Household Pesticides and the Risk of Wilms Tumor

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Background: Previous epidemiologic studies have suggested that exposure to pesticides in utero and during early childhood may increase the risk of development of childhood cancer, including Wilms tumor, a childhood kidney tumor.

Objectives: In this analysis we evaluated the role of residential pesticide exposure in relation to the risk of Wilms tumor in children using data from a North American case–control study.

Methods: The National Wilms Tumor Study Group (NWTSG) collected information on exposure to residential pesticides from the month before pregnancy through the diagnosis reference date using detailed face-to-face interviews. Pesticide use was grouped according to type of pesticide and where they were used.

Results: A slightly increased risk of Wilms tumor was found among children of mothers who reported insecticide use [odds ratio (OR) = 1.4, 95% confidence interval (CI), 1.0–1.8; adjusted for education, income, and the matching variables]. Results from all other categories of pesticides were generally close to the null.

Conclusions: This study is the largest case–control study of Wilms tumor to date. We were unable to confirm earlier reports of an increased risk for Wilms tumor among those exposed to residential pesticides during pregnancy through early childhood.

Key words: childhood cancer, environment, pediatric pesticides, Wilms tumor.

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The interview included a section on household pesticide use. Mothers were asked about the use of chemical products to control different pests from the month before pregnancy with the index child through the reference date. Residential pesticides were defined as chemical products used to control insects, fungus, rodents, and weeds, in the house or yard, insects on pets, insects on the parent or child’s body, and professional extermination of the home or lawn. If the mother answered yes, she was asked how many times she used the product in specific time periods reflecting the month before pregnancy through the pregnancy and after the child was born up until the reference date.

In the analysis, pesticides were categorized by the location where the chemicals were used (i.e., house, lawn, child, pet, or mother’s body), by type (i.e., insecticide, herbicide, fungicide, rodenticide), and by combination of location and type (e.g., household insecticide). We then evaluated pesticide use in the exposure time windows (month before pregnancy through the pregnancy, birth through the reference date).

We estimated odds ratios (ORs) and 95% CIs for the association between pesticide use and Wilms tumor using unconditional logistic regression models. We evaluated potential confounders, including household income, maternal education, breast-feeding, and maternal age, in combination with the frequency matching variables (child’s age at reference date and geographic region of residence). We used four models to determine whether the hypothesized confounders should be included in the final model. Model 1 included maternal age and breast-feeding and the matching variables as potential confounders; model 2 included income, education, maternal age, breast-feeding, and the matching variables; model 3 included education, income, and the matching variables; and model 4 included only the matching variables. None of the combinations of these variables materially changed the crude pesticide effect estimates. The final model included the matching variables and two a priori confounders, education and income, selected as potential surrogates of selection processes related to RDD and nonresponse. We also evaluated effect measure modification based on the significance \((p < 0.10)\) of the likelihood ratio test of the interaction term in the logistic regression model. Factors examined as potential effect measure modifiers included reference age at diagnosis, mother’s education, and breast-feeding.

**Results**

This analysis was based on information obtained in telephone interviews from 523 case mothers and 517 control mothers. We found that cases and controls and their mothers were similar with regard to basic demographic characteristics (Table 1). There was some indication that children of mothers in a household with an income < $10,000 were at slightly higher risk of Wilms tumor, but the OR was not very precise. A difference in the distribution of sex was found between the two groups with a higher percentage of female cases (57.2%) compared with controls (47.2%). African Americans and Hispanics had a slightly higher risk for Wilms tumor, although these estimates were imprecise due to small numbers.

Approximately 61% of the case mothers and 57% of control mothers reported using pesticides (Table 2). Overall, pesticide use was associated with a slight increase in risk of Wilms tumor, after adjustment for the matching variables, income and education (OR = 1.3; 95% CI, 1.0–1.7). This result may represent insecticide use, because 88% of those not using pesticide use reported using insecticides. The association between any insecticide use and Wilms tumor was similar (OR = 1.4; 95% CI, 1.0–1.8). Insecticides were used more commonly than other types of pesticides; yet 33% of women reported using more than one pesticide type. Elevated ORs were not found for herbicides or fungicides.

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Table 1. Maternal and child demographic characteristics [no. (%)] and associated ORs (95% CIs) for children diagnosed with Wilms tumor and age/region-matched controls, United States and Canada, 1999–2002.

| Maternal and child characteristics | Cases (n = 523)\(^a\) | Controls (n = 517)\(^b\) | OR (95% CI)\(^c\) |
|-----------------------------------|----------------------|----------------------|------------------|
| **Child’s age at reference date (years)** | | | |
| 0–1 | 146 (27.9) | 138 (26.7) | 1.2 (0.9–1.6) |
| 2–3 | 185 (31.6) | 145 (28.1) | 1.3 (0.9–1.7) |
| ≥ 4 | 212 (40.5) | 234 (45.3) | 1.0 |
| **Geographic region of residence** | | | |
| Midwest | 159 (30.4) | 154 (29.8) | 1.0 |
| Northeast | 69 (13.2) | 60 (11.6) | 1.1 (0.7–1.7) |
| South | 180 (34.4) | 183 (35.4) | 1.0 (0.7–1.3) |
| West | 58 (11.1) | 64 (12.4) | 0.9 (0.6–1.3) |
| Canada | 57 (10.9) | 56 (10.8) | 1.0 (0.7–1.6) |
| **Mother’s education** | | | |
| 0–11 years | 45 (8.6) | 41 (7.9) | 1.0 |
| High school | 137 (26.2) | 118 (22.8) | 1.2 (0.7–2.0) |
| > High school | 341 (65.2) | 357 (69.1) | 0.8 (0.5–1.3) |
| **Household income at birth (US$)** | | | |
| < 10,000 | 47 (9.0) | 39 (7.4) | 1.3 (0.7–2.4) |
| 10,000–20,000 | 81 (15.5) | 96 (18.0) | 0.9 (0.6–1.4) |
| 21,000–30,000 | 65 (12.4) | 67 (13.0) | 0.9 (0.5–1.4) |
| 31,000–40,000 | 66 (12.6) | 68 (12.8) | 1.0 |
| 41,000–50,000 | 64 (12.2) | 63 (12.2) | 1.0 (0.6–1.6) |
| ≥ 51,000 | 158 (30.2) | 146 (28.3) | 1.0 (0.7–1.6) |
| **Mother’s race** | | | |
| White | 390 (74.6) | 404 (78.1) | 1.0 |
| Black | 73 (14.0) | 59 (11.2) | 1.4 (0.9–2.0) |
| Hispanic | 42 (8.0) | 33 (6.4) | 1.4 (0.8–2.3) |
| Other | 18 (3.4) | 22 (4.3) | 0.9 (0.5–1.6) |
| **Mother’s age at child’s birth (years)** | | | |
| < 20 | 40 (7.7) | 39 (7.5) | 0.8 (0.5–1.4) |
| 20–24 | 114 (21.8) | 103 (19.9) | 1.0 |
| 25–30 | 182 (34.8) | 164 (31.7) | 1.0 (0.7–1.4) |
| ≥ 31 | 187 (35.8) | 211 (40.8) | 0.8 (0.6–1.1) |
| **Sex** | | | |
| Male | 224 (42.8) | 273 (52.8) | 1.0 |
| Female | 299 (57.2) | 244 (47.2) | 1.5 (1.2–1.9) |

\(^a\)Among cases, there were 42 missing values for household income. Among controls, there was one missing value for mother’s education and 41 missing values for household income. \(^b\)ORs adjusted by child’s age at reference date and geographic region of residence (matching factors).
stratum. Although ORs varied slightly by strata, none of the factors examined as effect measure modifiers were statistically significant ($p < 0.10$) on the basis of the likelihood ratio test. For example, the effect of any pesticide use by child’s age at diagnosis was 0–1 year of age (adjusted OR = 1.3; 95% CI, 0.8–2.2); 2–3 years of age (OR = 1.5; 95% CI, 0.9–2.4); and ≥ 4 years of age (OR = 1.1; 95% CI, 0.7–1.7).

Child’s sex was also examined as a potential effect modifier and a confounder. Sex was not an important confounder when included in our models, and when results were stratified by sex, no important differences were found. For example, the OR for insecticide use was 1.3 (95% CI, 0.9–1.9) among males and 1.4 (95% CI, 0.9–1.9) among females.

**Discussion**

Exposure to residential pesticides did not produce a strong pattern of increased risk of developing Wilms tumor in this study. We classified the pesticides by intended use as a proxy of their chemical makeup. This division was important to distinguish whether any particular pesticide group conveyed more risk than another. Except for slightly higher risk associated with insecticides, most associations between pesticides and Wilms tumor were weak. There was also no apparent elevation in risk associated with exposure during different time periods before compared with after the birth of the child, nor modification of the effects of pesticides by child’s age or sex.

The first NWTS study found an association with household insect extermination (OR = 2.16; 95% CI, 1.24–3.75) (Olshan et al. 1993). Our study found no association between extermination and Wilms tumor. The more detailed data collection through structured telephone interview for the current study may have better distinguished pesticide usage patterns compared with the earlier study’s broad self-administered mailed questionnaire with less detailed questions.

This is the largest case–control study of risk factors for Wilms tumor conducted to date and has detailed exposure information using computerized telephone interviews. Women were queried about the types of pesticides used and the timing and location of their use. Mothers were asked to remember their use of pesticides up to several years before the interview. Recall could be problematic because use of chemicals in and around the house was common and memory of details over time could be inaccurate. One recent study found a high correlation for residential pesticides between self-reported pesticide exposure and household dust samples (Hartge et al. 2005). However, another study suggested that underreporting is a common problem with self-reported pesticide exposure from surveys (Nieuwenhuijsen et al. 2005). According to a U.S. Environmental Protection Agency report, in 1999–2001 in the United States the three most commonly used pesticides outside of the agricultural market were glyphosate, atrazome, and metam sodium; the most common insecticide used was malathion (Kiely et al. 2004). However, because mothers were not asked to recall the specific type of pesticide they used, we had limited ability to evaluate specific chemicals.

When pesticide use was reported, we did not ascertain whether the mother took any preventive steps such as wearing protective gear, ventilating the space, or removing the child from the room while using the pesticide—which would affect the level of exposure. A study of childhood brain tumors reported elevated risk when these exposure mediators were considered (Pogoda and Preston-Martin 1997).

Another limitation of our study was our inability to assess father’s report of residential pesticide use because of the sparse nature of the data. Different risk pathways may be operating depending on whether the mother or the father is exposed. Mothers and fathers may differentially recall the use of pesticides in or around the home (Daniels et al. 2001). It is unclear which parent better reports pesticide use, but some reporting error may be based on who applied the pesticides. The exposure level may differ for the applicator compared with other members of the household. The resulting exposure misclassification may be differential or nondifferential, and predictions about the direction of the bias are difficult to infer.

The control participation proportion (76%) was good, but the RDD screening proportion was low. Only 50% of those households contacted agreed to complete the screening questionnaire. It is difficult to speculate about the direction or magnitude to which this bias may have affected our results because we do not know the characteristics of those who did not respond to the initial request. However, we do know that those who participated were not different in demographic characteristics from those families who completed the screen but then decided not to participate.

Although the association between residential insecticide use and Wilms tumor may warrant further investigation, overall these findings do not support other positive findings from studies of residential or occupational pesticide exposures (Fear et al. 1998; Kristensen et al. 1996; Olshan et al. 1993; Sharpe et al. 1995). It has been suggested that preconceptual exposure to pesticides may play a role in the development of Wilms tumor by causing damage to parental germ cells (Tsai et al. 2005). We were unable to assess the potential for preconceptual exposure of fathers in this study, and most fathers were not likely to have exposure to pesticides at a level comparable to those of occupationally exposed workers. The ability of future studies to better investigate the relation between pesticides and Wilms tumor directly relies on whether advanced technology is available to improve exposure assessment, possibly using dust or biologic samples, to reflect more accurately the exposure during relevant time windows before and during pregnancy.

| Table 2. ORs (95% CIs) for risk of Wilms tumor associated with exposure to pesticides, NWTS 1999–2002. |
|---------------------------------------------------------------|
| **Cases [no. (%)]** | **Controls [no. (%)]** | **Exposed** | **Unexposed** | **Exposed** | **Unexposed** | **OR (95% CI)** |
| **Pesticide** | 320 (61.2) | 203 (38.8) | 292 (56.5) | 225 (43.5) | 1.3 (1.0–1.7) |
| In home | 176 (34.5) | 334 (65.5) | 148 (29.5) | 353 (70.5) | 1.3 (1.0–1.7) |
| In yard | 158 (31.0) | 352 (69.0) | 157 (31.3) | 344 (68.7) | 1.0 (0.8–1.4) |
| On body | 148 (29.0) | 362 (71.0) | 147 (29.3) | 354 (71.0) | 1.0 (0.8–1.4) |
| Insecticide | 285 (54.5) | 238 (45.5) | 251 (48.6) | 266 (51.5) | 1.4 (1.0–1.8) |
| In home | 154 (30.2) | 356 (69.8) | 123 (24.6) | 378 (75.5) | 1.4 (1.0–1.8) |
| In yard | 103 (20.2) | 406 (79.8) | 94 (18.9) | 404 (81.1) | 1.2 (0.8–1.6) |
| On body | 80 (17.5) | 420 (82.5) | 89 (16.0) | 421 (84.0) | 1.2 (0.8–1.7) |
| In home | 91 (18.0) | 415 (82.0) | 82 (16.7) | 409 (83.3) | 1.2 (0.8–1.7) |
| Herbicides | 112 (21.4) | 411 (78.6) | 112 (21.7) | 405 (78.3) | 1.0 (0.7–1.4) |
| Fungicides | 32 (6.1) | 483 (93.9) | 31 (6.0) | 486 (94.0) | 1.0 (0.6–1.7) |
| In home | 27 (5.3) | 491 (94.7) | 22 (4.5) | 479 (95.5) | 1.2 (0.7–2.1) |
| In yard | 6 (1.2) | 500 (98.8) | 10 (2.0) | 490 (98.0) | 0.7 (0.2–1.9) |
| Rodenticides | 20 (3.9) | 490 (96.1) | 19 (3.8) | 482 (96.2) | 1.0 (0.5–2.0) |
| Exterminator | 145 (28.6) | 362 (71.4) | 149 (29.9) | 349 (70.1) | 1.0 (0.7–1.3) |

*For the broadest categorization of the pesticides into herbicides, fungicides, insecticides, there were no missing data. Some data were missing for 13 cases and 16 controls when pesticides were classified based on both type and location of use. Adjusted for age at reference date, geographic region, education, and income. Exposure during any time from pregnancy through childhood.*

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