

Household Solvent Exposures and Childhood Acute Lymphoblastic Leukemia

ABSTRACT

Objectives. This study explored the risk of childhood acute lymphoblastic leukemia (ALL) associated with participation by household members in hobbies or other home projects involving organic solvents.

Methods. Participants in this case-control study were 640 subjects with ALL and 640 matched controls.

Results. Childhood ALL was associated with frequent (>4 times/month) exposure to model building (odds ratio [OR]=1.9; 95% confidence interval [95% CI]=0.7, 5.8) and artwork using solvents (OR=4.1; 95% CI=1.1, 15.1). We also found elevated risk (OR=1.7; 95% CI=1.1, 2.7) among children whose mothers lived in homes painted extensively (>4 rooms) in the year before the children's birth.

Conclusions. In this exploratory study, substantial participation by household members in some common household activities that involve organic solvents was associated with elevated risks of childhood ALL. (*Am J Public Health*. 2001;91:564-567)

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Little is known about the role of environmental exposures in childhood leukemia.¹ Several epidemiologic studies have described elevated risks of childhood leukemia associated with parents' exposure to occupational chemicals,²⁻¹⁰ including solvents^{3,6,8,9} and paints.^{3,5,7,10} Children may also be exposed to solvents and paints at home through their own or their parents' hobbies and household maintenance activities. To our knowledge, few studies¹⁰ have examined the risks of childhood leukemia associated with exposures to solvents in the home other than pesticides.

As part of a large comprehensive case-control study of potential risk factors for childhood acute lymphoblastic leukemia (ALL) conducted by the Children's Cancer Group, we undertook an exploratory study to examine the relationship between childhood leukemia and exposure to selected household chemicals during childhood, as well as indoor house painting during preconception, pregnancy, and childhood. We focused on common home activities likely to result in exposures to solvents.¹¹⁻¹⁴

Methods

Case subjects were children, aged birth to 14 years, who were newly diagnosed with ALL between 1989 and 1993, resident in any of 9 midwestern and mid-Atlantic states, and enrolled through the Children's Cancer Group, a cooperative clinical trials group.^{15,16} Eligibility criteria included a residential telephone and an English-speaking biological mother available for an in-person interview. Control subjects were selected through random-digit dialing and were individually matched to the case subjects by age (within 25% of the case's age at diagnosis), the first 8 digits of the telephone number, and race.¹⁷ The overall participation rates were 88% for case subjects and 64% for control subjects. After exclusion of patients with Down syndrome, which has been associated with a high risk of ALL,¹⁸ there were 640 matched case-control pairs.

For each of 3 hobbies (model building, artwork using solvents, and furniture stripping) and 2 household maintenance activities (motor vehicle and electronic equipment repair), interviewers asked mothers whether household members engaged in any of the 5 activities in and around their home. Because pretesting revealed that many mothers could not remem-

ber early activities or gave identical answers for each year of the child's life, the interview focused on activities during the reference year (the year preceding the date of diagnosis for the case and its matched control). Interviewers asked the mother about which household members participated in the activities, as well as the frequency and duration of each episode. Interviewers also asked questions about painting inside the subjects' homes within 3 months of conception, during the pregnancy, and after the subjects' birth, including the specific rooms painted, the frequency of the painting, who painted (mother or others), and whether members of the family remained at home overnight during the house painting.

For each hobby or household activity other than house painting, we analyzed 2 measures of exposure: frequency (defined as the number of times engaged in the activity per month) and cumulative exposure (defined as the product of the frequency of the activity and its duration per episode). Because fewer control than case mothers provided information about duration, our analysis emphasized frequency as a more unbiased exposure measure. Before any analysis, we arbitrarily classified frequency and cumulative exposure into common time categories. We categorized frequency of exposure as low (<1 time/month), medium (1-4 times/month), and high (>4 times/month); we categorized cumulative exposure as low (<10 minutes over a month), medium (10 minutes-1 hour over a month), and high (>1 hour over a month). For house painting, exposure was classified by the total number of rooms painted (1-2, 3-4, >4 rooms), as well as the frequency (1-2, 3-5, >5 times since birth) among those painting after the child's birth.

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We computed odds ratios by unconditional logistic regression so as to maximize the number of cases and controls included in this exploratory analysis. We confirmed our main findings by conditional logistic regression. Odds ratios were adjusted for age at the reference date, sex, mother's education level, and family income. We compared subjects by whether they ever or never participated in a given activity and by the 2 measures of exposure. We analyzed the total population, as well as 2 age strata: younger than 5 years (the peak ages are 2–4 years for ALL¹) and 5 years and older. Except for model building, there was an insufficient number of children participating

in the various activities to assess the risk of ALL among child participants. For house painting, we investigated the timing of painting before and after birth.

We also examined 2 strata based on length of time between diagnosis and interview (≤ 24 months vs >24 months). We explored trends in risk by entering exposure variables ordinally into the models.

Results

Case subjects and control subjects were demographically similar, except that the for-

mer came from families with lower income and had mothers with less formal education. Both groups were predominantly White (Table 1).

Exposures From Hobbies, Vehicle Maintenance, and Electronic Repair

No significant excess risk of childhood ALL was observed with ever vs never participation in any of the activities by a household member (Table 2). Moreover, neither automotive and truck maintenance nor electronic repairs reflected a pattern of risk with increasing exposure.

Elevated risks of childhood ALL, however, were associated with the highest levels of participation in some activities (Table 2). Risks were elevated for model building in the highest-frequency category (odds ratio [OR]=1.9; 95% confidence interval [CI]=0.7, 5.8) but did not vary by age group or the child's involvement. Artwork requiring solvents was linked with significantly elevated risks of childhood ALL in the highest-frequency exposure category (OR=4.1; 95% CI=1.1, 15.1), and risks increased as exposure rose (P trend=.07). Although the numbers were small, similar risks were observed in both age groups (data not shown). The associations with high cumulative exposure were similar to those with frequent exposures for both model building and artwork (data not shown).

For furniture stripping, risk was not elevated among children in families with the highest frequency of exposure. Risk was, however, significantly elevated among children in those families with the highest cumulative exposures (OR=2.9; 95% CI=1.1, 9.1).

In general, when the subjects were stratified by time between diagnosis and interview dates, the odds ratios among those interviewed close to the diagnosis date were about the same as or stronger than the unstratified odds ratios.

Exposure From Household Painting

We observed no significant overall increase in risk (OR=1.2; 95% CI=0.9, 1.5) of childhood ALL associated with interior house painting during the 12 months before the subject's birth, although the risk was elevated among children whose mothers lived in homes in which more than 4 rooms were painted during this period (Table 3). Risk of ALL was not higher among children whose mothers, rather than other people, did the painting (Table 3).

When risk was analyzed by 3-month periods in the year before birth, we also found no significant risk during each period except for

TABLE 1—Characteristics of 640 Children With Acute Lymphoblastic Leukemia and 640 Matched Controls,^a From Interview Data on Use of Household Solvent Exposures

Characteristics	Cases N (%)	Controls N (%)
Sex		
Male	333 (52.0)	337 (52.7)
Female	307 (48.0)	303 (47.3)
Age at diagnosis/reference date, y		
<2	68 (10.6)	85 (13.3)
2–4	312 (48.8)	289 (45.2)
5–9	179 (28.0)	185 (28.9)
≥ 10	81 (12.7)	81 (12.7)
Race		
White	585 (91.4)	612 (95.6)
Black	20 (3.1)	16 (2.5)
Other	35 (5.5)	12 (1.9)
Household income during reference year, \$		
<20 000	113 (17.7)	77 (12.0)
20 000–29 999	122 (19.1)	86 (13.4)
30 000–39 999	133 (20.8)	112 (17.5)
40 000–49 999	98 (15.3)	105 (16.4)
$\geq 50 000$	168 (26.2)	255 (39.8)
Missing	6 (0.9)	5 (0.8)
Mother's education		
<High school	57 (8.9)	30 (4.7)
High school	220 (34.4)	224 (35.0)
Some college	210 (32.8)	199 (31.1)
College graduate	153 (23.9)	187 (29.2)
Mother's occupation		
Professional	131 (20.5)	148 (23.1)
White collar	156 (24.2)	172 (26.9)
Blue collar	45 (7.0)	29 (4.5)
Housewife	308 (48.1)	291 (45.5)
Father's occupation		
Professional	190 (29.7)	200 (31.3)
White collar	103 (16.1)	119 (18.6)
Blue collar	285 (44.5)	240 (37.5)
Missing	62 (9.7)	81 (12.7)
Residential status		
Urban	169 (26.4)	136 (21.3)
Suburban	271 (42.3)	293 (45.8)
Rural	200 (31.3)	210 (32.8)
Time between reference date and interview, mo		
7–12	86 (13.4)	3 (0.5)
13–18	256 (40.0)	107 (16.7)
19–24	134 (20.9)	196 (30.6)
25–36	129 (20.2)	238 (37.2)
≥ 37	35 (5.5)	96 (15.0)

^aExcludes 11 pairs in which 1 member of the pair had Down syndrome.

TABLE 2—Distribution of Cases and Controls by Frequency^a of Hobby and Household Maintenance Activity During Year of Diagnosis, With Odds Ratios^b (ORs) and 95% Confidence Intervals (CIs)

	Cases	Controls	OR (95% CI)
Hobbies			
Model building			
Never ^c	549	555	1.0
Ever ^d	90	83	1.1 (0.8, 1.5)
Low	51	60	0.9 (0.6, 1.3)
Medium	29	18	1.5 (0.8, 2.8)
High	10	5	1.9 (0.7, 5.8)
P trend			.21
Artwork (using solvents)			
Never ^c	566	571	1.0
Ever ^d	73	65	1.3 (0.9, 1.8)
Low	34	35	1.1 (0.7, 1.8)
Medium	28	27	1.2 (0.7, 2.0)
High	11	3	4.1 (1.1, 15.1)
P trend			.07
Furniture stripping			
Never ^c	574	579	1.0
Ever ^d	65	59	1.1 (0.8, 1.6)
Low	32	35	0.9 (0.6, 1.5)
Medium	24	14	1.8 (0.9, 3.6)
High	8	8	1.0 (0.4, 2.7)
P trend			.33
Household maintenance			
Auto/truck maintenance			
Never ^c	378	383	1.0
Ever ^d	260	255	0.9 (0.7, 1.2)
Low	121	129	0.9 (0.7, 1.2)
Medium	107	107	0.9 (0.6, 1.2)
High	31	19	1.5 (0.8, 2.7)
P trend			.91
Electronic repair			
Never ^c	604	612	1.0
Ever ^d	35	25	1.4 (0.8, 2.4)
Low	20	14	1.5 (0.7, 3.0)
Medium	13	5	2.7 (1.0, 7.7)
High	2	6	0.3 (0.1, 1.5)
P trend			.50

^aFrequency refers to occasions per month: "low" is less than once a month, "medium" is 1 to 4 times a month, and "high" is more than 4 times a month.

^bAdjusted for child's age at the reference date, sex, household income at the reference date, and maternal education.

^cReferent category.

^dNot all respondents reporting participation specified frequency.

a small borderline risk in the 3 months before conception (data not shown). However, when the study population was analyzed by length of time from diagnosis to interview, this association appeared to be due to responses from those interviewed at a more distant time from the reference date.

Among children residing in homes painted *after* the subject's birth, a small, but borderline significant, excess risk was seen (OR=1.3; 95% CI=1.0, 1.6). Risk was elevated for painting more rooms (for >4 rooms, OR=1.6; 95% CI=1.2, 2.2) and painting more frequently (for >5 times, OR=1.8; 95% CI=1.1, 2.8). When the associations among those interviewed close to the diagnosis date were examined, risk remained about the same, but

those associations disappeared among subjects interviewed later.

Discussion

This study found elevated risks for childhood ALL associated with substantial postnatal exposure to some household activities and prebirth and postnatal exposure to indoor house painting. There are, however, several limitations to this study. As in any retrospective interview study, exposures are likely to be misclassified owing both to imperfect respondent recollections and to the crudeness of the information requested. The questionnaire obtained only limited information on the child's

proximity to the activity and none on other activities that may involve solvents, particularly home renovation, such as floor refinishing. Moreover, little is known about the relevant time frame for exposure—whether exposures occurred before conception (germ cell mutations), during pregnancy (transplacental fetal exposure), or after birth. With the exception of house painting, the survey was restricted to postnatal exposures.

Our greatest concern in interpreting the findings is the possibility that differential reporting errors by case and control mothers exaggerated estimates of effect.¹² The weaker association with house painting before conception among mothers interviewed near the reference date substantially weakens the credibility of an association with preconception painting. However, the consistency between the other odds ratios and those limited to mothers interviewed close to the reference date supports the findings. Unfortunately, the disproportionate delay in interviewing control mothers limited our ability to check the consistency of associations at interview times very close to the events in question.

Selection bias due to differential socioeconomic status potentially could have resulted from use of random-digit dialing for control selection. Family income, however, was not associated with substantial participation in model building, artwork using solvents, or furniture stripping. Moreover, indoor house painting was more common among high-income controls, which suggests that a selection bias could have underestimated the association with house painting. Finally, socioeconomic factors do not appear to have confounded the relationship between ALL and the activities assessed, because controlling for family income and maternal education did not appreciably affect the results.

Despite the study limitations, there are several arguments for the plausibility of the findings. Some epidemiologic studies have shown an association between paternal occupational exposure to organic solvents and childhood leukemia in the postnatal period.^{2,3,10} Exposure of children could occur through inhalation of solvents used at home or brought home from the workplace on the parents' breath.¹⁹ Previous epidemiologic studies have found positive associations between childhood leukemia and painting on the job during the prenatal^{7,10,20} and postnatal¹⁰ periods.

Each of the activities associated with an elevated risk of childhood ALL involves exposure to organic solvents, some of which are known or possible human carcinogens. Benzene, a typical constituent in hobby glues in model building¹¹ and in paints,¹² is an established adult leukemogenic solvent.²¹ There is a case report of childhood leukemia following intense exposure to toluene-containing glues used in model

TABLE 3—Distribution of Cases and Controls by Indoor House Painting in Subject's Home During Year Before Birth, With Odds Ratios^a (ORs) and 95% Confidence Intervals (CIs)

	Cases	Controls	OR	95% CI
Ever painted				
No	346	359	1.0	
Yes	289	278	1.2	0.9, 1.5
No. of rooms painted				
Never painted	346	359	1.0	
1–2	161	188	1.0	0.8, 1.3
3–4	62	48	1.4	0.9, 2.1
>4	64	40	1.7	1.1, 2.7
P trend			.01	
Family stayed at home overnight ^b				
Never painted	346	359	1.0	
Not at home	25	17	2.3	0.6, 8.9
At home	102	109	1.9	0.6, 6.4
Painter				
Never painted	346	359	1.0	
Mother	160	152	1.1	0.9, 1.5
Other	128	124	1.3	0.9, 1.7

Note. Not all respondents who reported painting provided information about number of rooms painted, whether family stayed at home overnight, or who performed the painting.

^aAdjusted for child's age at the reference date, sex, household income at the reference date, maternal education, and painting during other periods.

^bAlso adjusted for number of rooms painted.

building.²² Methylene chloride, the main constituent of furniture strippers,¹³ is also a possible carcinogen,²³ and trichloroethylene, which may be found in paints and varnishes,²⁴ has been found to cause cancer in animals.²³

As the first large case-control study of childhood ALL evaluating associations with hobbies and household activities that may involve carcinogenic solvent exposures, our study is primarily exploratory. Because of the number of exposures examined, confirmation is required to rule out false-positive results. Further study is also warranted of additional household activities involving solvents, with exposure information for individual chemicals and levels and better delineation of specific time frames of exposure (prenatal vs exclusively postnatal) to illuminate the relevant biological pathways. □

Contributors

D.M. Freedman was principal author and analyst of the paper. P. Stewart and R.E. Tarone were involved in interpretation of data, analysis, and revisions of the paper. R.A. Kleinerman was involved in data collection, interpretation of data, analysis, and revisions of the paper. S. Wacholder was involved in the design of the entire study of which this study is a part, interpretation of data, and revision of the paper. E.E. Hatch was involved in data collection, the design of the study—including selection of cases and controls—interpretation of data, and revisions of the paper. L.L. Robison and M.S. Linet were involved in the design of the entire study of which this study is a part, data

collection, interpretation of data, and revisions of the paper.

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The study was approved by the National Cancer Institute Special Studies Institutional Review Board and obtained the consent of participants.

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