)	(0)	(0)	(0)	
20-24	12 135	11 721	3.7 (5)	1.6 (2)	3.7 (5)	1.6 (2)	0.8 (1)	0.8 (1)	3.0 (4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
25-29	11 456	11 242	6.3 (8)	4.9 (6)	0.8 (1)	0.8 (1)	0.8 (1)	(0)	3.0 (4)	(0)	(0)	(0)	2.4 (3)	(0)	(0)	(0)	
30-34	11 373	10 868	8.8 (11)	(0)	2.4 (3)	0.8 (1)	0.8 (1)	0.8 (1)	1.6 (2)	0.8 (1)	0.8 (1)	0.8 (1)	0.8 (1)	0.8 (1)	(0)	(0)	
35-39	11 142	10 180	0.8 (1)	0.9 (1)	1.6 (2)	0.9 (1)	0.9 (1)	(0)	1.6 (2)	0.8 (1)	0.8 (1)	0.8 (1)	0.8 (1)	1.8 (2)	(0)	(0)	
40-44	9 496	8 399	4.8 (5)	1.1 (1)	3.8 (4)	3.2 (3)	3.2 (3)	(0)	(0)	1.9 (2)	1.9 (2)	2.2 (2)	1.9 (2)	2.2 (2)	(0)	(0)	
45-49	8 135	7 061	3.4 (3)	2.6 (2)	4.5 (4)	1.3 (1)	1.3 (1)	2.6 (2)	(0)	3.9 (3)	3.9 (3)	2.2 (2)	2.2 (2)	2.6 (2)	3.4 (3)	(0)	
50-54	7 742	6 788	(0)	1.3 (1)	17.6 (15)	5.4 (4)	5.4 (4)	(0)	(0)	2.6 (2)	2.6 (2)	2.7 (2)	2.7 (2)	(0)	1.2 (1)	(0)	
55-59	7 631	7 199	(0)	1.3 (1)	8.3 (7)	10.1 (8)	10.1 (8)	(0)	(0)	(0)	(0)	2.7 (2)	2.7 (2)	(0)	1.2 (1)	(0)	
60-64	7 524	7 573	(0)	1.2 (1)	16.9 (14)	13.2 (11)	13.2 (11)	1.3 (1)	2.4 (2)	18.1 (15)	18.1 (15)	3.8 (3)	3.8 (3)	(0)	1.2 (1)	(0)	
65-69	7 875	7 959	2.3 (2)	(0)	2.4 (2)	2.4 (2)	2.4 (2)	1.2 (1)	2.4 (2)	20.8 (18)	20.8 (18)	7.2 (6)	7.2 (6)	(0)	1.2 (1)	3.6 (3)	
70-74	7 349	7 473	3.7 (3)	(0)	16.2 (14)	14.8 (13)	14.8 (13)	(0)	3.5 (3)	11.4 (10)	11.4 (10)	4.6 (4)	4.6 (4)	2.3 (2)	2.3 (2)	(0)	
75-79	4 829	4 868	3.8 (2)	(0)	18.6 (15)	15.8 (13)	15.8 (13)	(0)	4.9 (4)	26.0 (21)	26.0 (21)	9.7 (8)	9.7 (8)	2.4 (2)	2.4 (2)	(0)	
80-84	2 433	2 953	3.7 (1)	6.2 (2)	35.8 (19)	13.1 (7)	13.1 (7)	5.6 (3)	9.4 (5)	32.0 (17)	32.0 (17)	24.3 (13)	24.3 (13)	7.5 (4)	7.5 (4)	(0)	
85+	1 318	2 159	6.9 (1)	(0)	37.4 (10)	12.3 (4)	12.3 (4)	3.1 (1)	(0)	22.4 (6)	22.4 (6)	27.7 (9)	27.7 (9)	6.2 (2)	6.2 (2)	(0)	
Total	177 705	170 623	2.4*(47)	0.9*(17)	6.2*(122)	3.8*(72)	3.8*(72)	1.0*(18)	2.7*(52)	4.2*(82)	4.2*(82)	3.3*(61)	3.3*(61)	1.9*(38)	1.0*(18)	0.5*(10)	0.2*(3)

Statistics Office (CSO). Subjects were first categorised according to age, sex, and geographical location for the time period as a whole and comparisons undertaken. Cancers were classified and coded for analysis according to the standard ICD 9 (International Classification of Diseases) as testicular, lymphomas of either Hodgkin's (HD) or non-Hodgkin's lymphoma in variety. Leukaemias were organised in the following subcategories according to that classification system; acute lymphocytic leukaemia (ALL), chronic lymphocytic leukaemia (CLL), hairy cell leukaemia, acute myeloid leukaemia (AML)/acute non-lymphoid leukaemia (ANLL), and chronic granulocytic leukaemia (CGL).

Occupation was also recorded, if available from case notes. Where such was not recorded on the patient's chart the information was subsequently sought from the general practitioner. Occupation was classified using the Irish socioeconomic classification.<sup>7</sup> Occupations are first categorised into socioeconomic groups (SEGs), a nominal classification, and can be further organised and ranked according to a class scale. For the purposes of this part of the study, although information on both sexes was collected, it was decided a priori to examine male occupational data only because the population of primary interest was the working one and data for men were considered to be more reliable.

As no detailed exposure data were available in case notes it was also decided to survey a sub-section of cases with half as many age matched controls. All cases of testicular tumours, and of leukaemia and lymphoma cases of both sexes aged between 16 and 65 at diagnosis in one of the counties, Galway, were identified. One hundred and twenty five cases (M: 75; F: 50) were identified but 16 of these had no listed general practitioner and so were not considered further. Forty three of the remainder had died. Permission was sought from the local faculty of the Irish College of General Practitioners to have the general practitioner interview these patients, if still alive, or their relatives, if deceased, about their exposure history. A questionnaire was designed and piloted for the study that included details of all past residences, past medical history, reproductive history, occupational history, and chemical exposures at work and at home, including the garden. A specific section for farmers detailed manner of use of pesticides. Controls were to be selected through two general practices, one within five miles of the city and one rural, felt to be sociodemographically representative of the region as a whole. Patients presenting to these practices during the study period for a routine consultation who were in the right age group were asked to complete the questionnaire with their doctor.

STATISTICAL ANALYSIS

Average annual rates per 100 000 were calculated using the direct method and standardised to the World Standard Population. Significance comparison by region and occupation was by the standardised incidence ratio method, using





Table 4 Responses to pesticide use and practice among interview participants with a farming occupation. Note that there may be more than one positive response per person

	Cases 31 of 90						Controls 20 of 54			Odds ratio for difference (95% CI) cases/controls
	Men			Women			Men	Women	All	
	Testicular	Leukaemias	Lymphomas	Leukaemias	Lymphomas	All				
All	7	6	10	5	3		12	8		
Method of application										
Tractor mounted	2	2	2	0	0	6	8	3	11	0.19 (0.04, 0.80)
Hand held	1	2	3	1	0	7	3	2	5	0.87 (0.19, 4.18)
Back pack	6	1	5	4	3	19	5	2	7	2.94 (0.79, 11.25)
Protective equipment										
Overalls	1	1	2	0	0	4	1	2	3	0.83 (0.12, 6.46)
Gloves	2	1	2	1	0	6	3	3	6	0.56 (0.12, 2.56)
Mask	2	2	2	2	1	9	8	5	13	0.22 (0.05, 0.84)

similarly for chronic lymphocytic leukaemia in both sexes ( $r = 0.77$ ,  $p=0.005$  and  $r = 0.68$ ,  $p=0.02$  respectively). Acute myeloid leukaemia appeared to be declining in men ( $r = 0.71$ ,  $p = 0.01$ ). Testicular tumours display no definite trend.

Four hundred and fifty six male cases over the age of 15 years at diagnosis were identified and codable occupational data were available for 74% of these. Rates in men for each socio-economic group were computed using the appropriate census denominator data. Table 3 gives the SIRs with 95% confidence intervals for each SEG. It can be seen that testicular tumours were significantly more likely to occur in agricultural workers other than farmers and among semi-skilled persons. There were just five cases however, though four were fish farmers. The farmer category was particularly notable in having significantly higher ratios in four of the seven categories. The semi-skilled group also had higher rates of testicular tumours, Hodgkin's disease, and acute myeloid leukaemia. Overall, there was no pattern of geographical association between testicular cancers and any relevant industries in the region.

Interview data on previous chemical exposure were obtained for 90 cases (82.6%). Reasons for non-participation included no next of kin available (7), refusal (5) or non-response from next of kin (5). Data were collected from 54 controls, with no refusals to participate. One author (CMcDW) interviewed approximately half of the cases and controls or their relatives, as appropriate, the remainder were interviewed by their own general practitioners. There were no significant differences in reported uses of any specific pesticides between cases and controls, either in an occupational or a domestic setting. Thirty one (M: 23; F: 8) of the cases and 20 (M: 12; F: 8) of the controls had worked primarily as a farmer and gave detail of their pesticide application practice (see table 4). Farmer cases were less likely to wear protective masks than control farmers (odds ratio 0.22 (0.05, 0.84)). Cases were also less likely to spray herbicides using the tractor mounted method (odds ratio 0.19 (0.04, 0.80)). These differences remained significant when men only were compared. There was no difference between cases and controls in duration of employment as a farmer, acreage of farm, growth of specific crops types, and type of farming.

## Discussion

This study shows no excess of any of these categories of tumours compared with the only other part of the country for which there are contemporary available data and in the case of some tumour types, a lower rate is reported. The main findings were a rise in both sexes in the incidence of non-Hodgkin's lymphoma and chronic lymphocytic leukaemia in the region over time and patterns of association between occupational group and different categories of malignancy. This is in fact an increase in the number of cases ascertained or diagnosed in the 11 year period. In theory more cases could have been treated and referred, accounting for the rise in incidence. However, those with an address outside the Board area were excluded and our clinical treatment practices have not significantly changed during that time. Furthermore, the trends are not seen for every tumour type. Though we used the midpoint census data, the population variations were modest during the time and could not explain the effect. The newly established National Tumour Registry in Ireland can now monitor these effects systematically for the future. For epidemiological purposes, studies of leukaemias and lymphomas tend to group cases according either to end organ disease or cell line. In this study we used the ICD 9 system of categorisation to retain consistency with previous studies in the region. The age specific rates reported in this paper are consistent with the known epidemiology of these diseases.

The reasons for a change in incidence are not clear. Non-Hodgkin's lymphoma has shown a dramatic increase in incidence in the USA in the past 10 to 15 years<sup>10</sup> compared with Hodgkin's disease. Numerous medical conditions may predispose to non-Hodgkin's lymphoma, and include patients who have been treated with immunosuppressive drugs,<sup>11</sup> patients who have AIDS,<sup>12</sup> patients with longstanding infection with Epstein-Barr virus,<sup>13</sup> patients with coeliac disease,<sup>14</sup> and patients who have certain autoimmune diseases.<sup>15</sup> More recently patients who harbour the bacterium *Helicobacter pylori* in the stomach have been shown to have a higher incidence of gastric lymphoma.<sup>16</sup> Environmental carcinogens may be more likely to be implicated in the development of non-Hodgkin's lymphoma arising primarily in the lymph nodes, in contrast with those that arise at extranodal sites such as occur in patients who are immunosuppressed and that seem to

be linked to the Epstein-Barr virus. The vast majority of cases of non-Hodgkin's lymphoma reported in this study are nodal in type.

Other factors implicated in the medical literature include exposure to a wide range of agricultural chemicals<sup>17, 18</sup> used in farming and forestry and also exposure to various solvents used in the construction and paper industry. Exposure to toxic hazards, particularly at work are therefore an important aetiological possibility for lympho-proliferative tumours. This is rendered more likely if there is inadequate use of appropriate protective equipment or poor hygiene practice. We found an excess of leukaemias and non-Hodgkin's lymphomas among farmers generally but not for other agricultural workers. The finding confirms the trends seen in other studies elsewhere.<sup>19-21</sup> Our interview data on a small subsample lend support to the conclusion that inappropriate hygiene practices may have a role, though these should be interpreted with caution as numbers were small and there could be some recall bias.

We found a significant increase in testicular tumours in agricultural workers other than farmers, albeit with very small numbers; this group comprised predominantly those engaged in fish farming. Testicular tumours are rare, accounting for only about 1% of all male neoplasms.<sup>22</sup> There has been a remarkable 300% increase in this century in the United Kingdom and European countries generally. Prognosis has improved with treatment however. Cryptorchidism, drugs, and infections are possible aetiological factors. Testicular tumours are reported elsewhere to be rising in incidence in industrialised societies generally, including Ireland.<sup>23, 24</sup> The age distribution of these tumours is bimodal however and in the case of young men the environmental hazard may even be pre-natal. The relative risk of male infertility is also increasing, in part attributed to the increased prevalence of chemicals that have oestrogen-like actions.<sup>25</sup> One study showed an increased risk in both agricultural and petrochemical workers and suggested a viral explanation or some common toxic hazard.<sup>26</sup> Other studies indicate that the relation to occupation is not consistent, suggesting it may be a confounder for some other aspect of socioeconomic status.<sup>27</sup>

Comparisons were made across a variety of socioeconomic groups and for several different malignancy categories, thus increasing the probability of finding an association. There may be confounding exposures from other sources; for instance fish farm workers may well be engaged in other part time farming work. There is no evidence to date of an increase in this category of testicular malignancies in fish farm workers in other countries that retain adequate occupational surveillance data and have a significant fish farm industry such as Scotland and Scandinavia (personal communications) and there are no confirmatory studies of tumours among the fish themselves, though potential toxicity to Nuvan,

the principal agent used to control sea lice infestation has been studied at varying concentrations.<sup>28</sup> In a country with a strong dependence on agriculture the implications for further occupational surveillance and for attention to work practice, particularly the handling of potentially noxious materials, is clear.

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