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Hairy cell leukaemia, occupation, and smoking

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Summary. The roles of farm practices, occupational exposures to organic solvents, and ionizing radiation in the risk of hairy cell leukaemia (HCL) were examined in a French hospital-based multicentre case–control study including **291** cases **(229** men and **62** women) and **541** controls **(425** men and **116** women). No positive association was observed with occupations involving exposure to organic solvents or with selfdeclared exposures to solvents, but a significant association with self-reported exposure to petrol or diesel was found for men (OR= **1.5 CI95% [1·0–2·1]**). No association with ionizing radiation was detected. Agriculture employment gave an **odds** ratio **of** 1.7 (CI95% **[1·1–2·4]**) for men and **2·7 (CI95% [1·1–6·7])** for women. Among men, the association seems to affect farmers rather **than** agricultural workers. Self-declared exposure to pesticides **or** bovine cattle breeding was related to HCL risk in both genders. Finally, a signfficant negative association **with** smoking was observed in men, with an inverse exposure–risk relationship odds ratios of **0.6,** 0·5 and **0.2,** respectively, for cumulative consumptions of **<10, 10–23** and **≥24** pack-years), contrasting with an odds ratios clearly **>1** in women.

Keywords: hairy cell leukaemia, occupation, smoking, epidemiology, case–control study.

Hairy cell leukaemia (HCL) is a rare B-cell chronic lymphoid leukaemia, well defined by the specific microscopic pattern of lymphocytes, first described by Bouroncle *et al* **(1958).** Very few epidemiological studies of HCL have been conducted. The incidence of the disease is low, and HCL is estimated to constitute about **2%** of all leukaemias (Bouroncle *et al*, **1958:** Bernstein *et al*, **1990).** HCL affects exclusively adults, with a mean age of about **55** years. A striking epidemiological feature of this malignancy is the strong male predominance (with a male : female ratio of about **4 : 1)** consistently observed in all series, whereas the sex ratios of other leukaemias do not usually go beyond **2 : 1.** Flandrin & Collado **(1987).** having interviewed a large series of cases in the context of a clinical trial on interferon-alpha, suggested that this imbalance could be related to environmental factors, especially to benzene and ionizing radiation. This suggestion was the starting point of the present case–control study. To our knowledge, two analytical case–control studies have investigated satisfactorily the role of environmental factors in HCL (Oleske et *al*, **1985;** Staines & Cartwright, **1993).** These studies yielded some convergent findings with respect to occupational exposures and smoking. Long-term exposure to organic chemicals gave an odds ratio of **3·1** in the study by Oleske *et al* **(1985)** and exposure to solvents, petroleum products and benzene were associated with odds ratios of **1·5, 2·1** and **2.0,** respectively, in the study by Staines & Cartwright **(1993).** Odds ratios **>2** were also found with woodworking (Oleske *et al*, **1985)** or wood dust (Staines & Cartwright. **1993).** No clear effect of ionizing radiation was observed in either study. Odds ratios associated with tobacco smoking were **<1** in both studies, and even with a significant inverse dose–response relationship in the study by Staines & Cartwright **(1993).** Finally, elevated odds ratios were observed in farmers and foresters in the study by Oleske et *al* (1985), whereas in the study by Staines & Cartwright **(1993)** the overall odds ratio for farmers was not reported. Slightly elevated odds ratios were observed in the latter study for use of fertilizers and for exposure to farm animals, but not for pesticide exposure. which concerned only three cases. However, the small size of these two studies hampers the interpretation of their findings. This paper reports the initial results of a larger case–control study investigating the role of organic solvents, pesticides and ionizing radiation in HCL risk.

MATERIAL AND METHODS

Selection of cases and controls. Cases and controls were retrospectively recruited from **1990** to **1992** from 18

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Table I. Causes of hospitalization of the controls.

	Men	Women
Rheumatological diseases	166 (39·1%)	47 (40·5%)
Injuries	124 (29.2%)	22 (19.0%)
urological diseases	25 (5.9%)	3 (2.6%)
Osteopathies	21 (4.9%)	10 (8.6%)
Benign tumours (lipomas)	15 (3·5%)	7 (6.0%)
Neurological diseases	13 (3.1%)	12 (10.3%)
Cardiovascular diseases	12 (2.8%)	3 (2.6%)
Infectious diseases	8 (1.9%)	2 (1.7%)
Respiratory diseases	7 (1.6%)	1 (0·9%)
others	22 (5.2%)	6 (5.2%)
unknown	12 (2.8%)	3 (2.6%)
Total	425 (100%)	116 (100%)

hospitals located throughout France (Angers, Bayonne, Bordeaux, Caen, Chambéry, Lille, Limoges, Lyon, Nancy, Nantes, Nice, Nimes. Paris, Poitiers, Rennes, Rouen, Strasbourg, Toulouse). All cases diagnosed from January 1980 to January 1990. including those deceased, were identified and recorded, but only living cases were included in this study. Diagnoses were confirmed histologically.

Controls were chosen from among persons hospitalized at the same time in the same hospital (mostly in orthopaedic and rheumatology departments), using the admission records for the 10-year period. The choice of controls was guided both by the necessity of targeting the same age group as cases without selecting for particular diseases, habits or socio-economic status, and by the need to concentrate retrospective sampling on a few admission records in each city. Subjects admitted for cancers or for work-related diseases or accidents were not eligible as controls. For practical reasons, only those subjects whose addresses and telephone numbers correlated positively in the current telephone directory at the time of recruitment were retained as eligible. However, the cases were also checked in the telephone directory at the same time as the controls in order to verify further that no bias was introduced by this selection.

Two controls were individually matched with each case according to gender, date of birth (±3 years), date of admission (±3 years). and residence (inside/outside the hospital catchment area).

Cases and controls were sent by mail a self-administered questionnaire. Non-responders were sent the questionnaire at most twice more. If a control had still not answered after three attempts he was replaced by another control from the list using the same selection criteria.

In all, 474 cases (381 men and 93 women: sex ratio 4·1) were identified from the 18 haematology departments. Among them, 291 living cases (61%). 229 men and 62 women, were recruited. Among the 183 cases excluded, 112

Table II. Socio-demographic characteristics of cases and controls.

	Men		Women	
	Cases (229)	Controls (425)	Cases (62)	Controls (116)
Age				
Mean	55.6	56.0	55.8	56.0
Standard error of the mean	0 7	0 5	1.5	1.1
Residence inside/outside catchment area of hospital				
Inside	76%	78%	76%	72%
Outside	24%	22%	24%	28%
Socio-economic status (last job held)				
Professional. technical workers				
Administrators and managers:	31.6%	279%	24.2%	20.0%
Clerical, sales and service workers	23.7%	26.0%	46.8%	478%
Production and agricultural workers	44.3%	46·1%	16.1%	16.5%
Never employed	0.4%	0.0%	12·9%	15.7%
Education level (highest diploma)				
No diploma	21%	18%	20%	25%
Primary school	32%	33%	35%	34%
Juniorschool	31%	32%	30%	26%
High school or university graduate	16%	16%	15%	15%
No. of jobs held				
Mean	4·7	4.8	2.3	2·2
Standard error of the mean	0.2	0.1	0.2	0.2

* Including farmers.

had died (100 men and 12 women) – most of them (68%) having died before 1984 – and 71 living cases (52 men and 19 women) did not send back the questionnaire. A total of 1020 subjects were eligible as controls and were sent the questionnaire: 591 (58%) sent back the questionnaire. 50 responders were excluded because their matched case was dead or a non-responder and they could not be matched with another case. Thus, 541 controls (425 men and 116 women) were eventually included. The reasons for hospital admission are given in Table I.

Data collection. The questionnaire included questions on socio-demographic characteristics, tobacco smoking, and long-time occupations and leisures. Questions on smoking involved the number of cigarettes, cigars or pipes smoked per day, and the dates of beginning and stopped smoking. With regard to occupation, subjects were asked to describe, in a semi-structured form, their job history, the job titles and economic area of their various employments, the tasks they accomplished and the products they handled. They were also given a checklist of tasks involving exposure to solvents (use of paints, varnishes, adhesives, paint removers, machinery, metal degreasing, dry cleaning, use of solvents as chemical reactants), pesticides and ionizing radiation. Finally, the questionnaire included questions about contacts with animals (pets, breeding cattle).

Subjects identified from the questionnaire as possibly exposed to solvents were asked to undergo a supplementary telephone interview using structured task-oriented questionnaires, administered under case/control status blinding, in order to detail the exposures (exact nature of exposures, intensity). Subjects having been employed in farming were interviewed at home by occupational physicians specializing in agricultural work. The supplementary questionnaires were designed to enable case-by-case exposure assessment and are to be analysed in a second stage of this study. The present paper reports only results from the self-administered questionnaire.

Statistical analysis. Occupations were summarized by the job titles, coded using the 1968 International Standard Classification of Occupations (ILO, 1968). The employers' industrial sector was coded using the International Standard Industrial Classification (United Nations, 1975). Only employments with a duration of 6 months or more were considered.

Table III. Association between HCL risk and occupations a priori involving exposures to solvents or pesticides (odds ratios estimated by conditional logistic regression).

Job titles (ILO codes)	Cases	Controls	OR	CI95 (%)	Two-tailed Pvalue
MEN	(229)	(425)			
Jobs a priori involving exposure to organic solvents					
Painters (8.19.55–8.73.70–9.3)	6	15	0 8	0·3–2·0	ns
Artists and designers (1.61–1.62)	1	0			
Printers (9.2)	3	4	1.4	0·2–8·7	ns
Mechanics (8.43–8.44–8.49)	19	57	0·6	0·3–1·0	0·05
Electrical fitters (8.5)	17	36	0·9	0·5–1·7	ns
Machine tool operators (8.32–8.33–8.34–8.41)	14	44	0·6	0·3–1·1	0.07
Cabinet makers, joiners (8.1–9.54)	12	30	0.7	0·3–1·4	ns
Rubber and plastic product makers (9.01–9.02)	2	3	1.3	0·2–8·0	ns
Shoe and leather goods makers (8.0)	1	3	0 7	0·1–6·4	ns
Chemical industry*	2	10	0.3	0·1–1·6	ns
Housewives (5.5)	6	5	2·3	0·7–7·6	ns
Agricultural jobs					
Agricultural and forestry workers (6)	86	122	1.7	1·1–2·4	<0·01
Farmers (6.1)	37	38	2·3	1·3–3·9	<0·01
Agricultural and animal husbandry workers (6.2)	54	90	1.3	0·8–2·0	ns
Nursery workers and gardeners (6.27)	3	8	0·6	0·2–2·5	ns
Forestry workers (6.3)	9	9	2.4	0·8–6·8	ns
WOMEN	(62)	(116)			
Jobs a *priori* involving exposure to organic solvents					
Housewives (5.51–5.52)	6	7	1.7	0·5–5·4	ns
Nurses (0.71–0.72)	3	3	1.7	0·3–8·7	ns
Chemical industry*	1	1	1.4	0.1–24·0	ns
Other solvent-exposed workers†	2	6	0·6	0·1–3·2	ns
Agricultural jobs					
Farmers or agricultural workers (6.1–6.2)	14	13	2.7	1·1–6·7	<0·05

* ISIC code = 3510

† Painters, printers, mechanics. machine tool operators. woodworkers, rubber and plastic product makers, shoe and leather goods makers.

Odds ratios were estimated by conditional logistic regression for matched sets with a variable number of controls by pair, using SAS® procedure PHREG. Separate analyses were conducted for men and women because the distribution of the occupational factors of interest and of smoking was expected to vary with gender and because a sex-related factor seems to be involved in the aetiology of the disease (resulting in a sex ratio of 4) and might interact with the factors under study.

RESULTS

The mean age was about 56 years for both men and women. Age, sex and residence matched exactly (Table II), enabling satisfactory comparability of cases and controls for socio-economic status, as defined by the category of the last job held. level of education, and number of different jobs held.

Job titles

Table III reports the odds ratios associated with farming and with occupations *a priori* considered to involve exposure to solvents. Among the men, none of the jobs selected for their probable exposure to solvents was associated with the risk of HCL. A negative association was observed even with employment as a mechanic or as a machine tool operator. In contrast, overall, employment of men in agriculture was associated with an increased risk of HCL, and the odds ratio was higher for farmers. An elevated odds ratio was also found for forestry workers, but without reaching statistical significance. No other job was found to be associated with HCL risk and. in particular, there was no association with woodworking as defined by employment as a wood preparation worker, papermaker, cabinet-maker or joiner (OR = 0.8 – CI95% [0·4–1·4]). Only two cases and four controls were classified under the ILO title 'Other salesmen' which includes the job of petrol-pump attendant.

Only a few women worked in solvent-exposed jobs, mainly those normally perceived to involve oxygenated solvents (alcohol for nurses, alcohol and glycol ethers for cleaners and housewives). None of these jobs was associated with HCL risk. As was the case for men. farming was associated significantly with HCL risk.

Occupational exposures

The odds ratios associated with selfdeclared occupational tasks and exposures are reported in Table IV. Solvent exposure, as defined by exposure to paints, varnishes, paint strippers, adhesives, diluents, metal degreasers or use of

Table IV. Associations between HCL risk and self-declared occupational exposures (odds ratios estimated by conditional logistic regression).

	Cases	Controls	OR	CI95 (%)	Two-tailed *P* value
MEN	(220)	(425)			
Use of solvents					
Solvent exposure*	107	176	1.2	0·8–1·7	ns
Petrol/diesel	79	109	1·5	1·0–2·1	<0·05
Glass cleaning	17	23	1.3	0·7–2·5	ns
Dry cleaning	2	4	1·0	0·2–5·6	ns
Exposure to engine exhausts	43	53	1.6	1·0–2·6	0.05
Farm practices					
Use of pesticides	53	58	2.0	1·3–3·1	<0·01
Breeding Bovine cattle	50	58	1.9	1·1–3·1	<0·02
Ovine cattle	17	18	1.8	0·9–3·6	0.08
Swine	16	20	1.4	0·6–2·8	ns
Ionizing radiation	8	17	0.9	0·4–2·2	ns
WOMEN	(62)	(116)			
Use of solvents					
Solvent exposure*	11	21	1.1	0·5–2·4	ns
Petrol/diesel	3	3	2.1	0·4–10·6	ns
Glass cleaning	7	8	1.8	0.5–6·1	ns
Dry cleaning	1	1	2.0	0·1–32·0	ns
Farm practices					
Use of pesticides	8	7	2·7	0·8–8·7	0.10
Breeding Bovine cattle	8	8	2.0	0·6–6·9	ns
Ovine cattle	3	2	3.3	0·5–19·6	ns
Swine	3	9	0·5	0·1–2·2	ns
Ionizing radiation	4	5	1·3	0·3–5·0	ns

*Paints, varnishes. paint strippers. adhesives, diluants, metal degreasers, solvents as chemical reagents.

Table V. Association between risk of HCL and tobacco smoking in men and women (odds ratios estimated by conditional logistic regression).

	Cases	Controls	OR	a 9 5 (%)	Two-tailed P value
MEN					
Smoking status					
Non-smokers	83	100	1·0	—	<0·001
Former smokers	79	145	0 6	0·4–0·9	
Current smokers	57	163	0.4	0·3–0·6	
Unknown	10	17			
Total	229	425			
Cumulative cigarette consumption					
Non-smokers	83	100	1·0	—	<0·001
<10 pack-years	46	71	0 6	0·4–1·0	
10–23 pack-years	40	85	0.5	0·3–0·8	
⩾24 pack-years	27	92	0 2	02 – 05	
unknown	33	77			
Total	229	425			
WOMEN					
Smoking status					ns
Non-smokers	39	84	1.0	—	
Former smokers	3	8	1·0	0·2–4·2	
Current smokers	15	15	2.4	0·9–6·2	
Unknown	5	9			
Total	62	116			
Cumulative cigarette consumption					0.10
Non-smokers	39	84	1.0	—	
<6 pack-years	8	8	2.9	09 – 9.7	
⩾6 pack-years	8	8	2·8	0·8–9·6	
Unknown	7	16			
Total	62	116			

solvents as chemical reagents, was not associated with the risk of HCL in either gender. A significantly increased risk was observed among men declaring exposure to petrol or diesel. An elevated odds ratio was also found with exposure to petrol or diesel among women, but the number of cases was very small.

Table VI. Odds ratios for some occupations estimated by conditional logistic regression adjusting for smoking status.

Job title (ILO codes)	Cases	Controls	OR	C195 (%)	Two-tailed P value
MEN	(229)	(425)			
Painters (8.19.55–8.73.70–9.3)	6	15	0.9	0·3–2·7	ns
Printers (9.2)	3	4	1.4	0·2–8·4	ns
Mechanics (8.43–8.44-8.49)	19	57	0·7	0·4–1·2	ns
Electrical fitters (8.5)	17	36	0.9	0·5–1·7	ns
Machine tool operators (8.32–8.33–8.34–8.41)	14	44	0·7	0·4–1·3	ns
Cabinet makers, joiners (8.1–9.54)	12	30	0.6	0·3–1·4	ns
Agricultural and forestry workers (6)	86	122	1.5	1·0–2·2	<0·05
Farmers (6.1)	37	38	2·0	1·1–3·5	<0·05
Agricultural and animal husbandry workers (6.2)	54	90	1·2	0·8–1·9	ns
WOMEN	(62)	(116)			
Housewives (5.5 1–5.52)	6	7	2.4	0·7–8·9	ns
Farmers and agricultural workers (6.1–6.2)	14	13	2.2	0·8–5·7	0·10

Very few subjects were exposed to ionizing radiation, and it was not possible to categorize them according to the type of radiation or duration of exposure. No association with radiation was found for either gender.

An increase in risk was observed in both genders for subjects who used pesticides and for those who declared involvement with bovine or ovine cattle breeding, although the association was not statistically significant for women.

Tobacco smoking

Table V reports the odds ratios associated with tobacco smoking. There were contrasting results for men and women. For men, smoking was significantly negatively related to the risk of HCL, with lower odds ratios for current smokers than for former smokers compared to non-smokers. and with the lowest odds ratios for the heaviest smokers. In contrast, odds ratios >1, on the borderline of statistical significance, were observed in women.

Control of confounding and selection bias

Because of the high proportion of prevalent cases in the study sample, the analysis was also restricted to pairs in which the cases were diagnosed after **1984,** when mortality was 3 times lower (about **15%).** This restriction did not modify the relationship with either tobacco smoking or occupation.

The association between smoking and HCL was not affected by adjustment for blue collar/white collar status.

Adjustment for having been employed as a farmer or as an agricultural worker did not modify the odds ratios associated with solvent-exposed jobs. In contrast, smoking appeared to confound. at least partly, the negative relationships observed with mechanics and machine-tool operators (Table VI).

DISCUSSION

This study was designed specifically to investigate the role of occupational exposures to solvents, pesticides and ionizing radiation in the risk for hairy cell leukaemia. The present analysis, based on self-reported data, produced mainly the following results: (i) no positive association was observed with occupations supposed to involve an exposure to organic solvents or with self-declared exposures to solvents, but a significant association was found with self-reported exposure to petrol or diesel. Significantly decreased odds ratios were found with employment as a mechanic or as a machine-tool operator, but the relationships seems at least partly confounded by smoking. (ii) Employment as a farmer, self-declared exposure to pesticides, and bovine or ovine cattle breeding were related to the risk of HCL. Among men. the association seems to involve farmers rather than agricultural workers. (iii) No association was found with exposure to ionizing radiation, without any distinction as regards the nature or extent of exposure. (iv) Finally, a significant negative association in men was observed with smoking, with an inverse exposure–risk relationship contrasting with the finding of odds ratio clearly >1 in women.

Due to the rarity of the disease, recruitment was Performed restrospectively and prevalent cases were enrolled. This design could give rise a selection bias if survival were related to the factors under study, i.e. if survival were better in farmers and poorer in mechanics or smokers. An attempt was made to obtain data from surrogates of cases who had died and of matched controls who had died, but the response rate was weak (30%), the information obtained was poor, and the control selection very complex. The cost-effectiveness of the process was, in consequence, discouraging. Mortality from HCL was high before the introduction of interferon-alpha in **1983.** In our sample, the proportion of cases who had died was **59%.** and **15%** for cases diagnosed prior to and after **1984,** respectively. The main results of the study were not affected when the analysis was restricted to pairs in which cases were diagnosed after **1984.** Moreover, selection of farmers by better survival is unlikely, because farmers accounted for **27%** of the cases diagnosed before **1984** and for **35%** of those diagnosed after **1984,** when mortality was lower. Similarly, current smokers accounted for **37.5%** of the cases diagnosed before **1984** and for **21.5%** of the cases diagnosed afterwards. This is not consistent with selection by survival of those cases who smoked less.

The selection of controls listed in the telephone directory, although all cases were included, could also bias the results. **49** cases **(39** men and **10** women) were included in the study although they were not listed in the directory at the time of recruitment. Among them, **27%** were farmers, whereas farmers were **32%** of the remaining sample. It is unlikely, therefore. that retaining unlisted cases may have introduced an excess of farmers. Similarly. **22.6%** of the cases listed in the telephone directory were current smokers, compared to 35·9% among those unlisted. Retaining the latter is therefore unlikely to lower the proportion of smokers among cases. The proportion of non-smokers was the same **for** the cases listed in the directory and those unlisted.

Smoking

The negative association between smoking and HCL risk does not seem to be explained by an excess of smokers in the hospitalized control group. Hospital controls may tend to be of lower social class and may be more likely than population controls to be cigarette smokers, as has been observed in the U.K. (Staines & Cartwright, **1993).** However, in the present study, smoking habits of the control group were very similar to those of the general population: the proportion of current smokers for the ages **35–44, 45–54, 55–64, 65+** was **49%.** 43%, 41% and **27%.** respectively, for the study controls, and 50%, **45%.** 40% and **30%** in a population-based survey conducted in **1980** in France on a representative **16000**-person sample (Hirsch *et al,* **1988).** The distribution of heavy smokers by age among the controls also parallels the figures from this survey. The association between smoking and HCL risk is also unlikely to be explained by socio-economic status or level of education, which were similar in the cases and controls. In addition, adjustment for blue collar/white collar status produced no change in the estimates. The negative association with smoking in men is consistent with the results published by Oleske **et *al*** **(1985)** and by Staines & Cartwright **(1993).** Although a positive relationship seems to exist between smoking and acute non-lymphocytic

leukaemia, none has been demonstrated for chronic lymphocytic leukaemia (CLL) (Austin & Cole, **1986;** Garfinkel & Boffetta, **1990;** Severson *et al*, 1990; Siegel, **1993;** Brownson *et al*, **1993)** or multiple myeloma (Linet *et al*, **1992:** Heineman *et al*, **1992).** The contrast in the results between men and women for smoking was unexpected. However, this result correlates in an interesting manner with some other facts: (i) the sex ratio of the disease suggests the existence of a sex-related factor that could interact with smoking; (ii) some sex hormone related malignancies such as breast and uterine neoplasms are also negatively associated with smoking (IARC monograph no. **38. 1986);** (iii) sex hormones and smoking share common metabolic pathways, providing an opportunity for interactions. In addition, the activity of the oxidative enzyme systems differs between males and females and is influenced by hormone levels (Sipes & Gandolfi, **1991).** It may therefore be suggested, for instance, that male hormones could have adverse effects counterbalanced by smoking, or that a carcinogen is cleared through a metabolic pathway activated both by smoking and female hormones.

Occupations

The comparability of cases and controls in terms of socio-economic status, educational level and number of jobs was good. Selection of controls is therefore unlikely to explain the findings of the study with respect to occupation.

The absence of a positive association between self-declared solvent exposure and the risk of HCL does not definitely rule out the existence of an association with more specific chemicals, such as benzene (present mostly in petrol), other aromatic solvents, chlorinated solvents and glycol ethers (present mostly in glass-cleaning products). The finding of an elevated odds ratio associated **with** petrol or diesel use suggests an association with benzene exposure. Unfortunately, diesel and petrol exposure were sought by the same question and so cannot be separated. Such a finding would be consistent with the 2-fold HCL risk found by Staines & Cartwright **(1993)** among subjects exposed to benzene and, more generally, with the well-known association between benzene and leukaemia (Austin *et al*, **1988).** although this association could be restricted to myelocytic leukaemias (Lamm *et al*, **1989:** Enterline. **1993).** However, this increase in odds ratio contrasts with the low odds ratio associated with employment as a mechanic, which can be regarded as a more objective anamnestic marker of petrol exposure (only two cases and four controls were classed under the ILO title 'Other salesmen' which includes petrol-pump attendants). Recall bias might explain the discrepancy: benzene is a known risk factor for leukaemias and, in France, compensation may be awarded for benzene-related leukaemias. Cases might be better informed by their doctors and those whose jobs involved, even only slightly or occasionally. exposure to petrol might then be more likely to declare it in the self-administered questionnaire than controls with similar exposure. The supplementary questionnaires have been structured and standardized in order to provide more objective, specific and semi-quantified information. and will be explored further in the subsequent analyses.

The absence of an association between exposure to ionizing radiation and HCL risk is difficult to interpret categorically in the present study. because the number of exposed subjects was small and the exposures not well-defined. *An* association was suggested in the study by Stewart & Keating **(1980).** However, the risk of CLL has not been found to increase in atomic bomb survivors and CLL is generally considered to be the only form of leukaemia unrelated to ionizing radiatiun (Cartwright, **1992).**

The role of farming in B-cell malignancies is receiving considerable attention. With respect to HCL, Oleske *et al* **(1985)** reported a 3-fold increase in risk for farmers and forestry workers, not indicated in the study by Staines & Cartwright **(1993).** although contact with farm animals yielded an odds ratio of **1.7.** Some studies on B-cell leukaemias, lymphomas and myelomas suggest an effect of pesticide use. The main suspects are chlorinated aromatic compounds such as phenoxyacetic acid herbicides, pentachlorophenols. DDT and other organochlorinated insecticides (Pearce & Reif. **1990;** Hoar Zahm & Blair, **1992).** The IARC classified insecticides, in general, in group 2A of 'probably carcinogenic products', based on both epidemiological and experimental data (IARC monograph no. **53, 1991).** In addition to pesticide use, farming usually involves exposures to cattle. This applies particularly to the past when ***mixed*** farming was usual. Several studies have also raised the possibility of animal virus transmission to man among farmers, abattoir workers or veterinarians. Bovine leukaemia virus has most frequently been proposed for investigation, but there is no evidence yet for such transmission, as reviewed by Pearce & Reif **(1990)** and Blair *et al* (1992).

The present study found an association with pesticide use and with bovine and ovine cattle breeding in both genders, but these variables are highly correlated in the present sample of farmers who began work around **1940** and in traditional mixed farming. A further stage of the analysis will examine ad hoc detailed questionnaires analysed by agricultural-work and chemical industry specialists.

The results of this study suggest that it would be of interest to investigate further the relationship between farming and hairy cell leukaemia, study solvent exposure with respect to specific chemicals such as benzene (for which the strongest hypotheses have been formulated), and try to account for the confounding or modifying effect of smoking.

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