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A case-referent study of soft-tissue sarcoma and Hodgkin's disease

Farming and insecticide use

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HOAR ZAHM S, BLAIR A, HOLMES FF, BOYSEN CD, ROBEL RJ. A case-referent study of soft-tissue sarcoma and Hodgkin's disease: Farming and insecticide use. *Scand J Work Environ Health* 14 (1988) 224–230. A population-based case-referent study in Kansas examined the relationship between exposure to insecticides and the development of soft-tissue sarcoma (STS) and Hodgkin's disease (HD). Data from telephone interviews for 133 STS cases, 121 HD cases, and 948 referents indicated that STS was associated with use of insecticides on animals, but not on crops. HD was not significantly associated with either use. STS risk was higher among the farmers who themselves mixed or applied insecticides to animals than among farmers who did not. Farmers who failed to use any protective equipment to reduce insecticide exposure were at a significantly elevated risk of STS. Risk rose with early calendar year of first use. The excess risk appeared to be primarily among fibrous and myomatous sarcomas with little association seen for lipomatous or other STS neoplasms. Myomatous sarcomas increased significantly with duration and time since first use of insecticides on animals. If the reported association between STS and insecticides is causal, the data suggest that exposure to the agent(s) responsible may have been reduced in the mid-1950s or the agent(s) have an average latency period for STS of at least 20 years.

Key terms: agriculture, chlorinated hydrocarbons, insecticides, lymphoma.

Reports from Sweden, Denmark, Italy, and the United States have suggested that persons exposed to phenoxy-acetic acid herbicides and chlorophenols have up to a sixfold excess risk of soft-tissue sarcoma, Hodgkin's disease, and non-Hodgkin's lymphoma (3, 4, 6, 8, 9, 13, 14, 17, 19, 24, 30, 31). A population-based case-referent study was conducted to assess the role of agricultural exposures and other factors in the development of these disorders in the United States. Data supporting an association between herbicide use and non-Hodgkin's lymphoma but not soft-tissue sarcoma or Hodgkin's disease have been presented previously (12); this report deals only with soft-tissue sarcoma, Hodgkin's disease, and insecticide use.

Table 1. Number of cases of soft-tissue sarcoma and Hodgkin's disease in different phases of the study.

	Soft-tissue sarcoma	Hodgkin's disease
Initial diagnosis	200	173
Pathology review	170	153
Confirmed cases	139	132
Telephone interview	133	121

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Subjects and methods

Cases

All new cases of soft-tissue sarcoma (STS)⁴ and Hodgkin's disease (HD)⁵ diagnosed during 1976–1982 among white male Kansas residents aged 21 years or older were identified through the University of Kansas Cancer Data Service, a population-based cancer registry covering the state of Kansas. There were 200 men diagnosed with soft-tissue sarcoma and 173 men with Hodgkin's disease (table 1).

Pathology specimens for 87 % of the cases were available for review to confirm the diagnoses and to standardize the subgroup terminology. For the soft-tissue sarcoma and Hodgkin's disease cases reviewed, 81 and 85 % were confirmed, respectively. In addition two cases initially diagnosed as non-Hodgkin's lymphoma were classified as Hodgkin's disease, yielding 139 cases of soft-tissue sarcoma and 132 histologically confirmed cases of Hodgkin's disease for inclusion in the study.

⁴ STS International Classification of Diseases for Oncology (ICDO) (29) histology codes (all topographical codes examined): 8800–8811, 8813, 8830–8855, 8860, 8890–8891, 8894–8902, 8910–8920, 8980–8981, 8990–8991, 9040–9044, 9120, 9130, 9140, 9150, 9170, 9540, 9560, 9581.

⁵ HD ICDO histology codes (all topographical codes examined): 9650–9663.

Referents

The referents were selected from white men in the general population of the state of Kansas. Three referents per case were frequency matched by age (± 2 years) and vital status to the combined age distribution of the three cancer case series ($N = 1\ 005$). For living cases, referents aged 65 years or older were selected from the Health Care Financing Administration file (the Medicare file), whereas referents aged 64 years or younger were selected by telephone with the use of a two-staged random digit dialing technique (25). For approximately one-half of the persons with soft-tissue sarcoma and one-third of those with Hodgkin's disease who had died before the initiation of the study, referents were selected from Kansas state mortality files with the additional matching factor of year of death. Persons with a cause of death of soft-tissue sarcoma, Hodgkin's disease, non-Hodgkin's lymphoma, a malignancy of an ill-defined site (ICDO 195), homicide, or suicide were excluded.

Interview

The persons with histologically confirmed cases and the referents, or their next-of-kin, were interviewed by telephone between December 1982 and January 1984. Questions on farming practices included crops and animals raised, farm locations and sizes, insecticides and herbicides used, years and acres treated, method of application, and use of protective equipment.

Interviews were obtained for 133 cases of soft-tissue sarcoma and 121 cases of Hodgkin's disease and 948 referents, the response rate among eligible subjects being 94 % for both the cases and the referents. The overall response rate, a weighted average which includes the product of the initial response (92.3 %) in the random digit dialing process and the interviewing rate for the random digit dialing referents, was 93 %.

Risk measurements

The measure of association was the odds ratio (OR). All risk estimates were adjusted for the effects of age by stratification. Maximum likelihood estimates of the overall risk and 95 % confidence intervals (95 % CI)

were computed by Gart's method (7). For duration-response relationships, significance was assessed by means of Mantel's one-tailed linear trend test (15).

Results

A total of 95 persons with soft-tissue sarcoma and 71 persons with Hodgkin's disease were reported to have worked or lived on farmland in comparison to 662 of the referents, yielding odds ratios of 1.0 (95 % CI 0.7–1.6) for soft-tissue sarcoma and 0.8 (95 % CI 0.5–1.2) for Hodgkin's disease. No trend with years spent working or living on a farm was observed. The risks did not vary significantly by type of crop or animals raised or farm size.

Insecticides

Insecticide use on crops or animals was reported by 50 persons with soft-tissue sarcoma (OR 1.3, 95 % CI 0.8–2.2), 38 persons with Hodgkin's disease (OR 0.8, 95 % CI 0.5–1.4), and 275 referents (table 2). The increased risk of soft-tissue sarcoma appeared limited to farmers who reported use of insecticides on animals (OR 1.6, 95 % CI 0.9–2.5). There was no significant association between soft-tissue sarcoma and duration, latency, frequency, or any other measure of exposure to insecticides used on crops or between Hodgkin's disease and any measure of insecticide exposure.

The risk of soft-tissue sarcoma among farmers who had used insecticides on animals rose with early calendar year of first use, but not consistently with duration (table 3). The duration-adjusted odds ratios for soft-tissue sarcoma among farmers who first used insecticides on animals after 1965, during 1956–1965 and 1946–1955, and prior to 1946 were 1.0 (reference category), 0.3 (95 % CI 0.01–4.7), 2.6 (95 % CI 0.3–26.7), and 4.9 (95 % CI 0.6–64.1), respectively (trend P -value = 0.009). We did not collect information on frequency, ie, days per year, of exposure to insecticides used on animals.

Risk varied according to farmers' work practices and insecticide application methods, increasing with level

Table 2. Number of cases of soft-tissue sarcoma and Hodgkin's disease and the referents and the odds ratio (OR) and 95 % confidence interval (95 % CI) by insecticide use on crops or animals.

	Referents	Soft-tissue sarcoma cases			Hodgkin's disease cases		
		N	OR	95 % CI	N	OR	95 % CI
Nonfarmers	286	38	1.0	·	50	1.0	·
Farmers							
Never used insecticides	315	32	0.7	0.4–1.3	20	0.6	0.3–1.0
Used insecticides ^a	275	50	1.3	0.8–2.2	38	0.8	0.5–1.4
Crops	132	14	0.8	0.4–1.6	25	1.1	0.6–1.9
Animals	214	46	1.6	0.9–2.5	32	0.9	0.5–1.5
Use unknown	72	13	·	·	13	·	·

^a Farmers could report use on both crops and animals.

Table 3. Number of soft-tissue sarcoma cases and referents and the odds ratio (OR) by duration and first calendar year of insecticide use on animals. (95 % CI = 95 % confidence interval)

	Cases	Referents	Age adjusted		Age and duration or latency adjusted ^a	
			OR	95 % CI	OR	95 % CI
Nonfarmers	38	286	1.0			
Farmers						
First year of use						
1966—	3	31	0.9	0.2—3.3	1.0	
1956—1965	3	38	0.7	0.2—2.4	0.3	0.01—4.7
1946—1955	11	50	1.5	0.7—3.4	2.6	0.3—26.7
—1945	25	87	1.8	1.0—3.4	4.9	0.6—64.1
Unknown	4	8				
Chi for trend			2.250		2.350	
P-value (one tailed)			0.012		0.009	
Duration (years)						
1—5	8	55	1.2	0.5—2.9	1.0	
6—10	14	46	2.2	1.0—4.5	2.6	0.7—9.4
11—20	5	50	0.8	0.3—2.2	0.5	0.1—2.9
≥21	14	60	1.6	0.7—3.3	1.0	0.3—3.7
Unknown	5	6				
Chi for trend			1.156		—0.566	
P-value (one tailed)			0.124		0.286	

^a Figures for first year of use adjusted for age and duration; figures for duration adjusted for age and latency.

Table 4. Number of soft-tissue sarcoma cases and referents and the odds ratio (OR) for farmers who mixed or applied insecticides to animals, by application method. (95 % CI = 95 % confidence interval)

	Cases	Referents	OR	95 % CI
Nonfarmers	38	286	1.0	
Farmers ^a				
Spraying	31	131	2.0	1.1—3.4
Dusting	7	27	1.9	0.7—5.1
Dipping	2	18	0.9	0.1—4.3
Pouring	4	20	1.6	0.4—5.3
In Feed	0	1	—	
Other	4	19	1.5	0.4—5.1

^a Farmers could use more than one method.

of exposure. Farmers who themselves mixed or applied the insecticides for use on animals had higher risks of soft-tissue sarcoma (OR 1.7, 95 % CI 1.0—2.9) than farmers who usually had someone else perform these tasks (OR 1.1, 95 % CI 0.4—2.6). Among the various and multiple application methods reported by the farmers who applied insecticides to animals themselves, spraying (OR 2.0, 95 % CI 1.1—3.4) and dusting (OR 1.9, 95 % CI 0.7—5.1) were associated with the highest risks (table 4). (No application method for crop insecticides showed excess risk of soft-tissue sarcoma: tractor-mounted or mist-blower sprayer, OR 1.0 and 95 % CI 0.4—2.2; into or on the soil, OR 0.8 and 95 % CI 0.3—1.9; aerial, OR 1.0 and 95 % CI 0.4—2.4; other, OR 0.9 and 95 % CI 0.3—2.3.) Farmers who failed to use protective equipment while mixing or applying insecticides on animals had a greater risk of soft-tissue sarcoma (OR 1.9, 95 % CI 1.1—3.3) than farmers who took some precautions to reduce exposure (OR 1.2, 95 % CI 0.4—3.1).

On farms where insecticides were first used on animals prior to 1956, the farmers who applied the chemicals themselves and who failed to use protective equipment had higher risks (OR 2.1, 95 % CI 1.2—3.9) than those who used protective equipment (OR 1.2), but the small numbers prohibit the calculation of duration-adjusted risk estimates. The trends with first years of use are significant for farmers who applied the pesticides themselves ($P = 0.031$) or who failed to use protective equipment ($P = 0.038$), but not for those who had someone else apply the insecticide ($P = 0.093$) or who used protective equipment ($P = 0.251$).

Table 5 presents risk according to the chemical group of insecticides ever used on animals. The subjects could report use of multiple insecticides, so the groups are not independent. Almost every group was associated with excess risk, including chlorinated hydrocarbons, organophosphates, and “other” and not otherwise specified insecticides, such as “fly spray.” The “other” group consisted of miscellaneous chemicals such as pyrethrum, creosote, nicotine, rotenone, and combinations. The risks for farmers who usually mixed or applied the insecticides to animals themselves were similar or slightly higher than for farmers who did not, except for the category “other,” for which the OR rose from 3.8 to 9.4. The numbers of subjects reporting use of most individual insecticides were small, but for 10 soft-tissue sarcoma cases and 28 referents use of dichlorodiphenyltrichloroethane (DDT) on animals (OR 2.3, 95 % CI 0.9—5.6) was reported.

The dates of use of specific chemicals were not collected in the interviews; however, the dates of use of any insecticide used on animals were available and are presented in table 6. Although the numbers are small, an examination of risks for first and last year of use

Table 5. Number of soft-tissue sarcoma cases and referents and the odds ratio (OR) by insecticide group ever used on animals. (95 % CI = 95 % confidence interval)

	Ever used on farm animals				Usually mixed or applied by study subject			
	Cases	Referents	OR	95 % CI	Cases	Referents	OR	95 % CI
Nonfarmers	38	286	1.0	—	38	286	1.0	—
Farmers ^a								
Chlorinated hydrocarbons	11	40	1.8	0.8–4.2	10	33	2.0	0.8–4.8
Organophosphates	5	15	2.1	0.6–6.9	5	15	2.1	0.6–6.9
Carbamates	—	1	—	—	—	1	—	—
Metals	1	1	5.9	0.2–225.0	1	1	5.9	0.2–225.0
Other	4	7	3.8	0.8–16.7	4	3	9.4	1.5–64.8
Not otherwise specified ^b	37	188	1.4	0.9–2.4	31	138	1.6	0.9–2.8

^a Farmers could report more than one method.

^b Fly, tick, or lice powder, spray, or treatment; cattle, sheep, or hog dip; or insecticide: not otherwise specified.

Table 6. Number of soft-tissue sarcoma cases and referents and the odds ratio (OR) by insecticide group and year of first and year of last use of any insecticide used on animals. (C = Cases, R = referents, 95 % CI = 95 % confidence interval)

	Ever use of insecticides on animals ^a															
	Chlorinated hydrocarbons				Organophosphates				Other				Not specified			
	C	R	OR	95 % CI	C	R	OR	95 % CI	C	R	OR	95 % CI	C	R	OR	95 % CI
First year of use of any insecticides on animals ^b																
1966–	—	2	—	—	1	2	3.6	0.1–56.1	—	—	—	—	2	30	0.6	0.1–2.9
1956–1965	—	8	—	—	—	3	—	—	—	1	—	—	3	29	0.9	0.2–3.2
1946–1955	4	12	2.0	0.5–7.8	2	3	4.2	0.4–34.4	2	—	—	—	9	42	1.5	0.6–3.6
—1945	6	16	2.4	0.8–7.3	1	7	0.9	0.04–7.9	3	5	3.9	0.6–22.8	19	81	1.5	0.8–3.0
Chi for trend			1.737				0.688				2.248				1.477	
P-value (one tailed)			0.041				0.246				0.012				0.070	
Last year of use of any insecticides on animals ^b																
1970–	3	20	1.0	0.2–3.9	5	14	2.3	0.7–7.5	2	2	6.9	0.6–82.0	13	84	1.2	0.6–2.5
1960–1969	2	7	1.8	0.2–10.7	—	1	—	—	—	—	—	—	4	41	0.8	0.2–2.7
1950–1959	4	9	3.0	0.7–12.0	—	—	—	—	—	1	—	—	5	12	2.1	0.6–6.6
—1949	2	3	4.5	0.5–37.8	—	—	—	—	3	3	6.6	0.9–48.1	13	43	1.9	0.9–4.2
Chi for trend			2.249				1.148				2.398				1.740	
P-value (one tailed)			0.012				0.126				0.008				0.041	

^a Farmers could report more than one insecticide group.

^b Reference group is nonfarmers (38 cases, 286 referents).

of any insecticides on animals by insecticide groups ever used suggested that the risks associated with use in the early time periods were related to the use of chlorinated hydrocarbons and the “other” and not otherwise specified insecticides. Chlorinated hydrocarbons known to have been used in the early 1940s include DDT, benzene hexachloride, heptachlor, lindane, methoxychlor, and toxaphene (10, 11, 22). There were no significant trends for first year or last year of use of organophosphates on animals.

The excess risk of soft-tissue sarcoma for insecticide use on animals appeared to be primarily among cases with sarcomas of fibrous⁶ (OR 2.3, 95 % CI 0.8–7.2) and myomatous⁶ (OR 2.6, 95 % CI 1.0–7.3) tissues with no or little association seen for lipomatous⁶

⁶ STS histological subtypes, based on the ICDO groupings: fibromatous sarcomas: ICDO codes 8810–8811, 8813, 8830–8832; myomatous sarcomas: ICDO codes 8890–8891, 8894–8902, 8910–8920; lipomatous sarcomas: ICDO codes 8850–8855, 8860; other sarcomas: ICDO codes 8800–8804, 8840, 8980–8981, 8990–8991, 9040–9044, 9120, 9130, 9140, 9150, 9170, 9540, 9560, 9581.

(OR 0.9, 95 % CI 0.2–3.1) or other⁶ soft-tissue neoplasms (OR 1.1, 95 % CI 0.5–2.4). Although based on small numbers, the risk of myomatous soft-tissue sarcoma increased consistently with early first year (trend $P = 0.003$) and duration (trend $P = 0.027$) of insecticide use on animals (table 7). The number of exposed myomatous sarcoma cases was too small to allow analysis by duration and latency simultaneously. No trends in risk were observed for fibrous soft-tissue sarcoma. Farmers who personally mixed or applied the insecticides for use on animals had higher risks of fibrous (OR 2.5, 95 % CI 0.8–8.0) and myomatous (OR 3.0, 95 % CI 1.1–8.7) sarcomas than farmers who usually did not (fibrous: OR 1.7, 95 % CI 0.2–10.0; myomatous: OR 2.1, 95 % CI 0.4–9.8). Insecticide application to animals by spraying was associated with a 2.4-fold increase in fibrous sarcomas (95 % CI 0.7–8.2) and a 3.4-fold increase in myomatous sarcomas (95 % CI 1.2–10.1). Mixing and applying insecticides to animals did not significantly increase risk for lipomatous (OR 1.1, 95 % CI 0.3–4.0) or other

Table 7. Number of cases of fibrous and myomatous soft-tissue sarcoma and the referents and the odds ratio (OR) by duration and first calendar year of insecticide use on animals. (95 % CI = 95 % confidence interval)

	Referents	Fibrous soft-tissue sarcoma			Myomatous soft-tissue sarcoma		
		Cases	OR	95 % CI	Cases	OR	95 % CI
Nonfarmers	286	6	1.0	—	7	1.0	—
Farmers							
First year of use							
1966—	31	2	4.2	0.5—30.8	—	—	—
1956—1965	38	1	1.4	0.1—12.8	1	1.1	0.05—9.7
1946—1955	50	1	0.9	0.04—8.2	4	3.0	0.7—12.3
—1945	87	5	1.9	0.05—7.2	9	4.0	1.2—13.6
Unknown	8	2	—	—	—	—	—
Chi for trend			1.115			2.741	
P-value (one tailed)			0.132			0.003	
Duration (years)							
1—10	101	6	3.0	0.8—11.1	4	1.5	0.4—6.0
11—20	50	1	1.0	0.04—8.5	2	1.8	0.2—9.8
≥21	60	3	1.7	0.3—8.7	5	3.4	0.9—13.2
Unknown	6	1	—	—	3	—	—
Chi for trend			0.836			1.930	
P-value (one tailed)			0.202			0.027	

(OR 1.2, 95 % CI 0.6—2.8) soft-tissue sarcomas. The number of subjects was too small to investigate histology and insecticide group in great detail; in general, the results were similar to those for the total soft-tissue sarcoma series. Excess risks for fibrous and myomatous sarcomas were associated with chlorinated hydrocarbons and insecticides not otherwise specified.

The risk of soft-tissue sarcoma associated with insecticide use on animals was slightly lower for the subjects who were interviewed directly (OR 1.3, 95 % CI 0.7—2.7) than for those whose next-of-kin were interviewed (OR 1.8, 95 % CI 0.8—3.9). The difference between the living and deceased subjects probably reflects the age patterns of the two groups and the higher risk of older subjects who used insecticides on animals. Subjects diagnosed at age 80 or older had an odds ratio of 3.8, while younger subjects had an odds ratio of 1.5. The older users may have had greater exposure than younger farmers, who may have more recently used more mechanized techniques to apply insecticides to animals. A greater proportion of the subjects over 79 years of age (60 %) had next-of-kin proxies participate in the study, while only 43 % of the subjects aged 79 years or younger had proxy interviews.

Other pesticide exposures

Treating seeds with fungicides was related to a non-significant excess of soft-tissue sarcoma (OR 1.4, 95 % CI 0.7—2.6) but not to Hodgkin's disease (OR 0.9, 95 % CI 0.4—1.8). Nonfarming pesticide exposure in home gardens and yards was not associated with soft-tissue sarcoma (OR 0.7) or Hodgkin's disease (OR 0.7).

Eleven persons with soft-tissue sarcoma (OR 2.0, 95 % CI 0.9—4.1), eight persons with Hodgkin's disease (OR 1.5, 95 % CI 0.6—3.4), and 40 referents reported becoming ill at least once due to exposure to

pesticides. No attempt was made to confirm these self-diagnosed acute episodes with the subjects' medical care providers.

Discussion

This case-referent study conducted in Kansas found an association between soft-tissue sarcoma and the use of insecticides on animals, but not crops. Hodgkin's disease was unrelated to contact with insecticides. The risk of soft-tissue sarcoma increased with the potential for heavier exposures to insecticides, eg, among farmers who mixed or applied the insecticides to animals themselves or who failed to use protective equipment. The risk appeared to be limited to exposures occurring prior to the mid-1950s, primarily to chlorinated hydrocarbon insecticides, and to fibrous and myomatous sarcomas. Although organophosphates were associated with some elevated risks, the trends were not significant.

Although many of the same insecticides are used on animals and crops (5), the present study found an association only with use on animals. This specificity may reflect the potential for greater inhalation and dermal exposure associated with application on animals than on crops. Farmers usually spray crops only a few times a year, using methods such as tractor sprayers or aerial application; however, they spray animals much more frequently, usually by hand. For example, it was not unusual for farmers to spray dairy cattle twice a day by hand prior to milking. Use of hand-held equipment has consistently been associated with heavier dermal exposures than other application methods (27), and, in addition, the farmers would have been inhaling insecticide mists while milking the animals.

The excess risk of soft-tissue sarcoma associated with insecticide use prior to the 1950s has several possible

interpretations. The latency period for insecticide-related soft-tissue sarcoma may be long enough that exposures sustained after the mid-1950s have not yet resulted in excess cancer risk. An excess of lung cancer among pesticide applicators in Florida did not appear until 20 years after first exposure (1). The insecticides used, their contaminants, and methods of application may have changed since the mid-1950s. This study shows a decrease in the reported use of chlorinated hydrocarbons and an increase in reported use of organophosphate insecticides over time, consistent with reports from the United States Department of Agriculture and others (5, 18). Changes in farming practices may have affected risk. For example, as dairy farming became more mechanized, less insecticide may have been applied to animals, or farmers may have spent less time sitting near the cows and thereby sustained less exposure. We cannot distinguish between these hypotheses only on the basis of the data collected in this study.

The association between soft-tissue sarcoma and insecticide use on animals is not likely to be due to problems in the subjects' recall of exposure. There is no evidence that, in general, exposure was over-reported for the cases in comparison to the referents. No associations were observed for several measures of exposure, including herbicide use and insecticide use on crops. A survey of a sample of the subjects' pesticide suppliers did not reveal any major differences between the cases' and referents' confirmation rates for pesticides used on crops (12); unfortunately, the suppliers were not asked about insecticides used on animals. If exposures were underreported because of poor recall but were not biased with respect to case-referent status, then the reported odds ratios would underestimate the true risks (16). Unbiased under-reporting does not create spurious effects. In this study, although the association between soft-tissue sarcoma and insecticide use on animals was present among both living and deceased subjects, the odds ratio based on next-of-kin interviews alone were slightly higher than those for living subjects. This difference may be due to a small degree of recall bias by the next-of-kin, a more rapidly fatal outcome among cases exposed to insecticides used on animals, or the different age patterns of the living and deceased subjects.

Few of the other epidemiologic studies of soft-tissue sarcoma have separated insecticide and herbicide effects, or animal or crop exposures, because most were based on job title only and did not contain detailed information on farming practices (26). Eriksson et al (6), however, reported that among soft-tissue sarcoma cases 2.7 % utilized nicotine as an insecticide as compared to 0.5 % of the referents. Nicotine, first used as an insecticide in 1909 (10, 11, 22), was part of the "other" category associated with higher risk of soft-tissue sarcoma in this study. No association between soft-tissue sarcoma and chlordane or DDT was observed in the western part of the state of Washing-

ton (28). It is not known whether these reports represent use on crops, animals, or a combination. Other studies which collected detailed information on farming practices have focused on herbicide exposures and have left the role of insecticides in the development of soft-tissue sarcoma relatively unstudied (2, 20, 21).

Soft-tissue sarcomas are a heterogeneous group of tumors of various cell types that differ by etiology, incidence patterns, and survival (23). Although little is known about the causes of most soft-tissue sarcomas, it appears that risk factors vary by histological type. For example, thorotrast, vinyl chloride, and inorganic arsenic, well-established risk factors for soft-tissue sarcoma, induce hepatic angiosarcomas specifically (23). In this study, use of insecticides on animals was associated with fibromatous and myomatous soft-tissue sarcoma, but not lipomatous or other soft-tissue sarcoma neoplasms. The risk for myomatous soft-tissue sarcoma increased significantly with duration and latency of use of insecticides on animals.

In summary, this study found no association between Hodgkin's disease and insecticide use, but soft-tissue sarcoma, particularly myomatous cases, was associated with exposure to insecticides used on animals prior to the mid-1950s. The rising incidence and largely unknown etiology of soft-tissue sarcoma (23) indicates a need for further studies of this tumor. The findings of the present study suggest that insecticide exposure and farming practices should receive careful attention in future investigations.

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