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International Journal of Cancer

Exposure to house painting and the use of floor treatments and the risk of childhood acute lymphoblastic leukemia

Helen D. Bailey[1], Elizabeth Milne[1], Nicholas H. de Klerk[1], Lin Fritschi[2], John Attia[3], Catherine Cole[4] and Bruce K. Armstrong[5]; for the Aus-ALL Consortium

[1] Telethon Institute for Child Health Research, Centre for Child Health Research, The University of Western Australia, Perth, WA, Australia
[2] Western Australian Institute for Medical Research, The University of Western Australia, Perth, WA, Australia
[3] Centre for Clinical Epidemiology and Biostatistics, The University of Newcastle, Newcastle, NSW, Australia
[4] School of Paediatrics and Child Health, The University of Western Australia, Perth, WA, Australia
[5] Sydney School of Public Health, The University of Sydney, NSW, Australia

Painting in the home has been identified as a potential risk factor for childhood acute lymphoblastic leukemia (ALL). The aim of this analysis was to investigate whether exposure to house painting or floor treatments before birth or during childhood increased the risk of childhood ALL. Data from 389 cases and 876 frequency-matched controls were analyzed using unconditional logistic regression, adjusting for study matching variables and potential confounders. Overall, there was little evidence of an increased risk with painting inside the house in the year before the pregnancy, during the pregnancy, or after the child's birth; however, the risk appeared to be increased in certain circumstances. The odds ratio (OR) for more than three rooms being painted during pregnancy was 1.68 [95% confidence interval (CI) 1.01, 2.80]. The OR for someone other than the parents painting inside the house in the year before the pregnancy was 2.37 (95% CI 1.30, 4.30) and 3.07 (95% CI 1.46, 6.46) when more than three rooms were painted. The OR for the mother painting the outside of the house with oil-based paint in the year before the pregnancy was 2.97 (95% CI 1.06, 8.33). No association was found with having floor treatments in any time period. We found some evidence of an increased risk of ALL associated with house painting. An apparently increased risk associated with someone other than the parents painting inside the house may be related to the amount of paint used and the intensity of the dose received.

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer in developed countries. It is more common in boys and the majority of cases are diagnosed before the age of 5 years.[1] Little is known about the causes of ALL, although it is likely to involve both genetic factors and environmental exposures.[2] The early age at diagnosis suggests that parental (preconception) and fetal environmental exposures, in addition perhaps to exposures in early childhood, play a role in disease development.

Painting in the home has been identified as a potential risk factor for ALL in previous studies[3–5] and the International Agency for Research on Cancer concluded that that

Key words: case-control studies, child, leukemia, paint

The Aus-ALL consortium conducted the study and the Telethon Institute for Child Health Research (TICHR), The University of Western Australia, was the coordinating centre. Bruce Armstrong (Sydney School of Public Health), Elizabeth Milne (TICHR), Frank van Bockxmeer (Royal Perth Hospital), Michelle Haber (Children's Cancer Institute Australia), Rodney Scott (The University of Newcastle), John Attia (University of Newcastle), Murray Norris (Children's Cancer Institute Australia), Carol Bower (TICHR), Nicholas de Klerk (TICHR), Lin Fritschi (WA Institute for Medical Research), Ursula Kees (TICHR), Margaret Miller (Edith Cowan University) and Judith Thompson (WA Cancer Registry) were the research investigators as well as Helen Bailey (TICHR) was the project coordinator. The clinical investigators were: Frank Alvaro (John Hunter Hospital, Newcastle); Catherine Cole (Princess Margaret Hospital for Children, Perth); Luciano Dalla Pozza (Children's Hospital at Westmead, Sydney); John Daubenton (Royal Hobart Hospital, Hobart); Peter Downie (Monash Medical Centre, Melbourne); Lianne Lockwood, (Royal Children's Hospital, Brisbane); Maria Kirby (Women's and Children's Hospital, Adelaide); Glenn Marshall (Sydney Children's Hospital, Sydney); Elizabeth Smibert (Royal Children's Hospital, Melbourne); Ram Suppiah, (previously Mater Children's Hospital, Brisbane).

Grant sponsor: The National Health and Medical Research Council (NHMRC); **Grant number:** 254539; **Grant sponsor:** NHMRC Post Graduate Scholarship; **Grant number:** 513934; **Grant sponsor:** NHMRC Career Development Award; **Grant number:** 513910; **Grant sponsor:** NHMRC Fellowship; **Grant number:** 513706

DOI: 10.1002/ijc.25572

History: Received 29 Apr 2010; Accepted 14 Jul 2010; Online 23 Jul 2010

Correspondence to: Helen D. Bailey, Telethon Institute for Child Health Research, PO BOX 855, WA 6872, Australia, Tel.: +61-8-9489-7922, Fax: +61-8-9489-7700, E-mail: helenb@ichr.uwa.edu.au

there is "limited evidence" that painting is associated with childhood leukemia.[6]

There are two possible ways exposure to house painting may increase the risk of childhood ALL. Firstly, the mother or father may be exposed to paint fumes (either by living in the house or doing the painting themselves), causing damage to reproductive cells prior to the pregnancy. Secondly, the child may be exposed to the painting fumes *in utero* or during childhood. The evidence for exposure to paint increasing the risk of childhood ALL has been inconsistent, with three studies suggesting an association with maternal exposure around the time of the pregnancy,[3–5] two studies finding an association with the child's exposure[3,5] and two finding no association with exposure of the parents or child.[7,8] Other home maintenance activities such as floor treatments also involve exposure to similar substances to those found in paint, but they do not appear to have been investigated as possible causes of childhood ALL.

The Australian Study of Causes of Acute Lymphoblastic Leukaemia in Children (Aus-ALL) was a national study of the genetic, dietary and environmental causes of childhood ALL. The aim of this analysis was to investigate whether house painting or treating floors in the year before pregnancy, during the pregnancy or after birth increased the risk of childhood ALL.

Material and Methods

Study population

Aus-ALL was a national, population-based, multicentre case-control study, which recruited 416 cases and 1,361 controls aged younger than 15 years from mid 2003 to early 2007. For a child to be eligible, the biological mother needed to be available and have sufficient English skills to complete the questionnaires. Case families were identified and recruited through all ten pediatric oncology centers in Australia. Cases were eligible if they were diagnosed between July 1st, 2003 and December 31st, 2006 and had reached remission. Controls were recruited by random digit dialing (RDD) between 2003 and 2006 and were frequency matched to cases by age, sex and State of residence in a ratio of ~3:1. A full description of the study population and control recruitment process has been published elsewhere.[9–11] The study had Human Research Ethics Committee approval from participating hospitals.

Data collection

Both parents (where available) were mailed questionnaires about a range of potentially carcinogenic exposures, including painting the inside and outside of the home and treating floors. Mothers were asked if they or anyone else had done any painting or floor treatments in three time periods: the year before pregnancy, during pregnancy and after birth. Fathers were asked if they themselves had done any painting or floor treatments in the year before the pregnancy. Once these questionnaires were returned, computer assisted telephone interviews were conducted to collect further data on exposures listed in the questionnaire. Data were collected about the frequency of painting inside the house in each relevant time period and, for each individual painting episode, the person who did the painting (mother, father or another person), the type of paint used, the number of rooms painted and whether paint stripper was used. Information about whether painting was done during the pregnancy or after birth was provided by mothers, but both parents were asked independently about whether painting was done in the year before the pregnancy. If the painting was done during the pregnancy, information was sought about the trimester. We also asked whether the parents' bedroom was painted before the pregnancy, and if so, whether they slept in it within 3 days of it being painted. We asked similar questions about the mother's bedroom during pregnancy and the child's bedroom since birth.

Relevant questions were also asked about the painting done to the outside of the house. If either parent had painted in relevant time periods, information was collected about the type of paint used and the number of days painting was done in the time period.

If any floor treatments had been done, we asked about the type of floor (floorboards, tiles or slate, cork or other), type of treatment (sealant, stain, varnish, glue or other), the person who did the treatment (mother, father or other) and the frequency and number of rooms treated.

Exposure assessment

The data provided by both parents (where available) were collated to give a complete picture of the painting and floor treatments done in each time period. If either parent said painting or floor treatments were done, we classed the response as positive. Exposure was accumulated to the censoring date; for cases, this was the date of diagnosis, and for controls it was the date of return of the written questionnaires. There were several reasons for this approach; the control questionnaire asked about exposures "since your child was born" and as controls were frequency matched, there was no corresponding case whose date of diagnosis could have been used.

When mothers were asked who did the painting or floor treatments, the options were "mother," "father," or "another person," and it was possible to give more than one response. This allowed us to identify whether the parents had done any painting or floor treatments in relevant time periods, or whether painting or floor treatments had only been done by another person, so the categories used were: "mother" (mother +/− father or another person), "father" (father +/− mother or another person) or "only someone other than the parents" (neither parent, only another person).

For each painting episode, parents were asked about the type of paint used: water-based, oil-based or both. As very few people (less than 6%) used only oil-based paints in any time period, the final categories were "water-based only" and "any oil-based (+/− water-based)." To estimate the total

dose of exposure to painting inside the house, the numbers of rooms painted in each episode were added to assign a dose for each time period. If the respondent said that something other than a room was painted (*e.g.,* door frames), "half a room" was used as the default exposure. For the final analyzes, the total number of rooms painted in each time period were categorized as "lower" or "higher" exposure, with the cut-off being the median number of rooms painted in control homes in each time period: before and during pregnancy, "lower exposure" was three rooms or less; since birth it was five rooms or less; and over all time periods it was seven rooms or less. If the father was not interviewed and the mother could not provide information about all painting episodes, the data about the number of rooms painted and type of paint were classified as unknown.

For painting the outside of the house, we hypothesized that there would be little direct effect on those living in the house, so the main focus was on establishing whether either parent had actually done any such painting during the relevant time period(s); that is, before conception for the father and before or during pregnancy for the mother. The total number of days during which the parent painted was used as the indicator of dose. "Lower" exposure was defined as 4 days or less and "higher" exposure as more than 4 days; 4 was the median number of days control parents painted before or during the pregnancy.

The types of floors treated were collapsed into two categories: "floorboards" and "other hard floor types (excluding carpet)." The types of treatments were classified as "sealant, stain, varnish or other coating," or "adhesives or glue." For the final analyzes, the total number of rooms treated in each time period were categorized as "lower" and "higher" exposure, with the cut-off being the median number of rooms treated in control homes in each time period: before and during pregnancy, lower exposure was two rooms or less and since birth it was three rooms or less.

Immunophenotype and cytogenetic classification of the leukemia

We obtained information about immunophenotype and cytogenetic sub-types of participating cases from the medical record details provided by clinicians. The latter were determined using metaphase cytogenetics and fluorescence *in situ* hybridization screening.

Statistical analysis

Odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated using unconditional logistic regression in SPSS for Windows version 15, released September 2006 (SPSS, Chicago, IL.). All models were adjusted for the study matching factors—age at diagnosis, sex and State of residence. Variables considered *a priori* to be potential confounders of the association between painting and risk of ALL (ethnicity, maternal age at the child's birth, birth order, paternal smoking within 2 years of birth, family income and highest parental education) were assessed for inclusion in the models. Variables that met the criteria for the empirical definition of confounding (independently associated with both the exposure and the outcome) were included in the final models. The final models contained the matching factors, maternal age at the child's birth, birth order and parental education. The reference category for all the indoor painting analyses was "no indoor painting done in any time period"; for all the outdoor painting analyses, it was "no outdoor painting done in any time period"; and for floor treatments it was "no floor treatments done in any time period."

We also analyzed the data by immunophenotype and cytogenetic subtypes with more than 50 cases.

Results

We were notified of 568 incident cases of ALL, of whom 49 were ineligible to participate: 30 from non-English speaking backgrounds, 12 overseas visitors, three whose biological mother was unavailable and four who did not reach remission, leaving 519 eligible cases. Parents of 416 (80.2%) cases consented to participate in the study, and 389 families (75.0% of eligible) returned at least one of the parent questionnaires. Of these, 327 (84.1%) returned both mother and father questionnaires (see Table 1).

Of the 2,947 eligible control families identified through RDD, 2,071 (70.3%) agreed to take part. Because of age and sex frequency-matching quotas, we only recruited 1,361 of these families to the study. Of the recruited families, 876 (64.4%) returned at least one of the parent questionnaires and 744 (54.7%) returned both questionnaires (Table 1). Over 97% of case and control parents who returned the questionnaires did the telephone interviews.

The demographic characteristics of cases and controls who returned the written questionnaire were generally similar, with some exceptions (Table 1). Control parents were more likely than case parents to be tertiary educated, have a higher income and to have been aged 35 years or older when the child was born. Case children were more likely to be the first born child (47.8%) than controls (41.7%) and to have a birth defect (5.7% *vs.* 3.1%, respectively).

Exposure to painting inside the house

Overall, there was little evidence of an increased risk of childhood ALL associated with any painting inside the house in the year before pregnancy, during pregnancy, or after the child's birth (Table 2), including in any trimester during pregnancy (results not shown). Neither was there an apparent increase in risk if painting was done at any time from 1 year before the pregnancy to the censoring date (OR 1.13, 95% CI 0.86, 1.48) (Table 2). There was a suggestion that OR increased with the child's age at the censoring date in each period; however, no p-value for the interaction between exposure and age was <0.10 (results not tabulated). Furthermore, there was little evidence of an increased risk associated, with the mother painting before or during the pregnancy (OR

Table 1. Demographic characteristics of cases and controls

	Cases		Controls	
	n	%	*n*	%
Total available (any written questionnaire completed)	389		876	
Both parents	327	84.1	744	84.9
Sex				
Boys	214	55.0	462	52.7
Girls	175	45.0	414	47.3
Age[1]				
0–1	34	8.7	62	7.1
2–4	177	45.5	392	44.7
5–9	111	28.5	291	33.2
10–14	67	17.2	131	15.0
State of residence[2]				
NSW/ACT	120	30.8	270	30.8
QLD	69	17.7	183	20.9
SA/NT	43	11.1	84	9.6
VIC/TAS	117	30.1	246	28.1
WA	40	10.3	93	10.6
Birth order				
1	186	47.8	365	41.7
2	118	30.3	295	33.7
3+	85	21.9	216	24.7
Birth defect				
No	366	94.3	841	96.9
Yes	22	5.7	27	3.1
Child's birth year				
1988–1996	97	24.9	223	25.5
1997–2000	83	21.3	192	21.9
2001–2002	103	26.5	239	27.3
2003–2006	106	27.2	222	25.3
Highest education of either parent				
Non-Tertiary	223	57.3	409	46.7
Tertiary	166	42.7	467	53.3
Ethnicity[3]				
European ethnicity	279	71.7	650	74.2
At least 50% European	79	20.3	166	18.9
At least 50% non-European and unknown if 50% European	14	3.6	23	2.6
Indeterminate	17	4.4	37	4.2
Yearly household income				
<$20,000	28	7.2	51	5.8
$20,001–40,000	67	17.2	141	16.2
$40,001–70,000	113	29.0	287	32.8
$70,001–100,000	93	23.9	194	22.1
>$100,000	85	21.9	198	22.6
Mother's age at child's birth				
<25 years	60	15.4	99	11.3
25–34 years	263	67.6	580	66.2
35+ years	66	17.0	197	22.5
Father's age at child's birth				
<25 years	23	6.4	32	4.3
25–34 years	221	61.9	448	59.6
35+ years	113	31.7	272	36.2

[1]Age groups are based on the child's age at the censoring date. For cases, this was the date of diagnosis and for controls it was the date the questionnaire was returned. [2]Abbreviations: NSW: New South Wales; ACT: Australian Capital Territory; QLD: Queensland; SA: South Australia; NT: Northern Territory; VIC: Victoria; TAS: Tasmania; WA: Western Australia. [3]European: at least three European grandparents; 50% European: 2 European grandparents; At least 50% non-European and not known if 50% European: two non-European grandparents and ethnicity of other 2 grandparents unknown; Indeterminate: no 2 grandparents with the same ethnicity (*i.e.,* European or non-European) and 2+ grandparents of unknown ethnicity.

1.27, 95% CI 0.87, 1.85 and OR 1.27, 95% CI 0.86, 1.87, respectively), or with the father painting before the pregnancy (OR 0.97, 95% CI 0.71, 1.32) (results not shown in tables).

The ORs for any use of oil-based (+/− water-based) paint inside the home were: 1.45 (95% CI 0.98, 2.15) before pregnancy, 1.20 (95% CI 0.76, 1.61) during pregnancy and 1.32 (95% CI 0.89, 1.97) after birth (Table 2). The ORs for any use of paint stripper were elevated in all time periods (Table 2); and its use in any period was associated with an OR of 1.65 (95% CI 0.99, 2.76). The OR for "only someone other than the parents" painting inside the house in any period was 1.78 (95% CI 1.24, 2.57), and in the year before the pregnancy, it was 2.37 (95% CI 1.30, 4.30). If that person used any oil-based (+/− water-based) paints, the latter OR was 3.50 (95% CI 1.35, 9.03) (Table 2).

The OR for more than three rooms being painted during pregnancy was 1.68 (95% CI 1.01, 2.80), and the OR for three or fewer rooms being painted was 0.97 (95% CI 0.68, 1.39) (Table 3). If only someone other than the parents painted, having more than seven rooms painted over all time periods was associated with doubling of the risk, OR 2.19 (95% CI 1.28, 3.75); for those having seven rooms or fewer painted the OR was 1.61 (95% CI 1.05, 2.46, p-value for trend <0.001) (Table 3). No association was seen with the parents' bedroom being painted in the year before pregnancy (OR 1.15, 95% CI 0.82, 1.61), or during the pregnancy (OR 1.06, 95% CI 0.64, 1.76), or with the child's bedroom being painted since birth (OR 1.19, 95% CI 0.85, 1.69) (results not shown in tables).

There was some evidence of an increased risk associated with exposure to painting in all time periods among cases

Table 2. Odds ratios and 95% confidence intervals for risk of ALL with exposure to painting inside the home or floor treatments in relevant time periods

	Year before pregnancy		During pregnancy		After Birth		Any time period	
	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)
Any painting done								
No painting done inside the home (reference group)	108/261	1.00	108/261	1.00	108/261	1.00	108/261	1.00
Any painting done inside the home	179/418	1.08 (0.80, 1.45)	118/261	1.11 (0.80, 1.53)	189/433	1.08 (0.81, 1.45)	280/614	1.13 (0.86, 1.48)
Use of water-based paints only	102/276	0.93 (0.66, 1.30)	71/161	1.11 (0.76, 1.61)	107/262	1.02 (0.73, 1.41)	144/339	1.04 (0.77, 1.41)
Use of oil-based paint (+/− water-based)	68/120	1.45 (0.98, 2.15)	39/78	1.20 (0.76, 1.92)	70/148	1.32 (0.89, 1.97)	121/246	1.28 (0.92, 1.77)
Use of paint stripper	18/30	1.70 (0.87, 3.30)	10/17	1.57 (0.66, 3.70)	15/27	1.77 (0.85, 3.67)	35/59	1.65 (0.99, 2.76)
Painting done only by someone other than the parents								
Painting done inside the home	28/30	2.37 (1.30, 4.30)	20/30	1.58 (0.83, 2.99)	58/97	1.64 (1.08, 2.49)	91/135	1.78 (1.24, 2.57)
Use of water based paints	14/17	2.02 (0.91, 4.47)	5/14	2.23 (1.00, 4.99)	31/56	1.36 (0.81, 2.27)	50/72	1.74 (1.11, 2.71)
Use of oil based paint (+/− water)	12/10	3.50 (1.35, 9.03)	6/15	0.97 (0.35, 2.64)	23/37	2.07 (1.11, 3.83)	37/56	1.93 (1.17, 3.18)

[1]Adjusted for matching variables (age group, sex and State), birth order, highest parent education and maternal age at birth. [2]The reference groups are all those with no indoor house painting from 1 year before the pregnancy to the censoring date.
Abbreviations: OR: odds ratio; CI: confidence interval.

Table 3. Odd ratios and 95% confidence intervals for risk of ALL relating to the number of rooms painted or floors treated at different time periods

	Year before pregnancy		During pregnancy		After birth		Any time period	
	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)
Rooms painted in the home by anyone								
None (reference group)	108/261	1.00	108/261	1.00	108/261	1.00	108/261	1.00
Low	76/191	1.01 (0.71, 1.45)	76/186	0.97 (0.68, 1.39)	108/231	1.16 (0.84, 1.61)	137/289	1.17 (0.86, 1.59)
High[3]	94/201	1.17 (0.83, 1.66)	33/51	1.68 (1.01, 2.80)	70/179	0.97 (0.67, 1.42)	118/261	1.12 (0.81, 1.55)
p trend		0.37		0.13		0.99		0.49
Rooms painted in the home only by someone other than the parents								
None (reference group)	108/261	1.00	108/261	1.00	108/261	1.00	108/261	1.00
Low	8/11	1.60 (0.60, 4.28)	10/17	1.20 (0.52, 2.78)	28/44	1.71 (0.98, 2.98)	54/86	1.61 (1.05, 2.46)
High[3]	19/17	3.07 (1.46, 6.46)	10/13	2.23 (0.89, 5.62)	28/50	1.55 (0.89, 2.68)	33/42	2.19 (1.28, 3.75)
p trend		<0.001		0.10		0.05		<0.001

[1]Adjusted for matching variables (age group, sex and State), birth order, highest parent education and maternal age at birth. [2]The reference groups are all those with no indoor house painting from 1 year before the pregnancy to the censoring date. [3]The following definitions were used for high exposure for indoor painting: Any time period, more than seven rooms; before and during pregnancy, more than three rooms; and after birth, more than five rooms. Seven, three and five were the median numbers of rooms painted in each of these time periods, respectively.
Abbreviations: OR: odds ratio; CI: confidence interval.

Table 4. Odds ratios (OR) and 95% confidence intervals for risk of ALL with exposure to painting inside the home in relevant time periods by immunophenotype and cytogenetic subtype

		Year before birth		During pregnancy		After birth	
		Any painting done		Any painting done		Any painting done	
	Case n	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)
All cases	388	179/418	1.08 (0.80, 1.45)	118/261	1.11 (0.80, 1.53)	189/433	1.08 (0.81, 1.45)
Pre-B cell	345	161/418	1.16 (0.85, 1.59)	107/261	1.18 (0.84, 1.66)	170/433	1.17 (0.86, 1.60)
T cell	37	16/418	0.72 (0.32, 1.62)	9/261	0.74 (0.29, 1.87)	17/433	0.74 (0.33, 1.65)
Normal karyotype	132	56/418	0.93 (0.59, 1.45)	38/261	1.01 (0.61, 1.66)	43/433	0.82 (0.52, 1.29)
Any genetic feature	249	118/418	1.10 (0.78, 1.56)	77/261	1.12 (0.77, 1.65)	129/433	1.17 (0.83, 1.65)
Chromosomal deletions	62	29/418	1.31 (0.67, 2.54)	16/261	1.12 (0.53, 2.38)	35/433	1.44 (0.75, 2.75)
ETV6-Runx-1 t(12;21)	60	33/418	1.59 (0.81, 3.12)	21/261	1.47 (0.69, 3.13)	31/433	1.40 (0.71 2.76)
Hyperdiploidy	113	53/418	1.15 (0.69, 1.89)	37/261	1.18 (0.69, 2.02)	62/433	1.33 (0.82, 2.16)
Trisomy (or greater) of chromosome 21	66	31/418	1.00 (0.53, 1.86)	22/261	1.10 (0.57, 2.15)	34/433	1.05 (0.57, 1.92)

[1]Adjusted for matching variables (age group, sex and State), birth order, highest parent education and maternal age at birth. [2]The reference groups are all those with no painting in the time period.
Abbreviations: OR: odds ratio; CI: confidence interval.

Table 5. Odd ratios and 95% confidence intervals for risk of ALL in the offspring relating to whether the parents painted the outside of the house during relevant time periods

	Mother (+/− father or other)				Father (+/− mother or other)	
	Year before pregnancy		During the pregnancy		Year before pregnancy	
	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)	Exposed cases/ controls	OR[1,2] (95% CI)
No painting (reference group)	218/480	1.00	218/480	1.00	218/480	1.00
Any painting	18/36	1.08 (0.59, 1.98)	12/26	1.00 (0.49, 2.07)	93/217	0.97 (0.72, 1.31)
Use of water-based paints	9/27	0.64 (0.29, 1.41)	7/23	0.64 (0.27, 1.56)	48/143	0.77 (0.53, 1.12)
Use of oil-based paint (+/− water-based)	9/7	2.97 (1.06, 8.33)	5/3	4.05 (0.91, 17.92)	31/57	1.26 (0.78, 2.03)

[1]Adjusted for matching variables (age group, sex and State), birth order, highest parent education and maternal age at birth. [2]The reference groups are all those with no outdoor house painting from 1 year before the pregnancy to the censoring date.
Abbreviations: OR: odds ratio; CI: confidence interval.

with t(12;21) translocations (ETV6-Runx-1) (Table 4), although these estimates lacked precision.

Painting the outside of the house

Overall, there was no evidence of an increased risk of childhood ALL associated with the mother or father painting the outside of the house in the year before pregnancy, or with the mother doing so during the pregnancy (Table 5). However, the ORs for the mother using any oil-based (+/− water-based) paint on the outside of the house before or during the pregnancy were 2.97 (95% CI 1.06, 8.33) and 4.05 (95% CI 0.91, 17.92), respectively (Table 5). There was no evidence of a dose-response in any time period (results not shown).

Floor treatments

The OR for any floor treatments were 0.91 (95% CI 0.64, 1.30) in the year before the pregnancy, 0.89 (95% CI 0.53, 1.49) during the pregnancy and 0.92 (95% CI 0.67, 1.28) after birth (Results not tabulated). There were too few exposed subjects in our sample to analyze the data by the type of floor or treatment.

Discussion

We found weak evidence that having more than three rooms painted inside the house during the pregnancy was associated with an increased risk of childhood ALL. Risk also appeared to be increased in all time periods if the painting was only done by someone other than the parents or if oil-based

paints or paint stripper were used. The increased risk associated with the former was greater if more rooms were painted. There was some evidence that the mother's use of oil-based paint to paint the outside of the house in the year before or during the pregnancy was associated with an increased risk of ALL.

Five previous studies[3–5,7,8] have investigated the association between house painting and the risk of childhood ALL. Differences in definitions of exposure, time periods and the types of leukemia or sub-populations of cases studied do not allow direct comparison with our data (see Table 6). However, the results of four of these studies[3–5,7] are consistent with our study in suggesting a weak association between exposure to painting and the risk of childhood ALL, which does not appear to be specific to exposure in any particular time period. As only minimal details were published about the fifth study,[8] comparison was not possible.

Some studies have reported similar findings regarding the person who did the painting and the number of rooms painted. Scelo *et al.*[5] reported an increased risk of childhood ALL associated with use of paints, stains and lacquers by someone other than the parents, although this was not specific to house painting (Table 6). However, the prevalence of painting by someone other than the parents among cases (19%) and controls (13%) in that study was similar to Aus-ALL (cases 24%, controls 16%), so it seems likely that many of those exposures involved house painting. "Someone other than the parents" is likely to be a professional painter, in which case more rooms may have been painted. It may also be that the intensity of the exposure is higher, as a professional painter is likely to complete the task in a shorter time. It may also be that more paint was used or that the types of paints or products used in the cleanup were different from those used by parents; however, this level of detail was not available.

Freedman *et al.*[3] also quantified exposure in terms of rooms painted and investigated the same time period after birth, but a different period of prenatal exposure: "the year before birth" (Table 6). They reported an OR of 1.7 (95% CI 1.1, 2.7) in children whose mothers lived in homes in which more than four rooms were painted in the year before birth, similar to our OR of 1.68 (95% CI 1.01, 2.80) if more than three rooms were painted during pregnancy. Like us, they only found an increased risk with a higher level of exposure and not with "any" exposure in this time period.

Paternal occupational exposure to paints has been associated with an increased risk of leukemia,[12] and specifically ALL,[13] in the offspring, but the effect of maternal occupational exposure to paint is not known. This may be due in part to the low prevalence of maternal occupational exposure to paints; for example, in the United Kingdom Childhood Cancer Study, none of the 3,818 case mothers or 7,600 control mothers reported exposure to paint in the workplace.[14]

We found that indoor house painting in the year before pregnancy, during pregnancy or after birth appeared to increase the risk of the most common subtype of childhood ALL characterized by the t(12;21) (ETV6-Runx-1), although these findings are based on small numbers. Scelo and coworkers, also reported an increased risk associated with exposure to paints, stains or lacquers in this subtype.[5] Translocations of t(12;21) are thought to occur *in utero* as they have been detected in newborn blood samples.[15] Individuals who are susceptible to these translocations may also be more susceptible to DNA damage from environmental exposures such as paint at other critical time periods such as after birth.

To our knowledge, no previous studies have reported the type of paint used, whether paint stripper was used, or differentiated between inside and outside house painting. This has the advantage of providing more insight to what specific exposures, if any, are associated with an increased risk of childhood ALL. However, a potential pitfall is that requesting more detail may have increased the level of misclassification in Aus-ALL.

Paint is a generic name for a diverse range of products containing various pigments and compounds such as resins, binders, extenders and solvents.[16] There are two main categories of paint, based on the type of solvent they contain. About 75% of modern paints use water as the base and the rest are oil-based and contain solvents such as mineral spirits, toluene and xylene.[16] However, even many water-based paints release volatile organic compounds (VOC) into the atmosphere, albeit at lower levels than oil-based paints.[16] There is evidence that VOC levels in homes that have been painted remain elevated for at least a month after the painting has occurred, and the levels are also elevated in rooms other than those painted.[17] These findings suggest that painting inside the home may have an effect throughout the house and last well beyond the painting period. Because of this, it may be hard to pinpoint the critical time period for exposure. For example, if the painting was done just before the pregnancy, VOC or other levels of chemical residues may be elevated in the early weeks of pregnancy as well.

As well as the actual paint, more exposure to potentially hazardous solutions may occur through materials used to prepare the surface, *e.g.,* paint stripper, or in the cleaning up process. Paint strippers may contain methylene chloride, a powerful solvent, with potential short- and long-term health effects.[18]

If some substances, either in paint or associated materials, are carcinogenic, it is plausible that exposure to them in critical time periods could increase the risk of childhood ALL. We found some elevated ORs in the year before pregnancy, during the pregnancy and after the child's birth. It is plausible that parental exposure before pregnancy could damage reproductive cells. It is also plausible that fetal cells could be damaged by paint residues *in utero* or that exposure after birth could cause somatic cell changes.

One of the challenges when comparing studies of the association between childhood ALL and painting is that the VOC composition of paint has changed over time. Since

Table 6. Selected characteristics of studies that have investigated the association between painting and the risk of childhood leukemia

First author	Country	Definition of cases	Years of case ascertainment	Cases/ controls	Source of controls	Matching variables	Variables adjusted for	Reference group	Definition of exposure	Before pregnancy		During pregnancy		After birth	
										Definition	Results	Definition	Results	Definition	Results
Lowengart *et al.*[4]	United States	Acute leukemia	1980–1984	123/123	Friends/ random digit dialing	Age (within 3 years), sex and ethnicity	Matching variables	Those not exposed during pregnancy or while breastfeeding	Any use of paints, lacquer by the mother	NA	NA	During pregnancy and while breastfeeding			1.8 ($p = 0.03$)
Infante-Rivard *et al.*[8]	Canada	ALL	1980–2000	790/790	Family allowance files, provincial universal health insurance files	Age and sex	Not stated	Not stated	Exposure to any painting in the home	One year before pregnancy	"No association"	During pregnancy	"No association"	From birth until diagnosis	"No association"
Freedman *et al.*[3]	United States	ALL	1989–1993	640/640	Random digit dialing	Age (within 25%), telephone area code and race	Matching variables, sex, income, maternal education and painting in other time periods	No exposure in that time period	Exposure to any indoor house painting in the home	Three months before pregnancy and during pregnancy			1.2 (0.9, 1.5)	From birth until diagnosis	1.3 (1.0, 1.6)
Scelo *et al.*[5]	United States	ALL	1995–2005	550/737	Birth certificates	Date of birth, sex, Hispanic ethnicity and maternal race	Matching variables, income, domestic exposure to solvents	No exposure in that time period	Exposure to any paints, stains, or lacquers in the home	Three months before pregnancy	1.10 (0.71, 1.69)	During pregnancy	1.21 (0.88, 1.67)	From birth until third birthday (or until diagnosis if diagnosed before third birthday)	1.39 (1.07, 1.81)
Alderton *et al.*[7]	United States	Down Syndrome with ALL	1997–2002	97/173	Doctors' practice lists	Age group	All: age, sex and mother's education. If estimate changed by >10% smoking during pregnancy, race, maternal age at delivery and gestational age	No exposure in that time period	Exposure to any paints, stains, or lacquers in the home	One month before pregnancy and during pregnancy			1.10 (0.65, 1.86)	From birth to 6 months before diagnosis	1.16 (0.65, 2.08)
Bailey (this study)	Australia	ALL	2003–2006	389/876	Random digit dialing	Age, sex and State of residence	Matching variables, maternal age, birth order and highest parental education	Those not exposed to indoor painting in any time period.	Exposure to any indoor house painting in the home.	One year before pregnancy	1.08 (0.80, 1.45)	During pregnancy	1.11 (0.80, 1.53)	From birth until diagnosis	1.08 (0.81, 1.45)

the mid 1990s, there has been a reduction in the VOC content in paints in the United States,[19] United Kingdom[20] and Australia.[21] Of the three previous studies that found evidence of association,[3–5] two had recruited cases before these changes were introduced[3,4] (see Table 6), whereas one[5] recruited over the time period in which VOCs were being reduced. In our study, about 75% of all participants were born after VOCs in paints were reduced, which may explain why our estimates of effect for any painting are generally lower than these other studies.

We investigated whether floor treatments were associated with risk of ALL, as many of the products used for treating wood floors—such as lacquers and varnishes—are "surface coatings" like paint and can contain similar compounds. Products used on other hard floor types include sealants, which may contain glues and solvents such as xylene and toluene. Shu and coworkers found some evidence of an increased risk of ALL associated with maternal occupational exposure to both solvents and glues before and during pregnancy.[22] We did not find any evidence associated with floor treatments. However, the categories we used for product types were very broad as we did not collect information that would allow us to classify treatments into those involving solvents or not.

Aus-ALL had strengths and limitations. Cases were ascertained from oncology centers that treat virtually all children with ALL in Australia and 75% of parents of eligible cases consented to participate in Aus-ALL; 70% of eligible controls recruited by RDD also agreed to participate. However, 64% of participating control parents returned the questionnaires compared with 93% of participating case parents, raising the possibility of selection bias. We had information on parental education for all participants, and on household income for all but three cases and four controls. Control parents were more likely than case parents to have a tertiary education and a higher household income. Using area-based measures, we have also shown that control parents were of higher SES than the general Australian population.[11] Among controls, homes of families with higher parental education and income were more likely to have been painted, by the parents or by someone else, and to have had more rooms painted. Therefore, participation bias in the controls may have made their prevalence of house painting higher than in the general population and thus biased ORs downward. We sought to control this bias by inclusion of parental education in our analytical models, but there could be some persisting underestimation of ORs for ALL with house painting.

Use of oil-based (with or without water-based) paint or paint stripper was defined as any use of these products in the time period of interest. We found that 42% of controls who painted used some oil-based paints, which seems high given it is estimated that only about 25% of modern paints are oil-based.[16] Therefore, as most people who reported the use of oil-based paint also reported use of water-based paint, it may be that the amount of oil-based paint was small in many cases, so we may have underestimated the effect of using oil-based paint.

Another source of misclassification could have been our indicator of dose, which was the number of rooms painted in each time period. This measure does not take into account the size of the rooms or the quantity of paint used as we thought it unlikely that parents would be able to report these factors reliably.

For controls, the censoring date was the date the questionnaire was returned, whereas for cases it was the date of diagnosis. Controls were frequency matched by age to cases, but they had the opportunity to accrue exposures for the time period between study recruitment and return of the questionnaire as the questionnaire asked about exposures "since your child was born," as cases were asked about exposures until diagnosis. The median time between control recruitment and return of the questionnaire was 44 days (inter-quartile range 42.5). It is unlikely that this short time would have had a significant impact on whether a child was exposed.

As with most case-control studies there was the potential for recall bias. We attempted to minimize this using standardized written questionnaires and structured telephone interviews, with the interviewer blinded to case-control status. Nonetheless, using these methods would not remove the potential for case parents to think more deeply about past exposures, and therefore to report them more frequently. However, there is no clear reason why recall of paint type should be different for cases and controls. Nor would one expect to see bias operating specifically in relation to painting done by someone other than the parents; if anything, these exposures ought to be recalled more easily and therefore be less prone to bias.

Some of our findings, such as the risk associated with someone other than the parents painting with oil-based (+/− water-based) paint, were based on small numbers so the estimates are imprecise. We also had missing values for a number of variables, mainly when the father was not interviewed and the mother did not know the details. However, these were generally similarly distributed across cases and controls and comparatively few: less than 40 missing values for individual exposure periods and less than 90 for all exposure periods. Because we made multiple comparisons, some of our positive findings may be due to chance.

In conclusion, we found some evidence of an increased risk of ALL associated with house painting under certain conditions: when more than three rooms were painted during the pregnancy; when oil-based paints or paint stripper were used indoors; when someone other than the parents painted indoors; and when the mother painted the outside of the house with oil-based paint before or during the pregnancy. Our findings of an increased risk when painting was done inside the house by someone other than the parents could be related to the amount of paint used or the intensity of the

exposure. The analysis of pooled data from international collaborations will increase our power to elucidate putative associations. Such analyzes are planned in the Childhood Leukemia International Consortium (see http://clic.berkeley.edu).

Acknowledgements

Helen Bailey was supported by NHMRC Post Graduate Scholarship, Elizabeth Milne by NHMRC Career Development Award and Lin Fritschi by NHMRC Fellowship.

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