Exposure to Animals and Selected Risk Factors Among Canadian Farm Residents with Hodgkin's Disease, Multiple Myeloma, or Soft Tissue Sarcoma

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*Exposures to farm animals has been associated with certain rare cancers. Simultaneously, using the same methodology and control group, we conducted a six-province incident, population-based study of Hodgkin's disease (HD), multiple myeloma (MM), and soft tissue sarcoma (STS). Farm residence or work was reported by 38% (*n *= 119) of HD, 45% (*n *= 178) of MM, 43% (*n *= 156) of STS cases and 45% (*n *= 673) of controls. We conducted conditional logistic regression analyses and report odds ratios (OR_{adj}) and 95% confidence intervals. After adjustment for covariates, exposure to farm animals had minimal effect on risk. The independent risk factors after adjustment for covariates were a family history of cancer (MM, STS), occupational uranium exposure (HD), professional driving (MM), and personal previous cancer (MM) or shingles (HD, MM).* (J Occup Environ Med. *2003;45:857–868*)

During the period 1971 to 1991,[1] the proportion of farms reporting animal production in Canada decreased for major classes of animals with the exception of farms raising sheep and lambs (Table 1). However, the average number of production animals per farm increased dramatically. Acute and chronic health effects of intensive livestock production have been investigated.[2–4] Exposure to farm animals has been studied in relationship to risk of hematopoietic and lymphoid tumors as well as soft tissue sarcomas with conflicting results.[5–20] The rationale for these studies included the following: 1) domesticated animals develop similar conditions[21–24]; 2) possible viral transmission from animals to humans,[25–34] 3) increased exposure of workers to mycotoxins and fungi, some of which are carcinogenic[2,25]; 4) chronic antigenic stimulation by exposure to animal hair, dander, saliva, feather and dusts[27,30,35,36]; and 5) previous epidemiological studies linking certain occupations to risk of developing these tumors.[15,10,27,37–54] In addition, farm animals are regularly treated with insecticides and fungicides,[51,54] exposure to a few of which have been associated with these types of cancer. We previously reported[5] that raising swine and exotic animals (bison, elk, ostriches) were independent risk factors for non-Hodgkin's lymphoma whereas a decreased risk was associated with

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TABLE 1
Census Overview of Canadian Agriculture: 1971 to 1991

	1971	1991	% change
Cattle and calves			
% of total farms	67.9	52.0	−23
Average number per farm	53	89	+68
Chickens			
% of total farms	32.7	15.2	−53
Average number per farm	732	2,224	204
Horses and ponies			
% of total farms	30.4	20.9	−31
Average number per farm	3	6	100
Swine			
% of total farms	33.5	10.6	−68
Average number per farm	66	345	422
Turkeys			
% of total farms	3.7	3.0	−19
Average number per farm	711	954	34
Sheep and lambs			
% of total farms	3.8	4.7	24
Average number per farm	61	71	16
Commercial fertilizer			
Area in acres	17,121,551	53,280,448	211
% of total farms	38.5	59.2	54
Average area in acres per farm	121	322	165
Herbicides			
Area in acres	21,179,650	53,371,080	152
% of total farms	39.6	49.4	25
Average area in acres per farm	146	386	164
Insecticides or fungicides			
Area in acres	2,257,327	6,856,737	204
% of total farms	9.9	14.4	46
Average area in acres per farm	62	170	174

During the period 1971 to 1991, the proportion of farms reporting animal production decreased with the exception of farms raising sheep and lambs. The number of animals raised per farm reporting animal production increased. The usage of agricultural chemicals including commercial fertilizer, herbicides, insecticides and fungicides increased dramatically for each variable (applied area in acres, % of total farms and average area in acres per farm).

raising cattle after adjustment for covariables.

Methods

Details of the methodology of the Cross Canada Study of Pesticides and Health have been previously published.[5] In brief, living males with an incident first diagnosis of Hodgkin's disease (HD; ICD-9 201; $n = 316$), multiple myeloma (MM; ICD-9 203; $n = 347$), or soft tissue sarcoma (STS; ICD-9 171 and selected morphology codes; $n = 365$) self-administered a postal questionnaire to record demographic, personal and family medical history, lifetime occupations, and occupational exposure information. Age, province, and sex-matched controls ($n = 1506$) selected from population based sources within each province completed the same questionnaires. The response rates varied by responder category as follows: HD (68.4%); MM (58.0%); STS (60.8%); and controls (48.0%).

A specific section of the questionnaire was completed only by those men who had lived or worked on a farm during any period of their lives. This section queried sources of drinking water, hygiene practices in relationship to pesticide exposure, and exposure to animals on the farm. This report focuses on the subset of cases (HD, $n = 119$; MM, $n = 178$; STS, $n = 159$) and controls ($n = 673$) who had lived or worked on a farm. We conducted conditional logistic regression analyses with adjustment for the matching variables of age and province of residence and report adjusted odds ratio (OR_{adj}) and 95% confidence intervals (95% CI).

Results

For each of the three types of tumor (HD, MM, STS) and controls, Table 2 first shows the proportion who had lived and/or worked on a farm, who reported farming as their current occupation or as their longest held job, and the mean number of years worked as a farmer. There was a higher proportion of "ever" farmers among MM cases (27%) compared with controls (15%). Controls had farmed more years than HD cases and fewer than MM or STS cases. The rest of Table 2 and subsequent tables refer to the analyses of the

TABLE 2
Farm Residents and Farming as an Occupation*

		Hodgkin's Disease		Multiple Myeloma		Soft Tissue Sarcoma		
		(*n* = 316)	Age and province Adjusted OR (95% CI)	(*n* = 347)	Age and province Adjusted OR (95% CI)	(*n* = 365)	Age and province Adjusted OR (95% CI)	Controls (*n* = 1506)
Ever lived on a farm or ranch	*n*	119		178		159		673
	%	37.7	0.92 (0.69, 1.22)	51.3	1.00 (0.77, 1.30)	43.6	0.89 (0.68, 1.13)	44.7
Current residence: on farm	*n*	24		44		22		151
	%	7.6		12.7		6.0		10.0
Farmer (ever)	*n*	35		95		51		229
	%	11.1	0.95 (0.61, 1.48)	27.4	**1.37 (1.00, 1.88)**	14.0	0.81 (0.57, 1.16)	15.2
Current farmer	*n*	17		40		26		106
	%	5.4	1.06 (0.60, 1.90)	11.5	1.37 (0.90, 2.08)	7.1	0.94 (0.59, 1.51)	7.0
Longest held job:								
Farmer	*n*	22		46		28		121
	%	7.0	1.08 (.62, .91)	13.3	1.36 (0.90, 2.07)	7.7	0.91 (0.61, 1.36)	8.0
Nonfarmer	*n*	294		301		337		1385
	%	93.0		86.7		92.3		92.0
Mean years farmed (mean ± SE)		19.1 ± 3.4	***P* = 0.002**	37.2 ± 2.1	***P* = 0.04**	39.2 ± 2.6	***P* = 0.02**	32.0 ± 1.4

	Hodgkin's Disease		Multiple Myeloma		Soft Tissue Sarcoma		Controls	
	n	%	*n*	%	*n*	%	*n*	%
Farm residence or work**								
Are you currently living on a farm?								
Yes (*n*, %)	20	16.8	34	19.1	23	14.5	126	18.7
How long have you lived on a farm (years)								
Mean ± SD	13.0 ± 14 (T = 3.21, *P* = 0.001)		23.5 ± 19 (T = 27.5, *P* = 0.007)		19.4 ± 19 (T = 0.21, *P* = 0.83)		19.0 ± 18	
Range	1–74		1–80		1–75		1–84	
Median	10.0		18.0		14.5		15.0	
If you have left the farm, at what age did you leave?								
Mean ± SD	20.3 ± 9.5 (T = −3.61, *P* < 0.001)		34.0 ± 19 (T = 3.78, *P* < 0.001)		24.0 ± 16 (T = 1.77, *P* = 0.08)		27.1 ± 16	
Range	2–59		3–81		3–73		3–73	
Median	19.0		27.0		19.0		21.0	

* % and OR (95% CI) based on total study population, each case group compared with controls.
** Means, ranges, and percentages based on "yes" to "ever" farm worker/resident.
Bold indicates statistically significant results.

subset of individuals who lived or worked on a farm during any period of their lives. Data in Table 2 demonstrate that 1) HD cases had lived fewer years on a farm and those who left were younger than controls who left; 2) MM cases lived longer on a farm and those who left were older than controls and (c) STS cases were similar in both duration and age at leaving to controls.

Exposure to individual types of farm animals (cattle, dogs, cats, chickens, horses, swine, turkeys, ducks, geese, sheep, rabbits, goats, exotics) was examined using cut points for dose based on distributions among control subjects. The proportions of subjects who reported personal care of the animals and the presence of animals on the farm diagnosed with leukemia or lymphoma were scrutinized. There were two statistically significant results, a decreased risk of MM associated with raising small (>1 and ≤ 15) numbers of turkeys and an increased risk of MM associated with the highest category of number of sheep (≥ 26). There were no significant associations with personally caring for farm animals or the presence of animals with leukemia or lymphoma on the farm.

Tables 3, 4, and 5 share the same format, a summary of reported exposures to pesticides and agricultural chemicals among those who reported a total of ≥ 10 hours per year to any combination of those listed, selected occupational exposures, types of animals and medical conditions/treatments. In addition, each table includes a conditional logistic model with adjustment for age, province of residence and covariates with a *P* value of 0.20 or less in univariate, age and province adjusted analyses. In univariate analyses of information related to HD cases and controls (Table 3), occupational exposure to uranium and a previous diagnosis of shingles were statistically significant predictors of HD. The conditional logistic model included exposure to dogs, to horses, personal care of animals, exposure to sheep/cattle dips/veterinary drugs/creosote wound dressing, fungicides, severe acne, shingles, treatment for lice/scabies and work related exposures to uranium or ultraviolet radiation. After adjustment for covariates, the statistically significant risk factors for HD were a previous medical diagnosis of shingles and exposure to uranium at work while treatment for lice/scabies lowered risk.

Table 4 displays the findings related to Multiple Myeloma. In univariate analyses, the occupational determinants were professional driving and a temporary job as a chicken farmer and ever holding a job in farming. The medical conditions of interest were shingles, previous diagnosis of cancer or rheumatoid arthritis. A positive family history of cancer in a first degree relative was also a risk factor. The conditional logistic model included those factors as well as exposure to chickens, turkeys, ducks, geese, sheep, goats, rabbits, sheep/cattle dip/veterinary drugs/creosote wound dressing, a history of allergies, and allergy skin prick tests. The statistically significant risk factors for MM were professional driving, a previous diagnosis of shingles, a previous diagnosis of cancer, and a positive family history of cancer in a first-degree relative. Exposure to animals on the farm did not have a substantial effect on risk.

Results related to STS are displayed in Table 5. Exposure to sheep/cattle dips/veterinary drugs/creosote wound dressing, significantly lowered risk, a temporary job in chicken farming increased risk, and a positive family history of cancer in first-degree relatives increased risk in univariate analyses. The conditional logistic model included those variables as well as exposure to cattle, personal care of farm animals, work-related exposure to radium or uranium, and exposure to potato seed dust. The statistically significant variables after adjustment for covariates, which increased risk, were a positive family history of cancer or a temporary job as a chicken farmer. Exposure to sheep/cattle dips/veterinary drugs/creosote wound dressing significantly decreased risk.

Discussion

Hodgkin's disease (HD)

For many years, the overall incidence rates of HD were declining or stable in the US SEER data for men and women.[55] In Connecticut,[56] the incidence rates approximately doubled for young adult men and women between 1935 and 1992. In Canada,[57] there has been a total decline in incidence rates of 1.4% between 1991 and 1998, which followed a significant decline between 1970 and 1995.[58] Incidence rates increased profoundly among young adults, aged between 15 and 39, for the nodular sclerosis subtype of HD[57] between 1991 and 1998. There has been a decline in incidence rates among the elderly due to a decline in misclassification between HD and NHL.[57]

The known or suspected risk factors for HD relate to occupational exposures among farmers or forestry workers,[59] socioeconomic status;[60] medical history, including late onset of certain childhood viral diseases,[61] infectious mononucleosis,[62] or Epstein-Barr virus positivity[63–65], previous cancer,[66] organ transplant,[67] and HIV or AIDS;[68] a positive family history of cancer or immune deficiency in a first-degree relative[69–71]; and a dose–response pattern for a diagnosis of lymphoma/leukemia in any first-degree relative, which increases if a sibling has HD.[72,73]

Epidemiologic studies of hematopoietic and lymphatic tumors in association with occupational exposure to animals have produced conflicting results including positive, negative and no effect.[5–20] Exposure to farm animals was investigated using several hypothetical scenarios: 1) domesticated animals develop similar conditions[21–24] and there may be direct transmis-

TABLE 3
Cases of Hodgkin's Disease and Controls: Selected Variables Investigated Among Farm Residents/Workers

	HD		Controls		
	n	%	*n*	%	OR_{adj} (95% CI)
Pesticides/agricultural chemicals ≥10 h/year					
Herbicides	29	24.4	137	20.4	0.98 (0.56, 1.70)
Insecticides	15	12.6	60	8.9	1.51 (0.75, 3.04)
Fungicides	5	4.2	13	1.9	2.22 (0.68, 7.25)
Fumigants	1	0.8	7	1.0	0.47 (0.03, 6.66)
Adjuvants/spreader/sticker	3	2.5	9	1.3	1.93 (0.41, 9.23)
Creosote/wood preservative/pruning paint/pentachlorphenol	7	5.9	34	5.0	0.99 (0.38, 2.57)
Sheep and cattle dip/veterinary drugs/creosote wound dressing	4	3.4	43	6.4	0.28 (0.08, 1.03)
Fruit tree spray	1	0.8	10	1.5	0.72 (0.08, 6.72)
Slimicides/algicide/water treatment	4	3.4	15	2.2	1.45 (0.36, 5.87)
Seed treatment	11	9.2	45	6.7	1.38 (0.60, 3.17)
Occupational exposures					
Uranium	8	6.7	7	1.0	**6.96 (2.04, 23.8)**
Ultraviolet light	18	15.1	80	11.9	0.55 (0.28, 1.09)
Exposure to farm animals					
Dogs					
0 (reference)	43	36.1	231	34.3	
1	33	27.7	262	38.9	0.70 (0.40, 1.22)
≥2	43	36.1	180	26.8	1.15 (0.67, 1.99)
Horses					
0 (reference)	71	59.7	302	44.9	
≥1 and ≤3	24	20.2	178	26.4	0.67 (0.37, 1.20)
≥4	24	20.2	193	28.7	0.91 (0.51, 1.63)
Personal case of animals (yes)	80	67.2	489	72.7	0.73 (0.44, 1.19)
Animals with lymphoma/leukemia (yes)	4	3.4	17	2.5	0.74 (0.21, 2.55)
Medical conditions/treatment					
Severe acne	16	13.4	25	3.7	1.79 (0.81, 3.94)
Shingles	14	11.8	33	4.9	**4.70 (2.11, 10.4)**
Allergy desensitization shots	7	5.9	44	6.5	0.69 (0.27, 1.74)
Treatment head, body lice/scabies	7	5.9	56	8.3	0.41 (0.17, 1.02)
Tonsillectomy	24	20.2	184	27.3	0.95 (0.54, 1.66)
Cancer in first-degree relative	37	31.1	247	36.7	1.22 (0.74, 2.01)

	Conditional Logistic Model*	
Variable	Parameter Estimate	OR_{adj} (95% CI)
Dogs (1)	−0.18	0.83 (0.43, 1.62)
Dogs (≥2)	0.39	1.48 (0.72, 3.02)
Horses (≥1 and ≤3)	−0.33	0.72 (0.35, 1.47)
Horses (≤4)	−0.10	0.90 (0.43, 1.91)
Personal care of animals (yes)	−0.24	0.79 (0.43, 1.43)
Sheep/cattle dips/veterinary drugs/creosote wound dressing (yes)	−0.78	0.46 (0.12, 1.77)
Exposure to fungicides (yes)	0.59	1.80 (0.43, 7.53)
Severe acne (yes)	0.66	1.94 (0.80, 4.71)
Shingles (yes)	1.54	**4.67 (1.96, 11.1)**
Treatment for lice/scabies (yes)	−0.97	**0.38 (0.14, 0.99)**
Uranium exposure (job) (yes)	1.55	**4.74 (1.28, 17.5)**
Ultraviolet exposure (job) (yes)	−0.47	0.63 (0.30, 1.29)

* Adjustments for age, province of residence, covariates with a *P* value of 0.20 or less in univariate analyses.
Bold indicates statistically significant results.

sion from animals to humans or a shared environment may produce the same disease in producer and animal; and 2) excessive antigenic stimulation by exposure to animal hair, dander, saliva, feathers, and dusts.[27,30,35,36] A personal history of autoimmune and allergic conditions is a known risk factor for HD. In this study, after adjustment for covariates, exposure to farm animals was not associated with HD whereas a personal history of shingles, an autoimmune disorder, was strongly associated (OR [95% CI] = 4.67 [1.96, 11.1]). The odds ratio for shingles was not appreciably attenuated by the adjustment for

TABLE 4
Cases of Multiple Myeloma and Controls: Selected Variables Investigated Among Farm Residents/Workers.

	MM		Controls		
	n	%	*n*	%	OR_{adj} (95% CI)
Pesticides/agricultural chemicals ≥10 h/year					
Herbicides	31	17.4	137	20.4	0.90 (0.56, 1.44)
Insecticides	17	9.6	60	8.9	1.19 (0.65, 2.19)
Fungicides	5	2.8	13	1.9	1.43 (0.46, 4.42)
Fumigants	1	0.6	7	1.0	0.64 (0.07, 5.66)
Adjuvants/spreader/sticker	2	1.1	9	1.3	0.89 (0.17, 4.67)
Creosote/wood preservative/pruning Paint/pentachlorphenol	8	4.5	34	5.0	1.10 (0.48, 2.54)
Sheep and cattle dip/veterinary drugs/creosote wound dressing	3	1.7	43	6.4	0.37 (0.11, 1.26)
Fruit tree spray	5	2.8	10	1.5	1.80 (0.57, 5.70)
Slimicides/algicide/water treatment	3	1.7	15	2.2	1.05 (0.28, 4.02)
Seed treatment	13	7.3	45	6.7	0.95 (0.48, 1.90)
Occupation					
Professional driver	31	17.4	82	12.2	**1.89 (1.15, 3.11)**
Chicken farmer (<1 year)	40	22.5	112	16.6	**1.56 (1.00, 2.43)**
Exposure to farm animals					
Chickens					
0 (reference)	72	40.4	297	44.1	
≥1 and ≤50	44	24.7	227	33.7	0.74 (0.48, 1.31)
≥51	62	34.8	149	22.1	1.42 (0.89, 2.28)
Turkeys					
0 (reference)	149	83.7	558	82.9	
≥1 and ≤15	8	4.5	60	8.9	0.46 (0.18, 1.17)
≥16	21	11.8	55	8.2	1.52 (0.80, 2.87)
Ducks					
0 (reference)	148	83.2	586	87.1	
≥1 and ≤10	13	7.3	53	7.9	0.88 (0.41, 1.91)
≥11	17	9.6	34	5.1	1.65 (0.81, 3.35)
Geese					
0 (reference)	149	83.7	590	87.7	
≥1 and ≤10	14	7.9	60	8.9	0.77 (0.36, 1.65)
≥11	15	8.4	23	3.4	1.79 (0.82, 3.92)
Sheep					
0 (reference)	145	81.5	594	88.3	
≥1 and ≤25	16	9.0	45	6.7	1.43 (0.65, 3.14)
≥26	17	9.6	34	5.1	1.95 (0.97, 3.91)
Rabbits					
0 (reference)	156	89.3	601	89.3	
≥1 and ≤10	6	3.4	43	6.4	0.60 (0.19, 1.86)
≥11	13	7.3	29	4.3	2.41 (1.03, 5.63)
Goats					
0 (reference)	164	92.1	635	94.4	
≥1	14	7.9	38	5.6	1.63 (0.78, 3.40)
Personal care of animals (yes)	125	70.2	489	72.7	0.16 (0.76, 1.80)
Animals diagnosed with lymphoma or leukemia (yes)	2	1.1	17	2.5	0.80 (0.16, 4.02)
Medical conditions/treatment					
Shingles	21	11.8	33	4.9	**2.12 (1.14, 3.93)**
Tonsillectomy	56	35.4	184	27.3	1.17 (0.79, 1.79)
Cancer in first degree relative	101	58.0	247	36.7	**1.71 (1.19, 2.45)**
Prior diagnosis of cancer	35	19.7	40	5.9	**2.84 (1.68, 4.81)**
Rheumatoid arthritis	7	3.9	48	7.1	**0.42 (0.18, 0.95)**
Allergies	34	19.1	166	24.7	0.76 (0.49, 1.17)
Skin prick allergy test	22	14.2	71	11.5	1.51 (0.85, 2.68)

(Table 4 continues)

covariates. Also of note, although based on small numbers, was the positive association between occupational exposure to uranium and HD (OR [95% CI] = 4.74 [1.28, 17.5]) and the inverse association of treatment for head/body lice or scabies and HD (OR [95% CI] = 0.38 [0.14, 0.99]). These treatments typically involve repeated applications of insecticides to the skin. These two associations were not

TABLE 4. CONTINUES

Variable	Conditional Logistic Model* Parameter Estimate	OR_{adj} (95% CI)
Chickens (≥1,≤50)	−0.16	0.85 (0.44, 1.63)
Chickens (≥51)	0.15	1.16 (0.60, 2.26)
Rabbits (≥1 and ≤10)	−0.68	0.50 (0.12, 2.06)
Rabbits (≥11)	0.28	1.32 (0.35, 5.06)
Turkey (≥1 and ≤10)	−0.62	0.54 (0.18, 1.60)
Turkey (≥11)	−0.10	1.10 (0.46, 2.63)
Ducks (≥1 and ≤10)	−0.14	0.87 (0.24, 3.15)
Ducks (≥11)	0.04	1.04 (0.28, 3.81)
Geese (≥1 and ≤10)	−0.66	0.52 (0.15, 1.78)
Geese (≥11)	0.33	1.40 (0.31, 6.32)
Sheep (≥1 and ≤25)	0.33	1.39 (0.46, 4.17)
Sheep (≥26)	0.26	1.30 (0.51, 3.33)
Goat (≥1)	0.26	1.30 (0.45, 3.75)
Temporary chicken worker (<1 year)	0.31	1.36 (0.72, 2.59)
Professional driver	0.69	**1.99 (1.06, 3.74)**
Farmer	0.11	1.12 (0.66, 1.88)
Sheep/cattle dips/veterinary drugs/creosote wound dressing (yes)	−0.77	0.46 (0.12, 1.82)
Rheumatoid arthritis (yes)	−0.33	0.72 (0.27, 1.92)
Diagnosed allergies (yes)	−0.42	0.65 (0.34, 1.27)
Shingles (yes)	0.96	**2.61 (1.12, 6.11)**
Allergy skin prick (yes)	0.44	1.56 (0.68, 3.54)
Prior diagnosis of cancer (yes)	1.35	**3.84 (1.87, 7.86)**
Family history of cancer (yes)	0.76	**2.14 (1.31, 3.50)**

* Adjustments for age, province of residence, covariates with a *P* value of 0.20 or less in univariate analyses.
Bold indicates statistically significant results.

included in our a priori hypotheses and should be viewed with caution until replicated.

Multiple Myeloma (MM)

Incidence rates for MM increased annually in the United States between 1973 and 1992.[55] Between 1992 and 1997, these rates have decreased annually. In Canada, between 1991 and 1998, there has been an average annual increase of 1.4%.[57] Known or suspected risk factors for MM include exposure among selected occupational groups (farmers,[6,74–79] forestry workers, precision metalworkers, transportation industry workers[75,79]), and to specific substances (occupational exposure to pesticides,[80] raising animals, including sheep and chickens[75,76]). A few studies have reported statistically significant increases in risk for specific exposures which increase in a dose-response relationship with duration and frequency of exposure while the association with farming[81–83] and with animals[84] were not confirmed in all studies. Variously defined measures of antigenic stimulation and autoimmunity have been investigated for associations with MM with often contradictory results. A US national cohort study[85] found that inflammatory conditions (gout, gallstones, enteritis, and pleurisy,) increased risk of developing MM while allergies, autoimmune conditions and chronic bacterial conditions did not. A cohort study of rheumatoid arthritis patients[86] found a statistically significant association with MM. The first degree relatives of MM cases were at increased risk of rheumatoid arthritis but not of cancer.[87] A personal history of shingles,[88] rheumatic fever,[89,90] tuberculosis,[89,91] kidney/bladder infection,[89,90] scarlet fever[91] and pernicious anemia[92] have all been associated with increased risks of developing MM as have eczema[93] and musculoskeletal disorders.[93] An increased risk of multiple myeloma has also been reported among subjects with a family history of cancer;[94] ie, paternal prostate cancer[95] and MM[96] among first degree relatives.

In this study, after statistical adjustment for covariates, exposure to farm animals was not associated with MM. A diagnosis of shingles (OR [95% CI] 2.61 [1.12, 6.11]), a personal history of cancer prior to the diagnosis of MM (OR [95% CI] 3.84 [1.87, 7.86]), a family history of cancer in a first-degree relative (2.14 [1.31, 3.50]), and an occupational history of professional driving (1.99 [1.06, 3.74]) were statistically significant predictors of MM.

Soft Tissue Sarcoma (STS)

STS are a heterogeneous group of tumors, consisting of over 20 subtypes that are rare both individually and in the aggregate.[97] STS represents less than 1% of all new diagnosis of cancer per year among adults. These are mainly tumors of

TABLE 5
Cases of Soft-Tissue Sarcoma and Controls: Selected Variables Investigated Among Farm Residents/Workers

	STS		Controls		
	n	%	*n*	%	OR_{adj} (95% CI)
Pesticides/agricultural chemicals ≥10 h/year					
Herbicides	31	19.5	137	20.4	0.90 (0.56, 1.45)
Insecticides	17	10.7	60	8.9	1.26 (0.68, 2.36)
Fungicides	4	2.5	13	1.9	1.40 (0.41, 4.77)
Fumigants	2	1.3	7	1	1.59 (0.31, 8.25)
Potato seed dust	4	2.5	4	0.6	2.96 (0.70, 12.2)
Adjuvants/spreader/sticker	0	0	9	1.3	*
Creosote/wood preservative/pruning paint/pentachlorphenol	9	5.7	34	5.0	1.18 (0.54, 2.56)
Sheep and cattle dip/veterinary drugs/creosote wound dressing	1	0.6	43	6.4	**0.09 (0.01, 0.70)**
Fruit tree spray	3	1.9	10	1.5	1.31 (0.33, 5.12)
Slimicides/algicide/water treatment	0	0	15	2.2	*
Seed treatment	12	7.6	45	6.7	0.96 (0.48, 1.92)
*No exposed persons among cases					
Occupational exposures					
Uranium	5	3.1	7	1.0	3.44 (0.96, 12.32)
Pulp and paper (<1 year)	21	13.2	68	10.1	1.39 (0.79, 2.45)
Radium	4	2.5	6	0.9	3.35 (0.86, 13.12)
Chicken farming (<1 year)	40	25.2	112	16.6	**1.63 (1.05, 2.52)**
Exposure to farm animals					
Cattle					
0 (reference)	49	30.8	217	32.2	
≥1 and ≤30	63	39.6	255	37.9	1.05 (0.67, 1.64)
≥31	47	29.6	201	29.9	0.99 (0.79, 1.25)
Personal care of animals (yes)	107	67.3	489	72.7	0.68 (0.46, 1.01)
Animals diagnosed with lymphoma or leukemia (yes)	2	1.26	17	2.5	0.68 (0.15, 3.07)
Medical conditions/treatment					
Cancer in first-degree relative	75	47.2	247	36.7	**1.57 (1.07, 2.29)**
Allergy skin prick test	19	11.9	71	10.5	1.32 (0.73, 2.36)
Medical implant	4	2.5	7	1.0	1.96 (0.55, 7.00)

	Conditional Logistic Model*	
Variable	Parameter Estimate	OR_{adj} (95% CI)
Cattle (≥1 and ≤30)	+0.11	1.12 (0.71, 1.76)
Cattle (≥31)	−0.29	0.76 (0.44, 1.76)
Personal care of animals (yes)	−0.29	0.75 (0.48, 1.17)
Chicken farming <1 year (yes)	+0.54	**1.73 (1.07, 2.27)**
Family history of cancer (yes)	+0.46	**1.58 (1.07, 2.34)**
Exposure to radium (work) (yes)	+0.98	2.68 (0.56, 12.80)
Exposure to uranium (work) (yes)	+0.60	1.82 (0.42, 7.85)
Potato seed dust (yes)	+0.53	1.69 (0.33, 8.71)
Sheep/cattle dip/veterinary drugs/creosote	−2.28	**0.10 (0.01, 0.77)**

* Adjustments for age, province of residence, covariates with '*P*' value of 0.20 or less in univariate analyses.
Bold indicates significantly significant results.

muscle, fat and connective tissue but can also occur in visceral organs. Researchers have had difficulty accumulating large number of cases of specific biological subtypes while risk factors probably vary by body site and/or morphology. Between 1973 and 1987, in the United States SEER data,[55] the overall incidence rates were relatively stable with the exclusion of Kaposi's sarcoma. In Canada,[57] the mean age at diagnosis has increased between 1988 ($\bar{x}$ = 52.8) and 1993 ($\bar{x}$ = 55.8) whereas the male:female ratio has declined from 1.38:1 to 1.34:1.

Known and suspected risk factors for STS include selected medical conditions[98] (chicken pox, shingles, mumps), a personal[99] or family history of cancer[94] and work in certain occupations which involve exposure to selected pesticides[39,42,98, 100–102] and to certain types of farm animals. Zahm et al.[103] found increased risks of STS with insecticide use on animals but not on crops. Several studies[104–107] have reported no association of STS with agricultural, farming or pesticide use patterns. The reported types of immune dysfunction are induced and include increased risks as a second primary

tumor after radiation[108] and/or chemotherapy with alkylating agents as well as among AIDS patients.

Farmers, forestry and railway workers, meat packers, gardeners, and industrial chemical workers[39,42,99, 100–103,109,110] have all been reported to be at increased risk of developing STS compared to appropriate control groups. There has been at least one report of an association between a specific subtype, fibrohistiocytic sarcoma, and herbicide use and of an increasing risk of STS[109] with duration, frequency, and intensity of exposure to chlorophenol. Occupational exposure to phenoxyherbicides[100–102] as well as raising cattle, horses, and goats have also been associated with increases in risk. However, these reported risks have not been confirmed in all studies.[104–107]

After adjustments for covariates, a positive family history of cancer in a first degree relative (OR [95% CI] 1.58 [1.07, 2.34]) and a temporary (<1 year) job in chicken farming (but not raising chickens) were associated with increased risk of STS whereas exposure to sheep/cattle dips or veterinary drugs reduced risk (0.10 [0.01, 0.77]). Exposure to animals of any type, personally caring for animals or the presence of animals with lymphoma or leukemia had no effect on risk of STS.

Limitations

The limitations of this study include those inherent in the case–control design using postal questionnaires, lower than optimal response rates for both the case and controls and the fact that we investigated and reported results for a large number of agents not all of which were specified in the hypothesis. Therefore, the analyses related to these unspecified agents were considered exploratory. By requesting certain information and conducting statistical analyses based on case-control differences only among farmers, ranchers and farm residents, we lowered the number of eligible subjects, decreased our statistical power and may have overmatched. The wording of the question used to establish eligibility for this subanalysis: "Have you ever lived or worked on a farm" may have been too vague and diffuse as people who have lived the majority of their life span in nonfarm areas were included. However, several researchers have reported that early childhood exposure to agricultural chemicals, to animals or to the farm environment in general are risk factors for one or more of the conditions that we studied.

Strengths and Conclusions

This study encompassed farm workers/residents from six Canadian provinces with differing climates and therefore crops and types of animals grown. Farm practices are diverse. Measures of duration and intensity of exposure to animals were included. There were also questions concerning general measures of industrial hygiene practiced as well as a survey of customary safety habits (data not reported). This subanalysis included moderate numbers of cases and controls who were identified and recruited from population-based sources. Statistical adjustments for covariates including selected medical conditions, occupational exposures, exposure to pesticides classified into broad categories ie, herbicides, insecticides, fumigants and fungicides, personal and family history of cancer was conducted. After adjustments for covariates, we found that exposure to farm animals had no effect on risk except for an association between a temporary (< one year) chicken farming job and STS. Among these Canadian farm resident/workers, the independent risk factors after adjustment for covariates were: a positive family history of cancer in first-degree relatives (MM, STS), an occupation involving exposure to uranium (HD) or as a professional driver (MM) and personal previous cancer (MM) and shingles (HD, MM). Treatment for head lice/body lice (HD) and exposure to sheep/cattle dips/veterinary drugs/creosote wound dressing (STS) significantly decreased risk

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