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Family Pesticide Use and Childhood Brain Cancer

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Abstract. The relationship between family pesticide use and childhood brain cancer was examined in a case-control study. Telephone interviews were conducted from June 1989 through March 1990 with the natural mothers of 45 childhood brain cancer cases, 85 friend controls, and 108 cancer controls. In comparisons to friend controls, significant positive associations were observed for use of pesticides to control nuisance pests in the home, no-pest-strips in the home, pesticides to control termites, Kwell® shampoo, flea collars on pets, diazinon in the garden or orchard, and herbicides to control weeds in the yard. In comparisons to cancer controls, significant positive associations were observed for use of pesticide bombs in the home, pesticides to control termites, flea collars on pets, insecticides in the garden or orchard, carbaryl in the garden or orchard, and herbicides to control weeds in the yard. In general, positive associations in comparisons to one control group were supported by elevated odds ratios in comparisons to the other control group. Several potentially important associations were identified in this study. However, small sample sizes, potential recall bias, multiple comparisons, and lack of detailed exposure verification require further research to confirm these findings.

Childhood brain cancer etiology appears to be multi-factorial and there is no clear primary cause (Larson 1980). Several investigators have examined the potential link between childhood brain cancer and exposure to pesticides. In comparing brain cancer cases to normal controls, an odds ratio (OR) of 2.3 ($p = 0.10$) was found for children exposed to household pest exterminations (Gold *et al.* 1979). A comparison to children with other cancers showed no such relationship. Sinks (1985) found significant relationships between childhood brain cancer and maternal use of aerosol pesticides during pregnancy (OR = 1.65, $p = 0.04$) and after birth (OR = 1.66, $p = 0.04$). No significant risk was observed in this study for other pesticide exposures. Other studies have shown no association between pesticide use and childhood brain cancer (Preston-Martin *et al.* 1982; Howe *et al.* 1989). Several studies have also found a potential link between other childhood cancers (e.g., acute lymphocytic leukemia) and pesticide exposure (Lowengart *et al.* 1987; Schwartzbaum *et al.* unpublished).

Although it has not been precisely quantified, substantial pesticide exposure to children can occur in and around the home. A 1988 study conducted by the United States Environmental Protection Agency (EPA) found that seven percent, by volume, of all pesticides used in the United States were used in the home, garden, or yard (EPA 1989).

This article examines the potential relationship between family pesticide use and childhood brain cancer. Data reported in the article were collected as part of a larger case-control study of childhood cancer (Davis 1991).

Methods

Cases

Childhood brain cancer cases in this study were identified through the population based Missouri Cancer Registry (MCR). Reporting procedures, completeness, and accuracy of MCR data are discussed in detail elsewhere (Brownson *et al.* 1989). The study included 45 childhood brain cancer cases (ICD-O site code 191) from age zero to ten (WHO 1976). The brain cancer cases included 20 astrocytomas, 11 medulloblastomas, and a mix of other cancer types (89% histologically confirmed). All childhood brain cancer cases were Missouri residents diagnosed between 1985 and 1989. The study was limited to white children, due the small number of nonwhites. Children with Down's Syndrome ($n = 2$) were excluded due to its close association with childhood cancer (Alderson 1980). Seven of the case children were dead at the time of the interview with the mother. Table 1 characterizes study cases and controls according to demographic variables.

Controls

The primary control group consisted of 85 children who were identified as friends of childhood brain cancer and acute lymphocytic leukemia (ALL) cases reported to MCR. During the initial contact, mothers of children with cancer were asked to identify an age and sex matched child for participation in the friend control group. A second control group included 108 other childhood cancer cases age zero to ten reported to the MCR between 1985 and 1989. This group included 71

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Table 1. Distribution of cases and controls by age, gender, family income, and father's education

Demographic characteristics		Cases	Friend controls	Cancer controls
Child age (yrs)	0–1	5 (11%)	10 (12%)	21 (19%)
	2–3	12 (27%)	28 (33%)	37 (34%)
	4–5	4 (9%)	16 (19%)	26 (24%)
	6–10	24 (53%)	31 (36%)	24 (22%)
Child gender	Female	14 (31%)	35 (41%)	51 (47%)
	Male	31 (69%)	50 (59%)	57 (53%)
Family income	0–$20,000	12 (27%)	17 (20%)	40 (37%)
	$20,001–$30,000	17 (38%)	24 (28%)	26 (24%)
	$30,001–$40,000	9 (20%)	19 (22%)	16 (15%)
	>$40,001	7 (16%)	25 (29%)	24 (22%)
	Refused	0 (0%)	0 (0%)	2 (2%)
Father's education	Less than 12 yrs	2 (4%)	3 (4%)	8 (7%)
	HS graduate	11 (24%)	15 (18%)	37 (34%)
	Post HS training	18 (40%)	29 (34%)	31 (29%)
	College graduate	11 (24%)	34 (40%)	28 (26%)
	Refused	3 (7%)	4 (5%)	4 (4%)

cases of ALL, nine sarcomas, eight lymphomas, and a mix of other cancer types (99% histologically confirmed). Eleven of the cancer control children were dead at the time of the interview with the mother.

Exposure Variables

The study was limited to pesticide use for nuisance pests (roaches, ants, spiders, and mosquitoes), termites, lice, pet pests (fleas and ticks), garden or orchard pests, and weeds in the yard. Due to the large number of products available, it was not possible to assess use of specific products for controlling nuisance pests in the home or pests on pets. For these situations, exposure was assessed for all products combined and for product formulations (liquid spray, dust, shampoo, flea collar). It was possible to assess use of selected pesticide products for termites, lice, garden or orchard pests, and yard pests (weeds), since only a limited number of products were available in Missouri for use in these situations.

For each pesticide use situation, respondents from the case and cancer control groups were asked the number of times that pesticides had been used for these pests during pregnancy and in the interval from birth to six months of age, and the average number of times per year during the interval from seven months of age to the diagnosis of cancer. Respondents from the friend control group were asked the same questions for pregnancy and birth to six months of age. They were then asked the average number of times per year that pesticides were used during the interval from seven months of age of their child to the age of cancer diagnosis of the matched child with cancer. Respondents were also asked whether several specific pesticide products had been used at any time from pregnancy to diagnosis. For termite control, questions were also asked about overall termite pesticide use in the home within one year prior to the time the respondent moved into the home (nearly all respondents lived in several homes).

Data Collection and Analysis

Telephone interviews were conducted with the natural mothers of all study participants from June 1989 through March 1990. Immediately after scheduling telephone interviews with a participant's natural mother, a packet was mailed containing a handout designed to improve recall. The handout included a description of the time periods covered by the study and lists of specific pesticide products examined in the study.

The Mantel-Haenszel method was used for initially determining odds ratios (OR) and 95% confidence intervals (CI) (Mantel and Haenszel 1959; Rothman 1982). Logistic regression was used to adjust odds ratios and confidence intervals for the potential confounders identified by the larger study (Engelman 1988). These potential confounders included child's age at diagnosis, child's exposure to environmental tobacco smoke during birth to six months of age and seven months of age to diagnosis, family income, father's education, mother's education, and family member in the construction industry. The time between diagnosis and interview was also included in the logistic model for comparisons to cancer controls.

Quantitative trends in pesticide use were analyzed with Mantel's one-tailed test (Mantel 1963). Pesticide use categories were "no pesticide used," "pesticides used one to five times," and "pesticides used more than five times." The "no pesticide used" category was the reference level.

Overall, 83% of eligible study participants completed a questionnaire. Participation varied by case or control status. Friend controls showed the highest participation rate with 94% completing a questionnaire. Brain cancer cases and cancer controls showed lower participation rates at 73% and 78%, respectively.

Human Subjects Review

The entire project was reviewed and approved by the Missouri Department of Health's Human Subjects Review Committee.

Results

A composite variable was used to assess the relationship between childhood brain cancer and overall pesticide use. This variable was scored "yes" if the respondent indicated some level of use on any interview question asking how many times pesticides were used during a specific time period. Odds ratios for overall pesticide use during pregnancy, birth to 6 months of age, and 7 months of age to diagnosis varied in magnitude from 0.5 to 1.4 (not shown in the Tables). No trends were observed in ORs of low pesticide use families versus high pesticide use families.

Pesticide use for nuisance pests showed several elevated ORs in comparisons with friend controls (Table 2). A significant OR of 3.4 (95% CI = 1.1–10.6) was observed during the seven months of age to diagnosis period. Several ORs were also elevated for specific types of pesticide products used in the home for nuisance pests (Table 2). In general, the positive findings associated with comparisons to friend controls were supported by elevated ORs in comparisons to cancer controls. Odds ratios for use of pesticide spray cans, spray liquids, and dusts on nuisance pests were generally near or below one and no variables were significantly associated with childhood brain cancer.

Pesticide use for termites was examined using several variables. The variable "prior termite treatment" was scored "yes" if the respondent answered "yes" for termite treatment for any home treated within 1 year prior to residence. The ORs for this variable were elevated for both control groups (Table 2).

The variable "pesticides used for termites" examined termiticide use during pregnancy, birth to 6 months of age, and 7 months of age to diagnosis. This variable showed slightly ele-

Table 2. Childhood brain cancer and pesticide use for nuisance pests, termites, and lice, Missouri, 1985–1989[a]

Exposure variable	Time period	Ex/unex cases[b]	Control group	Odds ratio[c]	95% CI
Pesticides used for nuisance pests	Preg.	30/15	Friend	1.8	0.8–4.0
			Cancer	1.2	0.5–2.9
Pesticides used for nuisance pests	0–6	28/16	Friend	1.9	0.8–4.3
			Cancer	1.9	0.8–4.4
Pesticides used for nuisance pests	7–Dx.	38/6	Friend	3.4	1.1–10.6
			Cancer	1.7	0.5–5.4
Bomb used for nuisance pests	Preg.	5/40	Friend	2.1	0.5–8.3
			Cancer	6.2	1.4–28.4
Bomb used for nuisance pests	7–Dx.	6/38	Friend	1.1	0.3–3.7
			Cancer	0.6	0.2–2.0
No-Pest-Strip used for nuisance pests	Preg.	8/37	Friend	5.2	1.2–22.2
			Cancer	1.9	0.6–5.9
No-Pest-Strip used for nuisance pests	0–6	6/38	Friend	3.7	0.9–15.2
			Cancer	2.5	0.7–9.4
No-Pest-Strip used for nuisance pests	7–Dx.	8/36	Friend	3.7	1.0–13.7
			Cancer	2.0	0.6–6.3
Prior termite treatment	—	11/34	Friend	2.6	0.9–7.5
			Cancer	2.3	0.8–6.4
Pesticides used for termites	7–Dx.	12/33	Friend	1.4	0.5–3.9
			Cancer	1.4	0.5–3.8
Any termite treatment	—	21/24	Friend	2.9	1.3–7.1
			Cancer	3.0	1.3–7.4
Chlordane used for termites	—	7/35	Friend	1.5	0.5–4.9
			Cancer	1.5	0.5–5.1
Pesticides used on lice	7–Dx.	8/36	Friend	1.3	0.4–4.1
			Cancer	1.7	0.5–5.4
Kwell® used on lice	7–Dx.	7/37	Friend	4.6	1.0–21.3
			Cancer	1.9	0.6–6.9

[a] Data for time periods with three or fewer exposed cases were excluded from the Table

[b] Number of exposed and unexposed cases

[c] Adjusted by logistic regression for child's age at diagnosis, child's exposure to environmental tobacco smoke, family income, father's education, mother's education, family member in the construction industry, and time between diagnosis date and interview

vated ORs during seven months of age to diagnosis, with small sample sizes precluding meaningful analysis during the other time periods (Table 2).

The variable "any termite treatment" was scored "yes" if any home had been treated for termites within 1 year prior to residence or if a residence home was treated during any time from the beginning of pregnancy to cancer diagnosis. This variable was significantly related to childhood brain cancer with an OR of 2.9 (95% CI = 1.3–7.1) in comparison to friend controls and 3.0 (95% CI = 1.3–7.4) in comparison to cancer controls (Table 2).

The ORs for lice pesticide use were slightly elevated during the seven months of age to diagnosis period. Inadequate sample sizes were available during pregnancy and birth to six months of age. Our study also showed that use of Kwell® was significantly associated with childhood brain cancer in comparison to the friend controls (OR = 4.6; 95% CI = 1.0–21.3). This finding was supported by an elevated OR in comparison to cancer controls (OR = 1.9; 95% CI = 0.6–6.9).

Table 3. Childhood brain cancer and pesticide use for pests of pets, Missouri, 1985–1989

Exposure variable	Time period	Ex/unex cases[a]	Control group	Odds ratio[b]	95% CI
Pesticides used on pets	Preg.	11/34	Friend	0.9	0.4–2.0
			Cancer	0.4	0.2–1.0
Pesticides used on pets	0–6	10/34	Friend	1.0	0.4–2.5
			Cancer	0.5	0.2–1.2
Pesticides used on pets	7–Dx.	21/23	Friend	1.1	0.5–2.6
			Cancer	0.6	0.2–1.3
Pesticides used on pets plus exposed	Preg.	8/37	Friend	0.6	0.2–1.5
			Cancer	0.4	0.1–1.0
Pesticides used on pets plus exposed	0–6	5/39	Friend	4.8	0.9–24.7
			Cancer	1.8	0.5–6.6
Pesticides used on pets plus exposed	7–Dx.	21/23	Friend	1.4	0.6–3.1
			Cancer	0.7	0.3–1.5
Flea collar used on pets	Preg.	16/29	Friend	1.0	0.4–2.1
			Cancer	0.6	0.3–1.4
Flea collar used on pets	0–6	18/26	Friend	1.5	0.7–3.2
			Cancer	1.0	0.5–2.3
Flea collar used on pets	7–Dx.	25/19	Friend	1.9	0.9–4.2
			Cancer	1.1	0.5–2.4
Flea collar used on pets plus exposed	Preg.	12/33	Friend	0.9	0.4–2.1
			Cancer	0.6	0.2–1.3
Flea collar used on pets plus exposed	0–6	9/35	Friend	5.5	1.5–20.0
			Cancer	4.4	1.4–14.3
Flea collar used on Pets plus exposed	7–Dx.	25/19	Friend	2.4	1.1–5.6
			Cancer	1.3	0.6–2.9
Shampoo used on pets	Preg.	10/35	Friend	0.8	0.3–1.9
			Cancer	0.8	0.3–2.0
Shampoo used on pets	0–6	9/35	Friend	1.1	0.4–3.0
			Cancer	0.7	0.3–1.8
Shampoo used on pets	7–Dx.	16/28	Friend	0.9	0.4–2.2
			Cancer	0.8	0.3–1.7
Shampoo used on pets plus exposed	Preg.	7/38	Friend	0.5	0.2–1.4
			Cancer	0.6	0.2–1.5
Shampoo used on pets plus exposed	0–6	5/39	Friend	4.2	0.9–20.3
			Cancer	2.6	0.7–10.4
Shampoo used on pets plus exposed	7–Dx.	16/28	Friend	1.1	0.5–2.7
			Cancer	0.8	0.4–1.8

[a] Number of exposed and unexposed cases

[b] Adjusted by logistic regression for child's age at diagnosis, child's exposure to environmental tobacco smoke, family income, father's education, mother's education, family member in the construction industry, and time between diagnosis and interview

Pesticide use for pests of pets was examined at several levels. Overall pesticide use on pets, "pesticides used on pets" showed ORs near or below one for all time periods and both control groups (Table 3). A borderline significantly low OR was ob-

served during pregnancy in comparison to cancer controls.

A composite variable was also created requiring both pesticide use on pets and exposure to pets during the same time period. This composite variable was developed using the pesticide use questions and separate questions that asked whether the mother was exposed to pets during pregnancy and whether the index child was exposed to pets during the periods of birth to six months of age and seven months of age to diagnosis. This variable, "pesticides used on pets plus exposed," showed mixed results over the time periods (Table 3). During the birth to 6 months of age period, this composite variable showed elevated ORs for exposure to pets that had received some type of pesticide treatment. There was also a slight ($p = 0.06$) increasing trend for level of pet pesticide use plus exposure to pets during the birth to 6 months of age period (not shown in a table). Again, a significantly low OR was observed during pregnancy in comparison to cancer controls.

Several elevated ORs were observed for use of flea collars and shampoos on pets (Table 3). The most consistent and substantial elevations were seen for the pesticide use plus exposure to pets variables during the birth to 6 months of age period. Positive findings for friend controls were supported by elevated ORs in comparisons to cancer controls. The elevated ORs during birth to 6 months of age contrasted with the lower ORs during pregnancy and seven months of age to diagnosis. Odds ratios for use of pesticide spray cans, spray liquids, and dusts on pets were generally near or below one, with small sample sizes precluding meaningful analyses for several variables.

Interpretation of the pesticide use plus pet exposure results were complicated by findings of elevated odds ratios for simple exposure of the index child to pets. Results in comparisons to friend controls were OR = 4.2 (95% CI = 1.4–12.8) for exposure to pets during birth to six months of age and OR = 1.7 (95% CI = 0.7–4.0) for exposure to pets during seven months of age to diagnosis. Due to the nature of the construction of the composite variables (*e.g.*, "flea collar on pets plus exposed"), we were unable to use logistic regression to determine whether the observed relationships were due to pesticide use or simple exposure to pets. However, separate examination of unadjusted pet exposure odds ratios for the subpopulation that used pet pesticides versus the subpopulation that did not use pet pesticides clarifies the relationships. In the case of "flea collar on pets plus exposed" during birth to 6 months of age, the odds ratio for exposure to pets was 4.8 for the subpopulation that used a flea collar and only 2.3 for the subpopulation that did not use a flea collar. For this variable during seven months of age to diagnosis, the odds ratio was infinity for the subpopulation that used a flea collar (all 25 brain cancer cases were exposed to pets while five of the 32 friend controls were not exposed to pets) and it was 0.6 for the subpopulation that did not use a flea collar. It appears that flea collar use played a major role in the observed relationship between childhood brain cancer and simple exposure to pets.

Several elevated ORs were observed for use of garden insecticides during birth to six months of age and seven months of age to diagnosis (Table 4). Carbaryl also showed a significantly elevated OR of 2.4 (95% CI = 1.1–5.6) in comparison to cancer controls. Diazinon use in the garden was also associated with childhood brain cancer (OR = 4.6; 95% CI = 1.2–17.9) in comparison to friend controls. Small sample sizes precluded meaningful analyses for several other specific garden pesticides (*i.e.*, spectracide, malathion, and Round-Up®).

Table 4. Childhood brain cancer and pesticide use in the garden, orchard, or yard, Missouri, 1985–1989

Exposure variable	Time period	Ex/unex cases[a]	Control group	Odds ratio[b]	95% CI
Insecticides used in the garden or orchard	Preg.	11/34	Friend	1.5	0.6–3.9
			Cancer	1.2	0.5–3.0
Insecticides used in the garden or orchard	0–6	7/37	Friend	2.3	0.7–8.3
			Cancer	1.2	0.4–3.8
Insecticides used in the garden or orchard	7–Dx.	22/22	Friend	1.6	0.7–3.6
			Cancer	2.6	1.1–5.9
Carbaryl used in the garden or orchard	—	19/25	Friend	1.5	0.7–3.3
			Cancer	2.4	1.1–5.6
Diazinon used in the garden or orchard	—	7/37	Friend	4.6	1.2–17.9
			Cancer	1.4	0.4–4.7
Herbicides used on the yard	Preg.	12/33	Friend	1.1	0.5–2.5
			Cancer	1.0	0.4–2.4
Herbicides used on the yard	0–6	15/29	Friend	1.7	0.7–3.9
			Cancer	3.4	1.2–9.3
Herbicides used on the yard	7–Dx.	30/14	Friend	2.4	1.0–5.7
			Cancer	1.7	0.7–3.9
Weed-B-Gon used on the yard	—	16/26	Friend	1.1	0.5–2.5
			Cancer	0.9	0.4–2.1
Crab grass killer used on the yard	—	5/37	Friend	1.5	0.4–5.2
			Cancer	1.0	0.3–3.2

[a] Number of exposed and unexposed cases

[b] Adjusted by logistic regression for child's age at diagnosis, child's exposure to environmental tobacco smoke, family income, father's education, mother's education, family member in the construction industry, and time between diagnosis and interview

Yard herbicide use showed a significant relationship to childhood brain cancer during the birth to six months of age period (cancer controls) and the seven months of age to diagnosis period (friend controls) (Table 4). Both findings were supposed by elevated ORs in the other control group. Infrequent family use precluded meaningful analysis of the associations between childhood brain cancer and use of Round-Up®, Kleen-Up®, Grass-B-Gon®, Triox®, Poison Ivy and Poison Oak Killer®, and Brush-B-Gon®.

Discussion

Childhood brain cancer odds ratios varied substantially by pesticide use situation and time period of use. However, ORs in several pest control settings tended to increase as the pesticide use variable focused more tightly on a particular product. For example, use of pesticides to control lice during 7 months of age to diagnosis showed an OR of 1.3, while use of Kwell® during the same period showed an OR of 4.6. This pattern was also seen for use of no-pest-strips and flea collars. The finding is consistent with epidemiologic theory that a poorly or broadly defined exposure variable will result in a bias toward unity (Copeland *et al.* 1977).

An effort was made to more narrowly define exposure to pet pesticides by creating composite variables that required both

use of a pesticide and exposure to pets that were treated. Several of the composite variables showed higher ORs than the simple pesticide use variables. The composite variables that showed the most substantial increases in ORs were associated with the birth to six months of age period. The OR for overall pet pesticide use during the period increased from 1.0 to 4.8 and the ORs for flea collar use and shampoo use during the period increased from 1.5 to 5.5 and 1.1 to 4.2, respectively. These findings were supported by parallel, but smaller increases in comparisons to cancer controls.

High ORs for pet pesticide use during the birth to six months of age period may be partially explained by the increased susceptibility of infants to chemical exposures (WHO 1986). Future research on childhood cancer needs to fully examine the potential for exposure during this critical period.

Significant findings from this study should be interpreted in light of past carcinogenicity testing with experimental animals. Suspicions concerning the carcinogenicity of dichlorvos (a common active ingredient in no-pest-strips and several brands of flea collars during the study period) were supported by study results. Reuber (1981) has shown that dichlorvos causes tumors in the esophagus, endocrine organs, thyroid, liver, and mammary glands of mice and rats. Other studies have shown that dichlorvos causes chromosome abnormalities and sister chromatid exchanges and that dichlorvos may act as a tumor promoter as well as initiator (Lin *et al.* 1988; Dieter *et al.* 1989). On the basis of these studies, EPA has classified dichlorvos as a "probable human carcinogen" (EPA 1987).

The positive and significant findings on overall exposure to termite pesticides ("any termite treatment") support concerns about the carcinogenicity of chlordane (NCAMP 1988). Although chlordane was not significantly associated with childhood brain cancer in our study, this may be due in part to inadequate respondent knowledge concerning the use of specific termiticides by outside companies. Interviewer comments revealed low confidence in the accuracy of respondent knowledge and recall on the chlordane variable.

Several studies have also examined lindane (Kwell® shampoo) for carcinogenicity. Wolff and Morrissey (1986) demonstrated an increased level of lung and liver tumors when mice were treated with lindane. Other studies using mice and rats have shown the presence of liver and thyroid tumors after treatment with lindane (IARC 1979). Laboratory studies have also demonstrated that lindane acts as a tumor promoter (Schrotter *et al.* 1987). The International Agency for Research on Cancer (1979) has concluded that there is sufficient evidence to classify lindane as a carcinogen in mice. EPA (1985a) has classified lindane as a "possible human carcinogen."

The findings on carbaryl were potentially important since more than one fourth of the study respondents reported carbaryl use in the garden or orchard. Animal studies on the carcinogenicity of carbaryl are limited and study results are mixed (Andrianova and Alekseev 1970; IARC 1976; Triolo *et al.* 1982; Mount and Oehme 1981; Deutsch-Wenzel *et al.* 1985). Based on these and other studies, the EPA (1985b) has determined that carbaryl is not carcinogenic for experimental animals. However, concern has been expressed over the potential for transformation of carbaryl into nitrosocarbaryl, a proven carcinogen (Mount and Oehme 1981; Deutsch-Wenzel *et al.* 1985).

Odds ratios observed for comparisons of childhood brain cancer cases to cancer controls were generally lower than those for comparisons to friend controls. However, several positive findings in comparisons to friend controls were supported in comparisons to cancer controls (especially no-pest-strips, termiticides, Kwell®, flea collars, and pet shampoos).

The mixed results for the two control groups could be due to recall bias associated with the friend controls. However, the mixed results could also be caused by a potential, but unknown relationship between pesticide use and one or more of the cancer types included in the cancer control group. Past studies have implicated consumer pesticide use in childhood acute lymphocytic leukemia, the most common type of childhood cancer included in our cancer control group (Lowengart *et al.* 1987).

Interpretation of study results should take into account the potential effects of multiple comparisons. The complexity of family pesticide use (pest, applicator, time period, product) required creation of numerous variables to adequately assess use and exposure. Given the large number of comparisons in the study, several of the significant findings may be due to chance alone.

Small sample sizes, potential recall bias, multiple comparisons, and the lack of detailed exposure verification require that further research be conducted to confirm our results. Despite these limitations, our study has contributed substantial information on pesticide use in the home in relation to childhood brain cancer. Although our findings are not conclusive, they are suggestive of an association between childhood brain cancer and several pesticide use situations, product types, and specific products. The results of this study highlight the need for expanded research on the health effects of pesticide use.

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References

Alderson M (1980) The epidemiology of leukemia. Adv Cancer Res 31:1–77

Andrianova MM, Alekseev IV (1970) On the carcinogenic properties of the pesticides Sevin®, Manev®, Ciram® and Cineb®. Vopr Pitan 29:71–74

Brownson RC, Davis JR, Chang JC, DiLorenzo TM, Keefe TJ, Bagby JR Jr. (1989) A study of the accuracy of cancer risk factor information reported to a central registry compared with that obtained by interview. Am J Epidemiol 129(3):616–624

Copeland KT, Checkoway H, McMichael AJ (1977) Bias due to misclassification in the estimation of relative risk. Am J Epidemiol 105:488–495

Davis JR (1991) Childhood cancer and pesticide use in the home, garden, and yard. University of California, Berkeley, PhD dissertation, 161 pp

Deutsch-Wenzel RP, Brune H, Grimmer G, Misfeld J (1985) Local application to mouse skin as a carcinogen specific test system for non-volatile nitroso compounds. Cancer Lett 29(1):85–92

Dieter MP, Jameson CW, French JE, et al. (1989) Development and validation of a cellular transplant model for leukemia in Fischer rats: A short-term assay for potential anti-leukemic chemicals. Leuk Res 13(9):841–849

Engelman L (1988) Stepwise logistic regression. In: Dixon WJ, (ed) BMDP statistical software, Vol II. University of California Press, Berkeley, pp 941–968

Environmental Protection Agency (1985a) Lindane. Pesticide fact sheet. Office of Pesticide Programs. United States Environmental Protection Agency, Washington, DC

———(1985b) Carbaryl: Pesticide fact sheet. Office of Pesticide Programs, United States Environmental Protection Agency, Washington DC

———(1987) Dichlorvos: Pesticide fact sheet. Office of Pesticide Programs, United States Environmental Protection Agency, Washington, DC

———(1989) Pesticides industry sales and usage, 1988 market estimates. Economic Analysis Branch, Biological and Economic Analysis Division, Office of Pesticide Programs, United States Environmental Protection Agency, Washington, DC

Gold E, Gordis L, Tonascia J, Szklo M (1979) Risk factors for brain tumors in children. Am J Epidemiol 109(3):309–319

Howe GR, Burch JD, Chiarelli AM, Risch HA, Choi BCK (1989) An exploratory case-control study of brain tumors in children. Cancer Res 49:4349–4352

International Agency for Research on Cancer (1976) Carbaryl. In: Some carbamates, thiocarbamates, and carbazides. IARC monographs on the evaluation of carcinogenic risk of chemicals to man 12:282. International Agency for Research on Cancer, Lyon, France

———(1979) Hexachlorocyclohexame (Technical HCH and Lindane). IARC monographs of the evaluation of the carcinogenic risk of chemicals to humans. International Agency for Research on Cancer, Lyon, France, Vol 20, pp 195–239

Larson E (1980) The epidemiology of primary brain tumors. J Neurosurg Nursing 12(3):121–127

Lin SY, Lee TC, Cheng CS, Wang TC (1988) Cytotoxicity, sister-chromatid exchange, chromosome aberration and transformation induced by 2,2-dichlorovinyl-*O,O*-dimethyl phosphate. Mutat Res 206:439–445

Lowengart RA, Peters JM, Cicioni C, et al. (1987) Childhood leukemia and parents' occupational and home exposures. J Natl Cancer Institute 79(1):39–46

Mantel N, Haenszel W (1959) Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Institute 22:719–748

Mantel N (1963) Chi-square tests with one degree of freedom, extensions of the Mantel-Haenszel procedure. J Am Stat Assoc 58:690–700

Mount ME, Oehme FW (1981) Carbaryl. A literature review. Residue Rev 80:1–64

National Coalition Against the Misuse of Pesticides (1988) Chlordane, a pesticide review, health and environmental effects and alternatives. National Coalition Against the Misuse of Pesticides, Washington, DC

Preston-Martin S, Yu MC, Benton B, Henderson BE (1982) *N*-nitroso compounds and childhood brain tumors: A case-control study. Cancer Res 42:5240–5245

Reuber MD (1981) Carcinogenicity of dichlorvos. Clin Toxicol 18(1):47–84

Rothman KJ, Boice JD (1982) Epidemiologic analysis with a programmable calculator. USDHEW Pub. No. (NIH) 82-1649. US Gov Printing Office, Washington, DC

Schrötter C, Parzefall W, Schrötter H, Schulte-Hermann R (1987) Dose-response studies on the effects of alpha-, beta-, and gamma-hexachlorocyclohexane on putative preneoplastic foci, monooxygenases, and growth in rat liver. Cancer Res 47(1):80–88

Schwartzbaum JA, George SL, Pratt CB (unpublished) Childhood cancer: An exploratory analysis of environmental and medical factors. University of Tennessee, Memphis, TN 38163

Sinks TH Jr. (1985) *N*-nitroso compounds, pesticides, and parental exposures in the workplace as risk factors for childhood brain cancer: A case-control study. Dissertation Abstr Int 46(6):1888-B

Triolo AJ, Lang WR, Coon JM, Lindstrom D, Herr DL (1982) Effect of the insecticides toxaphene and carbaryl on the induction of lung tumors by benzo[a]pyrene in the mouse. J Toxicol Environ Health 9(4):637–649

Wolff GL, Morrissey RL (1986) Increased responsiveness of lean pseudoagouti AVY/A female mice to lindane enhancement of lung and liver tumorigenesis. In: Magee PN (ed) Proc Annual Meeting Am Assoc Cancer Res, Los Angeles, CA, Vol 27, p 138

World Health Organization (1976) International classification of diseases for oncology. World Health Organization, Geneva, Switzerland

———(1986) Principals for evaluating health risks from chemicals during infancy and early childhood: The need for a special approach. Environment and Health Criteria 59. World Health Organization, Geneva, Switzerland

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