

Adult-onset acute leukemia and employment in the meat industry: a New Zealand case–control study

Peter Bethwaite¹, David McLean^{2,3,*}, Josephine Kennedy² & Neil Pearce^{2,3}

¹Medical Laboratory, Wellington, CMC Bldg, 89 Courtenay Place, Wellington, New Zealand; ²Department of Medicine, Wellington School of Medicine, PO Box 7343, Wellington South, New Zealand; ³Centre for Public Health Research, Massey University Wellington Campus, Private Box 756, Wellington, New Zealand

Received 25 July 2000; accepted in revised form 19 March 2001

Key words: abattoir workers, butchers, case–control studies, leukemia, occupational exposures.

Abstract

Objectives: To assess the risks for adult-onset acute leukemia associated with employment in the New Zealand meat industry.

Methods: A total of 110 incident leukemia cases identified from referrals to one of six treatment centers between 1989 and 1991 were compared with 199 general population controls. Detailed occupational exposure histories were obtained by interview.

Results: There was an elevated risk associated with ever having worked in an abattoir (OR = 2.3, 95% CI 1.0–5.2), which appeared confined to those with over 2 years exposure (OR = 4.9, 95% CI 1.5–15.6). The excess risk was confined to abattoir workers having direct contact with animals or animal products (OR = 5.2, 95% CI 1.2–22.2). Ever having worked as a butcher was associated with elevated risk (OR = 2.9, 95% CI 1.1–7.2), confined to those individuals who worked as a butcher in an abattoir (OR = 4.8) or who butchered livestock on farms (OR = 8.2). No increased risk was found for work as a retail/wholesale butcher or meatpacker (OR = 1.2).

Conclusions: This study found increased leukemia risks associated with employment in the meat industry. These were confined to abattoir workers with over 2 years employment in the industry, and to persons whose jobs involved contact with animals or animal tissue, implying that biological exposures may be responsible.

Introduction

Although the subject of many epidemiological studies, relatively little is known about etiological factors for the leukemias. Previous studies have established that high-dose ionizing radiation [1–4], high-dose benzene exposure [5–7], and contact with cytotoxic drugs [8–10] are risk factors for leukemia. Recent evidence also implicates tobacco smoking [11]. In addition a range of studies suggest that occupational exposures to high levels of electromagnetic radiation [12, 13], to chlorohydrin [14], as well as work as a farmer [15–18], meat worker [19], butcher [20], or in a wood-related occupa-

tion [21–24] are associated with an increased risk for the development of an acute leukemia.

While a series of studies have shown a consistent excess of lung cancer associated with abattoir workers and butchers [25–34], leukemia risks among this group have been examined less frequently and the reported results are inconsistent. Two New Zealand case–control studies based on limited occupational information contained in registrations in the New Zealand Cancer Registry have examined leukemia risks in meat workers. An excess risk was an incidental finding in a larger case–control study (OR = 2.5, 95% CI 1.1–5.7) [15], and this was examined *a priori* in the later study which reported a modestly elevated risk (OR = 1.5, 95% CI 0.90–2.3) [19]. A non-statistically significant increase in risk (OR = 2.2, 95% CI 0.7–7.0) was reported in the case–control study by Loomis and Savitz for the occupational group “butchers and meat cutters” using death certificate data

* Address correspondence to: Dave McLean, Centre for Public Health Research, Massey University Wellington Campus, Private Box 756, Wellington, New Zealand. Ph.: 64-4-380-0609; Fax: 64-4-380-0600; E-mail: d.j.mclean@massey.ac.nz

from 16 US states [24]. Johnson and co-workers undertook cohort studies of members of the meat-cutters union in Baltimore, including 13,844 white male members (3025 abattoir workers) [30], 7261 white female members including 826 abattoir workers [31], and 5362 non-white male members including 851 abattoir workers [32]. No excesses of leukemia deaths were associated with work in an abattoir, meat-packing plant (in New Zealand this work is undertaken within the abattoir), supermarket, or chicken slaughterhouse, the only exception being a non-statistically significant two-fold increase in leukemia risk among women who worked in grocery stores primarily involved with wrapping meat for sale. An additional 9 years of follow-up of these cohorts has recently been reported, and although a number of epithelial tumors were over-represented in this series, again a non-statistically significant excess leukemia mortality was identified (OR = 2.3, based on 11 cases) [35]. However, these cohort studies had a very low study power to detect an increase in such rare cancers. A nested case-control study from the same cohort investigating risks for hematologic and lymphatic cancers observed excess risks throughout the meat industry (OR = 2.2, 95% CI 0.8–6.3) except in meat-packing plants, but this was due mostly to lymphomas (20 lymphoma cases and four leukemias) [36]. An historical cohort study of 862 self-employed butchers and their wives in Geneva reported an eight-fold increased leukemia risk amongst older butchers born between 1880 and 1899 [20]. We report here the findings of a population-based case-control study of the risks of adult leukemia associated with employment in the meat industry in New Zealand.

Methods

The vast bulk of incident leukemia cases in New Zealand, currently 92% of cases notified to the New Zealand Cancer Registry [37], are referred to one of six tertiary hematological oncology centers. A hematologist or research/oncology nurse within each center reported all presenting incident acute leukemia cases, plus information including name, address, telephone number, next-of-kin, usual medical practitioner, and current health status. The centers also provided information necessary to confirm the diagnosis of *de-novo* acute leukemia and subtype of the case based on the multi-parameter criteria established by the French-American-British (FAB) Cooperative Study Group [38].

Primary notification criteria for potential study subjects included cases with a primary diagnosis made by

standard criteria of acute lymphoid leukemia (FAB L1–3), acute non-lymphocytic leukemia (FAB M1–7), or acute leukemias of unspecified cell types (ICD9 209). Cases were required to have a primary diagnosis made between 1 January 1989 and 30 April 1991, and to be aged between 20 and 75 years at the time of initial diagnosis, but were excluded if the primary diagnosis was of an exacerbation of a chronic leukemia, or if the patient had a primary diagnosis of chronic leukemia, myelodysplastic syndrome, myeloproliferative disorder, or other hematological condition.

Cases that fulfilled the primary notification criteria were included as study subjects where they also had a current telephone connection, were enrolled on the electoral roll, possessed written consent from the primary hematologist and their general practitioner for participation in the study, and had themselves provided written informed consent, or where the patient was too ill to interview or was deceased the next-of-kin agreed to participate and provide written informed consent. Cases were ineligible for inclusion if the patient's hematologist or general practitioner advised that the patient or next-of-kin should not be contacted, the patient remained too ill for interview, or was deceased and no next-of-kin could be identified, cases were registered on electoral rolls outside the geographical area of the study, or significant language difficulties were encountered.

General population controls were selected at random from the most recent electoral rolls, from electorates aligned to the treatment centers' catchment areas. Individuals were included in the study if aged between 20 and 75 years, they had a telephone connection and no language or communication difficulties, they had no current or past history of acute or chronic leukemia, myelodysplastic or myeloproliferative disorder, or history of hospitalization for investigation or treatment of a hematological disorder, and they agreed to participate in the study and provided written informed consent. The study aimed to identify two controls for each case, but no formal matching procedures were employed.

Cases who met the eligibility criteria were sent a letter at least 2 months after diagnosis, inviting their participation in the study. Where the index case was deceased or remained too ill to be interviewed, a letter was sent to the next-of-kin. Controls were also initially approached with a similar letter sent to the address given on the electoral roll. Where no response was elicited, a further follow-up letter was sent, and this was followed by a telephone contact if no response could be established after the second mailing.

Information was collected using identical methods for cases and controls in the form of a telephone interview.

The occupational data obtained included a detailed lifetime work history, together with a detailed description of the tasks undertaken in each job. To assist in completion of the information on occupational history, participants were sent a work history diary sheet to complete 1 week before the telephone interview. The departments and job tasks undertaken in an abattoir were divided according to whether or not there was direct contact with live animals or animal tissues. The following job/task descriptions were classified as "animal contact": stock control (pen and move stock from trucks into works yards), stock cleaner (clean down stock before slaughter), slaughterman, meat inspector, pelt remover, butcher/boner on killing chain, carcass grader, offal packer and grader, butcher/boner on chilled carcass, meat packers (wrap and store chilled meat), and small goods workers. Freezing-store workers and packers were not classified with this group, as these workers only handle and load frozen, wrapped, and sealed meat.

Participant responses were recorded initially on questionnaires and then entered using the EPIINFO software (Centers for Disease Control, Atlanta, USA). Double-entry of all interview data was undertaken as a validity check, and the crude distribution of variables examined for outlying or missing information. Occupational histories were coded independently by three coders, using the *New Zealand Standard Classification of Occupations* [39], a modification of the *International Standard Classification of Occupations* [40]. Full analysis of the data was undertaken using the Statistical Analysis System [41]. Univariate analysis was undertaken using the Mantel-Haenszel odds ratio [42], with confidence intervals derived from a direct estimate of the variance of the log odds ratio [43]. Allowance was made in the analysis of these data for the potential confounding effects of age, social class (as assessed by highest educational attainment), and gender. Control of confounding was undertaken using the Mantel-Haenszel method [42], with confidence intervals derived by Miettinen's test-based method [44]. Logistic regression was used for multivariate analysis adjusting, in addition to the three confounders listed above, for other occupational exposures (ever/never worked on a farm, length of employment, farming activity as horticulture, mixed cropping or livestock, livestock species farmed, use of chemical sprays categorized as fungicides, herbicides or insecticides), non-occupational chemical exposures (paints, solvents, photographic development chemicals and hairspray products), and cigarette smoking (as ever/never smoked, exposure commencing at least 10, 15, or 20 years before diagnosis, and pack years as <1, 1-14, 15-30, and >30).

Results

From 165 cases notified and 312 controls selected, the overall response rate for the study was 86% (110) among the cases and 78% (199) among the controls. Thirty-eight notified cases were ruled ineligible as their age and date of diagnosis were outside the defined parameters. Of the remaining eligible cases, eight were unable to be contacted despite repeated attempts, with five declining to participate and four being too ill to be interviewed. The most common reason for ineligibility among the controls was age being outside the specified range, as age information was not available from electoral rolls. In addition, 14 controls gave a past history of investigation and/or treatment for a hematological disorder by a hematologist. Twenty-seven (10.6%) of the eligible controls refused to participate, and 28 (11%) of the target sample of controls could not be contacted despite recourse to multiple data sources. Eighty-nine of the 110 cases were interviewed directly, with interview data being collected from next-of-kin in 21 (19%) cases, *i.e.* 16 from surviving spouse, three from siblings, and two from parents of the index cases.

The age distribution, ethnicity, and socioeconomic status (as measured by highest educational qualification attained) for the cases and controls are compared in Table 1. The age distribution reflects the increasing incidence of acute leukemia with increasing age, with the general population controls, selected without *a-priori* information on age, being "younger." A significant difference in gender distribution between cases and controls is evident reflecting the recognized increased leukemia incidence in males. The ethnic balance of cases and controls is similar, while the controls show a higher proportion of individuals with higher secondary and tertiary qualification, presumably a cohort effect in the more youthful control population.

Table 2 summarizes the findings for acute leukemia associated with work in an abattoir. The leukemia risk was elevated for "ever work" in this industry (OR = 2.3), and when stratified on length of work in an abattoir the elevated risk was confined to persons with over 2 years employment in the industry (OR = 4.9). A significantly increased risk is seen for both ALL and ANLL among long-term abattoir workers (ORs = 6.2 and 4.6, respectively). The leukemia risks associated with work involving and work not involving animal contact are summarized in Table 3. The excess leukemia risk was confined to abattoir workers having ever worked in departments/tasks with animal contact (OR = 5.2), and the odds ratio is markedly elevated for ANLL (OR = 6.8).

Table 1. Distribution of the achieved sample by demographic parameters

	Cases	Controls	Crude OR	95% CI
Age at diagnosis				
< 30 years	14	24	1.0	–
30–49 years	31	85	1.6	0.68 – 3.7
50–69 years	41	71	1.0	0.44 – 2.3
> 70 years	24	19	0.5	0.17 – 1.2
Ethnicity				
Maori	10	14	1.0	–
Non-Maori	100	185	1.3	0.56 – 3.9
Gender				
Male	64	80	1.0	–
Female	46	119	2.1	1.30 – 3.3
Highest educational qualification				
Up to or including School Certificate	37	70	1.0	–
Up to senior secondary school	50	66	0.7	0.39 – 1.2
Tertiary qualification	23	63	1.5	0.74 – 2.8

Table 2. Odds ratio estimates for acute leukemia cases (ALL and ANLL) and work in an abattoir

Exposure	Exposed cases	Exposed controls	Adjusted OR ^a	95% CI
All cases				
Never worked	96	186	1.0	–
Ever worked	14	13	2.3	1.0–5.2
Up to 2 years	3	8	0.8	0.2–3.1
Over 2 years	11	5	4.9	1.5–15.6
ANLL				
Never worked	70	186	1.0	–
Ever worked	9	13	2.0	0.7–5.4
Up to 2 years	1	8	0.4	0.1–2.9
Over 2 years	8	5	4.6	1.2–17.5
ALL				
Never worked	26	186	1.0	–
Ever worked	5	13	3.0	1.0–6.3
Up to 2 years	1	8	0.8	0.1–8.3
Over 2 years	4	5	6.2	1.7–23.3

^a Adjusted for 10-year age groups, educational attainment, and gender.

Table 3. Odds ratio estimates for acute leukemia cases for abattoir work involving and not involving animal contact

Exposure	Exposed cases	Exposed controls	Adjusted OR ^a	95% CI
All Cases				
Animal contact	7	3	5.2	1.2–22.2
No animal contact	7	10	1.5	0.5–4.2
ANLL				
Animal contact	6	3	6.8	1.4–32.3
No animal contact	3	10	0.8	0.2–3.1
ALL				
Animal contact	1	3	2.7	0.3–29.6
No animal contact	4	10	2.9	0.9–9.8

^a Adjusted for age, educational attainment, gender, cigarette smoking history, and work as a butcher, using logistic regression.

Table 4. Odds ratio estimates for acute leukemia cases (ALL and ANLL) for work as a butcher

Exposure	Exposed cases	Exposed controls	Adjusted OR ^a	95% CI
All cases				
Ever exposed	17	12	2.9	1.1–7.2
Abattoir	7	3	4.8	1.1–20.0
Farm	5	1	8.2	0.9–77.4
Retail	6	9	1.2	0.4–3.6
ANLL				
Ever exposed	12	12	2.6	1.1–6.5
Abattoir	6	3	6.7	1.3–33.0
Farm	4	1	7.8	0.8–78.8
Retail	3	9	0.7	0.2–2.7
ALL				
Ever exposed	5	12	4.0	1.0–16.1
Abattoir	1	3	3.6	0.3–43.8
Farm	1	1	8.5	0.4–187.0
Retail	3	9	2.9	0.7–13.2

^a Adjusted for age group, educational attainment, gender, cigarette smoking, and other work as a butcher (abattoir, farm, or retail), using logistic regression.

Seventeen cases and 12 controls gave an occupational history which included work as a butcher, defined as the slaughtering of animals and/or cutting and handling of unprocessed animal meat excluding poultry. Significantly increased odds ratios for all acute leukemias (OR = 2.9) and ANLL (OR = 2.6) were found for “ever work” as a butcher (Table 4). The comparable odds ratio for ALL was 4.0 with the confidence intervals just including the null value. Work as a butcher occurred in three main settings: in an abattoir, butchering of stock as part of livestock farming, or as a retail or wholesale butcher or meat packer. Table 4 summarizes the risks associated with each task adjusted for potential confounders and for other work as a butcher. The odds ratios for all acute leukemias and both subtypes were elevated for butchering of stock by farmers (OR=8.2 for all acute leukemias) although these are based on small numbers and the confidence intervals are broad. The odds ratio for all acute leukemias and ANLL associated with butchery tasks in an abattoir (ORs = 4.8 and 6.7, respectively) are similar to those identified above for all abattoir workers having animal contact. No increased risk is identified associated with work as a retail/wholesale butcher or meat packer. Modestly elevated risks are seen for ALL with all three types of butchering; however, the estimates are again imprecise because of the small numbers involved.

The study also showed a mildly elevated risk for acute leukemia associated with a history of farming work (OR = 1.6, 95% CI 0.9–2.7), which when examined by major farming activity was seen among persons working in horticulture (OR = 2.6, 95% CI 1.1–5.8) and in mixed-crop farming (OR = 1.8, 95% CI 0.6–5.3)

rather than in livestock farming (OR = 1.0, 95% CI 0.6–1.8).

Discussion

This study has found elevated risks associated with having “ever worked” in an abattoir (OR = 2.3, 95% CI 1.0–5.2). The risks appear confined to those who had worked for over 2 years in this occupation (OR = 4.9, 95% CI 1.5–15.6), with no excess risk seen among short-term workers (OR = 0.8). The increased leukemia risk is seen both for ANLL and ALL cases, the risk being somewhat higher for ALL cases both overall and for those with longer work exposures.

The processing of meat and meat products is a significant industry in New Zealand’s predominantly agricultural economy, contributing almost 20% of total export earnings, and is therefore also a significant employer in New Zealand [45]. Abattoirs represent complex work environments organized into a number of defined departments involved with the slaughtering of animals and processing of meat and offal products. Major tasks include work with livestock, slaughtering of animals, removing and processing of pelts, butchering of meat and offal, secondary trimming and deboning of meat, grading and health inspection of meat and offal, primary and secondary refrigeration of products, wrapping and storage of products, digestion of unwanted products, and secondary processing and recovery of useful by-products from discarded meat and offal. Workers directly handle blood and internal organs of animals, and hence contact is intimate. The nature of the

work in abattoirs also means that cuts, wounds, crush injuries, and dermatitis are frequent among workers, and microbial agents have easy access into the body through the skin.

Potentially hazardous exposures in this industry are diverse, and in addition to zoonotic microorganisms, animal proteins, and dusts the opportunity exists for exposure to a range of potentially oncogenic products. The earliest suggestion regarding a possible etiology for the association between work in the meat industry and lung cancer was that the viral warts common in butchers could be responsible [46]. Butchers and abattoir workers are known to have a high rate of human papilloma virus-induced warts, and, in particular, the subtype HPV-7 is especially common in the skin lesions of these workers [35]. In addition, there is potential for aerosol transmission of agents in the abattoir environment, although Al-Ghamdi *et al.* found no evidence that HPV infection was a significant causal factor for lung cancers in butchers [47]. A number of viruses which are known to induce hematological tumors in animals, including bovine leukemia virus (BLV) in cattle, and avian leukosis virus and Marek's disease virus (MDV) in poultry [48], are present in healthy animals destined for human consumption. Most interest has centered on BLV, a retrovirus that has many features in common with HTLV-1. However, there is little direct evidence that BLV can cause leukemia in humans, and there is currently no serological evidence of human infection by the virus [16].

Chemical exposures in the industry have also received considerable attention as possible causes of cancers in meat workers [31]. These include the chlorophenols such as 2,4,6-trichlorophenol (2,4,6-TCP) previously used in the treatment of pelts [48], and the thermal decomposition products such as benzene, phthalic anhydride, and phthalates emitted when plastics used for wrapping and storage of meat are heated [31]. Other chemical exposures include nitrosamines and polycyclic aromatic hydrocarbons formed in meat-curing processes, and antioxidant agents, including butylated hydroxytoluene, used as preservatives [32]. The possibility of chronic antigenic stimulation has also been raised to explain the association between employment in the meat industry and hematological malignancies [49, 50]. However, apart from a suggested role in the etiology of multiple myeloma, there is little biological evidence for a significant role of chronic antigenic overload in leukemia etiology [51].

Leukemia risks associated with meat workers are higher in the current study than those previously reported; however, the study is the first interview-based case-control investigation using full employment histo-

ries to examine this association. All the previous studies have used either mortality records or registry-based information, which may underestimate the true associations because of non-differential information bias. In the previous New Zealand Cancer Registry-based studies, the excess leukemia risks in meat workers were seen for acute myeloid leukemia (OR = 2.5, 95% CI 1.3–4.7 and OR = 2.1, 95% CI 1.1–4.1) [16, 50] and ALL (OR = 2.5, 95% CI 0.8–8.0) [19]. In the case-control study by Loomis and Savitz, ALL risk was non-significantly elevated (OR = 2.2) while ANLL risk was not (OR = 0.5) [24]. In a UK case-control study of adult ALL cases, five of 33 cases gave a history of work in an abattoir or as a butcher compared to none of 33 controls [52].

Increased acute leukemia risks were largely confined to those abattoir workers having direct contact with animals or animal products (OR = 5.2), whereas there was little evidence of an increased risk in other workers (OR = 1.5). The difference in risk between these two groups was particularly marked for ANLL cases (ORs = 6.8 and 0.8, respectively). This pattern was not evident for ALL cases, although the numbers were small. The risks for both ANLL and ALL are elevated for abattoir butchers (ORs 6.7 and 3.6, respectively, although the later estimate is based on very small numbers). Work as a butcher is associated with a significantly increased acute leukemia risk (OR = 2.9), present in both ANLL and ALL subtypes (ORs = 2.6 and 4.0). In addition to abattoir work, high risks are seen amongst livestock farmers who slaughter their own stock (OR = 8.2), but not amongst retail butchers (OR = 1.2). No increase in leukemia risk was evident amongst persons whose work involved the slaughtering or processing of poultry.

An infectious etiology for the human leukemias has been supported by evidence linking animal leukemias and other hematological cancers with viral agents in a number of species including mice, chickens, cats, cattle, sheep, and primates. The identification of retroviral agents having an etiological role in human leukemia, albeit currently only in rare subtypes, has renewed interest in the possible role of animal retroviral agents in the development of the leukemias. In the current study, the greatest risks appear to be associated with persons involved in slaughtering and butchering sheep and cattle, and not with those slaughtering and processing poultry. Consistent with the current findings is the elevated leukemia risk in a cohort of self-employed butchers, confined only to older butchers who were a group who killed and processed their own stock [20]. The currently identified major oncogenic viruses in farm animals are bovine leukemia virus (BLV) associated

with lymphosarcoma in cattle, with potential to infect sheep and goats, papilloma virus causing gastrointestinal tract tumors in cattle, and avian leukosis virus and Marek's virus (a herpes virus) leading to malignant lymphoma in chickens [48].

Attention has focused on BLV, a C-type retrovirus, because of its similarities to HTLV-I. The virus has the ability to cross species barriers, both naturally and in experimental models, and has been able to induce leukemia in infant chimpanzees fed milk from infected cows [53]. Serological evidence of BLV infection in cattle herds is found in many countries including New Zealand [19]. A number of ecological studies have attempted to relate high BLV infection rates in cattle with high leukemia incidence in humans [48]. A small Swedish case-control study showed that bovine lymphosarcoma rates were higher in the cattle herds farmed by leukemia patients compared to neighborhood controls [54]. An ecological study in the USA also reported a strong correlation between male ALL incidence rates and cattle density, especially for dairy cows, with a significant excess of ALL in counties with bovine lymphosarcoma in cattle [55]. In a later case-control study, 223 persons with ALL from the 87 most rural counties in Iowa, and matched controls, were interviewed for history of residence, exposure to dairy cattle, and consumption of non-pasteurized dairy products. The BLV infection prevalence in dairy herds with which affected persons had contact was 20%, whereas the infection prevalence in the herds with which the controls had contact was higher at 38%. Also, in comparison to the earlier study, the density of dairy cows in townships where affected persons resided was generally less than that in townships where controls resided [56].

There is strong evidence linking BLV to hematological tumors in cattle. The viral infection has now been allied to a number of non-random chromosomal abnormalities in cattle with bovine lymphoma, including abnormalities of chromosome 5 and 7 which, interestingly, are often abnormal in human secondary acute leukemias [57]. In the experimental situation, BLV can infect human cells inducing a viral syncytial effect in tissue cultures; however, although the agent is found in meat and unpasteurized milk, there has not been substantiated evidence of clinical transmission, of BLV to humans. In a number of seroprevalence studies, using both traditional immunological and more recent molecular biological techniques, no serological evidence of human BLV infection has been elicited [58–61]. This cannot be taken as definite evidence against human infection as theoretically the virus may infect human cells without the expression of viral antigens on the cell surface [62], although this is unlikely

when compared to human infection with other retroviruses.

Recently a retrovirus from the lentivirus family has been identified in cattle and sheep, named bovine immunodeficiency virus (BIV). This virus is similar to human immunodeficiency virus (HIV types 1 and 2) and is found in leukocytes from cattle suffering from persistent lymphocytosis, lymph node enlargement, and central nervous system disorders [63]. Serological evidence suggests that many cattle herds are infected with both the BIV and BLV, although the two agents can exist independently [64]. It was hypothesized that indeterminate reactions to serological tests for HIV infection in humans may be due to co-reaction with human BIV infections; however, seroprevalence studies to date have failed to confirm transmission of BIV to humans, even in persons with close contact with dairy herds or who have ingested unpasteurized milk [60, 61].

In conclusion, this study found increased leukemia risks associated with employment in the meat industry, both in abattoir workers and butchers (but not retail butchers). Increased risks were confined to abattoir workers with over 2 years work in the industry and to persons whose jobs involved contact with animals or animal tissue. In contrast to several previous reports, the study found no evidence for increased leukemia risk amongst cattle, dairy, or sheep farmers, but non-statistically significant increased risks were seen in farmers who slaughtered their own stock. Increased risks were observed for both ANLL and ALL subtypes, and elevated risks for both subtypes of acute leukemias have been reported from several other studies of meat workers. The risk estimates were greater than reported by other investigators. However, the current study is the first to collect detailed exposure information on meat industry workers. The finding of similar risks in the different occupational groups would lend support to biological exposures being the likely common etiological factor across the groups. Although this would be a biologically plausible mechanism, with retroviral agents having a recognized etiological role in human leukemias, to date there is no experimental or serological evidence to prove transmission of zoonotic agents to humans. The potential for transmission of oncogenic viral agents is greatest with slaughtering and butchering of cattle and sheep, whereas retail butchers deal only with processed carcasses. Exposure to any putative viral agents would also occur in animal husbandry activities and the null effect seen amongst stock farmers remains unexplained, although this may be due to chance or to lower levels or different patterns of exposure.

The finding of an increased leukemia risk in meat workers deserves further attention. This finding

supports several earlier registry-based studies and should lead to industry-specific cohort investigations with sufficient power to examine rare cancers and determine etiology.

Acknowledgements

This study was funded by the Health Research Council of New Zealand and the Cancer Society of New Zealand. During the conduct of this research Peter Bethwaite and David McLean were funded by Public Health Research Training Fellowships from the Health Research Council of New Zealand. The authors acknowledge the contribution of Bridget Robson for her assistance with data collection.

References

- Shimizu Y, Schull WJ, Kato H (1990) Cancer risk among atom bomb survivors. The RERF Life Span Study. Radiation Effects Research Foundation. *JAMA* **264**: 601–604.
- Matanoski GM, Seltser R, Sartwell PE (1975) The current mortality rates of radiologists and other physician specialists: specific causes of death. *Am J Epidemiol* **101**: 199–210.
- Wang JX, Boice JD Jr, Li BX, Zhang JY, Fraumeni JF Jr (1988) Cancer among medical diagnostic X-ray workers in China. *J Natl Cancer Inst* **80**: 344–350.
- Darby SC (1986) Epidemiological evaluation of radiation risk using populations exposed at high doses. *Health Phys* **51**: 269–281.
- Infante PF, Rinsky RA, Wagoner JK, et al. (1977) Leukemia in benzene workers. *Lancet* **2**: 76–78.
- Rinski RA, Young RJ, Smith AB (1981) Leukemia in benzene workers. *Am J Ind Med* **2**: 217–245.
- Aksoy M (1985) Malignancies due to occupational exposure to benzene. *Am J Ind Med* **7**: 395–402.
- Gerson SI (1993) Molecular epidemiology of therapy-related leukemias. *Curr Opin Oncol* **5**: 136–144.
- Levine EG, Bloomfield CD (1992) Leukemias and myelodysplastic syndromes secondary to drug, radiation, and environmental exposure. *Semin Oncol* **19**: 47–84.
- Pedersen-Bjergaard J (1992) Radiotherapy and chemotherapy induced myelodysplasia and acute myeloid leukemia. A review. *Leuk Res* **16**: 61–65.
- Siegel M (1993) Smoking and leukemia: evaluation of a causal hypothesis. *Am J Epidemiol* **138**: 1–9.
- Savitz DA, Calle EE (1987) Leukemia and occupational exposure to electromagnetic fields: review of epidemiologic surveys. *J Occup Med* **29**: 47–51.
- Ahlbom A (1988) A review of the epidemiologic literature on magnetic fields and cancer. *Scand J Work Environ Health* **14**: 337–343.
- Benson LO, Teta MJ (1993) Mortality due to pancreatic and lymphopietic cancers in chlorohydrin production workers. *Br J Ind Med* **50**: 710–716.
- Pearce NE, Sheppard RA, Howard JK, Fraser J, Lilley BM (1986) Leukemia among New Zealand agricultural workers. A cancer registry-based study. *Am J Epidemiol* **124**: 402–409.
- Reif J, Pearce N, Fraser J (1989) Cancer risks in New Zealand farmers. *Int J Epidemiol* **18**: 768–774.
- Blair A, Zahm SH, Pearce NE, Heineman EF, Fraumeni JF Jr (1992) Clues to cancer etiology from studies of farmers. *Scand J Work Environ Health* **18**: 209–215.
- Kristensen P, Andersen A, Irgens LM, Laake P, Bye AS (1996) Incidence and risk factors of cancer among men and women in Norwegian agriculture. *Scand J Work Environ Health* **22**: 14–26.
- Reif J, Pearce N, Fraser J (1989) Cancer risks among New Zealand meat workers. *Scand J Work Environ Health* **15**: 24–29.
- Guberan E, Usel M, Raymond L, Fioretta G (1993) Mortality and incidence of cancer among a cohort of self employed butchers from Geneva and their wives. *Br J Ind Med* **50**: 1008–1016.
- Dubrow R, Wegman DH (1984) Cancer and occupation in Massachusetts: a death certificate study. *Am J Ind Med* **6**: 207–230.
- Morton W, Marjanovic D (1984) Leukemia incidence by occupation in the Portland–Vancouver metropolitan area. *Am J Ind Med* **6**: 185–205.
- Linet MS, Malker HS, McLaughlin JK, et al. (1988) Leukemias and occupation in Sweden: a registry-based analysis. *Am J Ind Med* **14**: 319–330.
- Loomis DP, Savitz DA (1991) Occupation and leukemia mortality among men in 16 states: 1985–1987. *Am J Ind Med* **19**: 509–521.
- Fox AJ, Lyng E, Malker H (1982) Lung cancer in butchers. *Lancet* **1**: 165–166.
- Griffith GW (1982) Lung cancer in butchers. *Lancet* **1**: 399.
- Lyng E, Anderson O, Kristensen TS (1983) Lung cancer in Danish butchers. *Lancet* **1**: 527–528.
- Doerken H, Rehpenning W (1982) Lung cancer in butchers. *Lancet* **1**: 561.
- Johnson ES, Fischman HR (1982) Cancer mortality among butchers and slaughterhouse workers. *Lancet* **1**: 913–914.
- Johnson ES, Fischman HR, Matanoski GM, Diamond E (1986) Cancer mortality among white males in the meat industry. *J Occup Med* **28**: 23–32.
- Johnson ES, Fischman HR, Matanoski GM, Diamond E (1986) Occurrence of cancer in women in the meat industry. *Br J Ind Med* **43**: 597–604.
- Johnson ES (1989) Mortality among non-white men in the meat industry. *J Occup Med* **31**: 270–272.
- Coggon D, Pannett B, Pippard EC, Winter PD (1989) Lung cancer in the meat industry. *Br J Ind Med* **46**: 188–191.
- Kristensen TS, Lyng E (1993) Lung cancer among butchers and slaughterhouse workers. *Scand J Work Environ Health* **19**: 137–147.
- Johnson ES, Dalmas D, Noss J, Matanoski GM (1995) Cancer mortality among workers in abattoirs and meatpacking plants: an update. *Am J Ind Med* **27**: 389–403.
- Metayer C, Johnson ES, Rice JC (1998) Nested case–control study of tumors of the hemopoietic and lymphatic systems among workers in the meat industry. *Am J Epidemiol* **147**: 727–738.
- Health Statistical Services (1992) *Cancer Registrations and Deaths, 1988 & 1989*. Wellington: New Zealand Department of Health.
- Bennett JM, Catovsky D, Daniel MT, et al. (1976) Proposal for the classification of the acute leukemias. French–American–British (FAB) Co-operative Group. *Br J Haematol* **33**: 451–458.
- Department of Statistics (1980) *New Zealand Standard Classification of Occupations*. Wellington: New Zealand Department of Statistics.
- International Labour Office (1968) *International Standard Classification of Occupations*. Geneva: ILO.

41. SAS Institute Inc (1988) SAS/STAT Users guide – Release 6.03. Cary, NC: SAS Institute Inc.
42. Mantel N, Haenszel W (1959) Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* **22**: 719–748.
43. Woolf B (1955) On estimating the relationship between blood group and disease. *Ann Hum Genet* **19**: 251–253.
44. Miettinen OS (1976) Estimability and estimation in case–referent studies. *Am J Epidemiol* **103**: 226–235.
45. Department of Statistics (2000) *New Zealand Official Yearbook 1999*. Wellington: New Zealand Department of Statistics.
46. Pegum JS (1982) Lung cancer in butchers. *Lancet* **1**: 561.
47. Al-Ghamdi AA, Sanders CM, Keefe M, Coggon D, Maitland NJ (1995) Human papillomavirus DNA and TP53 mutations in lung cancers from butchers. *Br J Cancer* **72**: 293–297.
48. Pearce N, Smith AH, Reif JS (1988) Increased risks of soft tissue sarcoma, malignant lymphoma and acute myeloid leukemia in abattoir workers. *Am J Ind Med* **14**: 63–72.
49. Pearce N, Smith AH, Howard JK, *et al.* (1986) Case–control study of multiple myeloma and farming. *Br J Cancer* **54**: 493–500.
50. Pearce N, Smith AH, Howard JK, *et al.* (1986) Non-Hodgkin's lymphoma and exposure to phenoxyherbicides, chlorophenols, fencing work and meat works employment: a case–control study. *Br J Ind Med* **43**: 75–83.
51. Gallagher RP, Spineli JJ, Elwood JM, Skippen DH (1983) Allergies and agricultural exposures as risk factors for multiple myeloma. *Br J Cancer* **48**: 853–857.
52. Whittaker JA (1991) Acute lymphoblastic leukemia in butchers and abattoir workers. *Br J Haematol* **79**: 649–651.
53. McLure HM, Keeling ME, Custer P, *et al.* (1990) Erythroleukemia in two infant chimpanzees fed milk from cows naturally infected with bovine C-type virus. *Cancer Res* **1974**: 2745–2757.
54. Kvarnfors E, Henricson B, Hugoson G (1975) A statistical study on farm and village level on the possible relations between human leukemia and bovine leukosis. *Acta Vet Scand* **16**: 163–169.
55. Donham KJ, Berg JW, Sawin RS (1980) Epidemiologic relationships of the bovine population and human leukemia in Iowa. *Am J Epidemiol* **112**: 80–92.
56. Donham KJ, Burmeister LF, VanLier SF, Greiner TC (1987) Relationships of bovine leukemia virus prevalence in dairy herds and density of dairy cattle to human lymphocytic leukemia. *Am J Vet Res* **48**: 235–238.
57. Schnurr MW, Carter RF, Dube ID, Valli VE, Jacobs RM (1994) Non random chromosomal abnormalities in bovine lymphoma. *Leukemia Res* **18**: 91–99.
58. Caldwell GG, Baumgartener L, Carter C (1976) Seroepidemiologic testing in man for evidence of antibodies to feline leukemia virus and bovine leukemia virus. *Bibl Haematol* **43**: 238–241.
59. Donham KJ, VanDerMaaten MJ, Miller JM, *et al.* (1977) Seroepidemiologic studies on the possible relationship of human and bovine leukemia: brief communication. *J Natl Cancer Inst* **59**: 581–583.
60. Sherman MP, Dock NL, Ehrlich GD, *et al.* (1995) Evaluation of HIV type 1 western blot-indeterminate blood donors for the presence of human or bovine retroviruses. *AIDS Res Hum Retroviruses* **11**: 409–414.
61. Whetstone CA, Sayre KR, Dock NL, *et al.* (1992) Examination of whether persistently indeterminate HIV type 1 western immunoblot reactions are due to serological reactivity with bovine immunodeficiency-like virus. *J Clin Microbiol* **30**: 764–770.
62. Kettman R, Burney A, Kleuter Y (1978) Distribution of BLV proviral DNA sequences in tissues of animals with enzootic bovine leukosis. *Leukemia Res* **3**: 23–32.
63. Egberink H, Horzinek MC (1992) Animal immunodeficiency viruses. *Vet Microbiol* **33**: 311–331.
64. Cockerell GL, Jensen WA, Rovnak J, Ennis WH, Gonda MA (1992) Seroprevalence of bovine immunodeficiency-like virus and bovine leukemia virus in a dairy cattle herd. *Vet Microbiol* **31**: 109–116.