Published in final edited form as:
Occup Environ Med. 2009 August ; 66(8): 557–560. doi:10.1136/oem.2008.040386.

Degreasing and risk of non-Hodgkin lymphoma

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Abstract

Objective—To investigate the relationship between selected solvent-related workplace tasks (degreasing, painting, gluing, stripping paint, staining) and risk of non-Hodgkin lymphoma (NHL).

Methods—We analyzed occupational data from a large population-based case-control study of NHL conducted in the United States. For participants reporting occupations with possible exposure to organic solvents, job-specific interview modules were administered to elicit in-depth information on solvent-related workplace tasks and other exposure-related factors (225 cases, 189 controls). Unconditional logistic regression models were fit to calculate odds ratios (OR) and 95% confidence intervals (CI) for average frequency, maximal frequency and cumulative number of hours having performed each task. Individuals with jobs rated as unexposed to organic solvents in the workplace (180 cases, 213 controls) were used as a reference group.

Results—We observed an increased risk of NHL among subjects in the highest category of maximal degreasing frequency (>520 hours/year: OR 2.1, 95% CI 0.9-4.9, trend test p=0.02). We found similar associations for the highest levels of average frequency and, among men, cumulative number of hours. Other solvent-related tasks were not associated with NHL.

Conclusion—Findings from this case-control analysis of solvent-related tasks suggest that frequent degreasing work may be associated with an elevated risk of NHL.

Keywords

non-Hodgkin lymphoma; solvents; case-control studies; degreasing

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COMPETING INTERESTS
The authors have no competing interests to declare.

INTRODUCTION

Several epidemiologic findings suggest that occupational exposure to organic solvents may be associated with an increased risk of non-Hodgkin lymphoma, but results are not conclusive.[1] Workers use solvents in a variety of work-related tasks (*e.g.*, degreasing, painting, gluing) likely to involve different levels of exposure to many different types of chemicals, so exposure assessment is challenging. Many past studies have not collected data in sufficient detail to permit investigations of specific solvent-related tasks. Consideration of such specific circumstances of exposure can provide important insight as to whether organic solvents influence lymphomagenesis. In a large population-based case-control study of NHL, we collected extensive information related to solvent exposure, including a detailed interview of subjects who reported jobs that typically involve solvent use. We used this detailed exposure data to investigate the relationship between risk of NHL and selected solvent-related workplace tasks, including degreasing, painting, gluing, stripping paint and staining.

METHODS

The NCI-SEER case-control study of NHL has been described previously.[2] In brief, between July 1998 and June 2000, subjects were enrolled from 4 US SEER registry areas: the state of Iowa, Los Angeles County, and the Seattle and Detroit metropolitan areas. Eligible cases were individuals 20-74 years old with incident NHL according to the International Classification of Diseases for Oncology, Second Edition. Cases of multiple myeloma and chronic lymphocytic leukemia (CLL) were not recruited for this study. Twenty-eight recruited cases of small lymphocytic lymphoma were later identified by pathology review to be CLL; however, because the two diagnoses comprise the same disease and differ only by initial presentation, we retained these CLL cases in the study. Controls were selected from the general population in the 4 registry areas, stratified on the basis of age (5-year intervals), sex and race to match the distribution in the cases. The study was approved by the institutional review boards at the NCI and the participating institutions, and study participants provided informed consent. Among all eligible subjects who we were able to locate, 1,321 case patients (76%) and 1,057 control subjects (52%) participated in the study.

Participants were mailed a residential and occupational history calendar. During the subsequent home visit, a trained interviewer administered a computer-assisted personal interview (CAPI) covering a wide variety of topics, including occupational history. The occupational portion of the questionnaire gathered general information on each job held by the subjects for 12 months or longer. In addition, for 32 selected occupations, job-specific modules developed by an industrial hygienist (P.S.) were administered to elicit more in-depth information on workplace tasks, exposures, and other exposure-related factors. The job modules were incorporated into the CAPI approximately one year into the interview phase of data collection.

In our analysis, we investigated five common solvent-related tasks that were assessed in multiple modules: degreasing, painting, stripping paint, staining, and gluing. Among subjects who were administered one or more job module (225 cases, 189 controls), data from the modules were combined to calculate three measures of exposure for each solvent-related task: the *average frequency* (calculated as the weighted average, across all modules, of the reported number of hours per year performing a particular task, weighted by the number of years worked at each corresponding job), the *maximal frequency* (the highest reported number of hours per year spent performing that task across all modules) and the *cumulative number of hours* (the sum, across all modules, of the product of the module-

specific hours per year performed a task and the number of years worked at the corresponding job). Each measure was grouped into exposure categories using the quintiles among controls as cut-points. To enable investigation of relative risk across a wider range of exposure, we subdivided the upper-most exposure category in some analyses using the intra-category median among controls as the cut-point.

Using SAS (Version 9) software, we calculated odds ratios (ORs) and 95% confidence intervals (CIs) describing the association between solvent-related tasks and NHL risk using unconditional logistic regression modeling. The reference group consisted of all study participants whose jobs did not result in administration of a solvent-related job module and who were determined to have probably been unexposed to organic solvents in the workplace, following a review of occupational history by an industrial hygienist (P.S.; 180 cases, 213 controls). This reference group includes individuals assessed as having been unexposed to solvents in the workplace who were interviewed prior to the incorporation of job modules into the CAPI (105 cases, 72 controls). Additional analyses with these subjects excluded from the reference group yielded virtually identical findings (findings not shown). Tests for trend were performed by modeling the exposure category medians among exposed subjects as a quantitative score. All regression models were fit adjusting for age (<45, 45-64, 65+), sex, race (White, Other/Unknown), education level (<12 years, 12-15 years, 16+ years) and study site (Detroit, Iowa, Los Angeles, Seattle). In addition to analyses of all subjects, we performed separate analyses for men and women, and analyses restricted to job module respondents (to enable the simultaneous adjustment of all solvent-related tasks in regression modeling). We also performed analyses assuming exposure effect latency periods of 5, 10, 15 and 20 years.

RESULTS

The case and control subjects included in our study of solvent-related tasks were found to be comparable with respect to their distributions by age, sex, SEER site, education level and race/ethnicity (findings not shown). The average frequency of degreasing among participants was low; the median hours per year spent degreasing among controls and cases was 12 (inter-quartile range 0-108) and 13.5 (0-173), respectively (Wilcoxon rank sum test: p=0.77). The amount of degreasing reported among controls varied widely among and within job modules. The highest median levels were found in the modules pertaining to mechanics (median 55 hours/year, inter-quartile range 10-156 hours/year), industrial machinery mechanics (32, 2-169 hours/year), aircraft mechanics (26, 2-52 hours/year), gas station attendants (9, 0-173 hours/year), and a general solvents module administered when it was not clear whether a particular module should be asked (4, 0-87 hours/year). Of the subjects who degreased, 88% reported using chemicals kept at room temperature.

Odds ratios describing the association between degreasing and NHL risk are summarized in Table 1. The typical degreasing frequency did not significantly differ between cases and controls in our study population, but a two-fold increase in risk of NHL was observed among subjects in the highest categories of average frequency (>478 hours/year) and maximal frequency (>520 hours/year), relative to individuals unexposed to organic solvents. Analyses of cumulative hours spent degreasing were null. Tests for trend were statistically significant for average frequency (p=0.01) and maximal frequency (p=0.02) but not for cumulative number of hours (p=0.18).

When the analysis was restricted to men, the associations with the highest levels of average and maximal degreasing frequency were slightly stronger (>478 hours/year of average frequency, OR 2.8, 95% CI 0.7-10.6; >520 hours/year of maximal frequency, OR 3.0, 95% CI 0.9-9.6), and evidence of an association with high cumulative number of hours spent

degreasing was observed (>2860 hours vs. unexposed: OR 1.9, 95% CI 0.9-4.3; trend test p=0.04). Risk estimates for women were highly unstable due to sparse data.

Our findings for degreasing did not materially change when we focused our analyses on degreasing performed using chemicals kept at room temperature (findings not shown). We also observed similar findings in analyses incorporating latency periods of 5, 10 and 15 years, although analyses assuming a latency period of 20 years yielded weak, inconsistent evidence of association (findings not shown).

The other solvent-related tasks that were assessed (painting, stripping paint, gluing, staining) were not found to be associated with NHL in our study population (findings not shown). When we modeled all five solvent-related tasks simultaneously in analyses restricted to job module respondents, associations with degreasing still remained (average frequency, p_{trend}=0.02; maximal frequency, p_{trend}=0.04; cumulative hours, p_{trend}=0.26).

DISCUSSION

Findings from this case-control analysis of solvent-related tasks suggest that degreasing work, if performed very frequently, may be associated with an elevated risk of NHL. The majority of degreasing reported by participants involved the use of chemicals kept at room temperature. Thus, the use in our study population of chlorinated solvents such as trichloroethylene (TCE) and tetrachloroethylene (PCE), which are typically heated for use in vapor degreasing applications, was low. Other solvent-related tasks were not associated with NHL in our study.

To our knowledge, this is the first report of degreasing work *per se* as a risk factor for NHL. Exposure to TCE and PCE have been linked to NHL risk in some cohort studies of highly-exposed industries, although the totality of evidence is equivocal.[3] Increased risk of NHL among aircraft and agricultural mechanics, who may perform degreasing tasks comparatively often, have also been observed in a few case-control investigations,[4,5] although several other case-control studies have not identified risk excesses in these occupations.[6-10] However, most job-based analyses have been limited in their ability to detect excess risks by the inherent assumption that workers in the same job/industry experience similar workplace exposures.[11,12] As our study demonstrates, degreasing work varies considerably among mechanics and other relevant jobs. The failure of job-based analyses to account for such variation would result in exposure misclassification and would likely bias of relative risk estimates towards the null. The availability of self-reported data regarding degreasing and other solvent-related tasks is thus an important strength of our study.

This study also has limitations, most notably the fact that the number of subjects in our study highly exposed to solvent-related tasks was small. One consequence of this is the possibility that the observed associations with heavy degreasing work, which were of borderline statistical significance, may have arisen due to chance. The other limitation of our small sample size is that we had limited statistical power to detect weak associations; consequently, we cannot rule out the possible existence of modest associations with NHL for the other solvent-related tasks found to be null in our study. We cannot rule out selection bias as an explanation for our findings, as the participation rate among controls was comparatively low (52%), although we previously estimated demographic and socioeconomic differences between control participants and nonparticipants to be generally minor [13]. Some relevant jobs did not trigger modules; this was due to multiple factors, the most prevalent of which were a 20-minute time limit on the occupational section of the interview and the incorporation of modules into the interview approximately one year after

beginning interviews. It seems unlikely that selection bias accounts for our findings, however, as it is improbable that study participation and module data missingness differ between controls and cases in an exposure-dependent manner.

In conclusion, this study suggests that holding jobs that involve frequent degreasing work may be associated with an increased risk of developing NHL. Additional studies are needed to clarify whether degreasing and specific degreasing agents clearly influence lymphomagenesis. For such studies to be informative, it is essential that they incorporate the collection of exposure data specific to individuals, such as from a module-based interview approach or the use of personal monitoring instruments.

MAIN MESSAGE

Occupations involving frequent degreasing work may be associated with an increased risk of non-Hodgkin lymphoma (NHL).

POLICY IMPLICATIONS

Our understanding of the relationship between degreasing work and NHL risk remains limited. Additional studies are needed, preferably incorporating more detailed exposure assessment methods (e.g., module-based interviews or the use of personal monitoring instruments) than have been typically used in past investigations.

Acknowledgments

FUNDING

This research was supported in part by the Intramural Research Program of the National Institutes of Health (National Cancer Institute) and by National Cancer Institute SEER Contracts N01-PC-65064 (Detroit), N01-PC-67009 (Seattle), N01-CN-67008 (Iowa) and N01-CN-67010 (Los Angeles).

REFERENCES

1. Hartge, P.; Wang, SS.; Bracci, PM., et al. Non-Hodgkin Lymphoma.. In: Schottenfeld, D.; Fraumeni, JF., editors. Cancer Epidemiology and Prevention. Oxford University Press; New York: 2006. p. 898-918.
2. Engels EA, Chatterjee N, Cerhan JR, et al. Hepatitis C virus infection and non-Hodgkin lymphoma: results of the NCI-SEER multi-center case-control study. Int J Cancer 2004;111(1):76–80. [PubMed: 15185346]
3. Mandel JH, Kelsh MA, Mink PJ, et al. Occupational trichloroethylene exposure and non-Hodgkin's lymphoma: a meta-analysis and review. Occup Environ Med 2006;63(9):597–607. [PubMed: 16644896]
4. Figgs LW, Dosemeci M, Blair A. United States non-Hodgkin's lymphoma surveillance by occupation 1984-1989: a twenty-four state death certificate study. Am J Ind Med 1995;27(6):817–35. [PubMed: 7645576]
5. Dryver E, Brandt L, Kauppinen T, et al. Occupational exposures and non-Hodgkin's lymphoma in Southern Sweden. Int J Occup Environ Health 2004;10(1):13–21. [PubMed: 15070021]
6. Blair A, Linos A, Stewart PA, et al. Evaluation of risks for non-Hodgkin's lymphoma by occupation and industry exposures from a case-control study. Am J Ind Med 1993;23(2):301–12. [PubMed: 8427258]
7. Fritschi L, Siemiatycki J. Lymphoma, myeloma and occupation: results of a case-control study. Int J Cancer 1996;67(4):498–503. [PubMed: 8759607]
8. Zheng T, Blair A, Zhang Y, et al. Occupation and risk of non-Hodgkin's lymphoma and chronic lymphocytic leukemia. J Occup Environ Med 2002;44(5):469–74. [PubMed: 12024692]

9. Mester B, Nieters A, Deeg E, et al. Occupation and malignant lymphoma: a population based case control study in Germany. Occup Environ Med 2006;63(1):17–26. [PubMed: 16361401]

10. Schenk M, Purdue MP, Colt JS, et al. Occupation / industry and risk of non-Hodgkin lymphoma in the United States. Occup Environ Med. 2007

11. Stewart PA, Stewart WF, Siemiatycki J, et al. Questionnaires for collecting detailed occupational information for community-based case control studies. Am Ind Hyg Assoc J 1998;59(1):39–44. [PubMed: 9438334]

12. Teschke K, Olshan AF, Daniels JL, et al. Occupational exposure assessment in case-control studies: opportunities for improvement. Occup Environ Med 2002;59(9):575–93. [PubMed: 12205230]

13. Shen M, Cozen W, Huang L, et al. Census and geographic differences between respondents and nonrespondents in a case-control study of non-Hodgkin lymphoma. Am J Epidemiol 2008;167(3): 350–61. [PubMed: 17989060]

Table 1

Relative risks of non-Hodgkin lymphoma in relation to average frequency, maximal frequency and lifetime cumulative hours performing degreasing tasks in the workplace

	All subjects[1]		Men only	
	N_{Co}/ N_{Ca}	OR[2] (95% CI)	N_{Co}/ N_{Ca}	OR (95% CI)
No module administered; assessed by IH as unexposed to solvents	180 / 213	1.0	103 / 112	1.0
Module(s) that do not ask about degreasing administered	45 / 53	1.0 (0.6-1.6)	23 / 32	1.3 (0.7-2.5)
Module(s) that ask about degreasing administered	144 / 172	1.0 (0.7-1.3)	115 / 135	1.1 (0.6-1.5)
Average degreasing frequency across modules (hours/year)				
0	53 / 71	1.1 (0.7-1.7)	39 / 50	1.1 (0.7-1.8)
1-9	20 / 13	0.5 (0.2-1.1)	18 / 10	0.3 (0.1-0.9)
10-26	17 / 18	0.8 (0.4-1.7)	13 / 17	1.1 (0.5-2.6)
27-80	18 / 18	0.7 (0.4-1.5)	17 / 17	0.6 (0.3-1.4)
81-259	22 / 21	0.7 (0.4-1.5)	20 / 18	0.7 (0.3-1.6)
>259	14 / 31	1.7 (0.9-3.4)	8 / 23	2.0 (0.8-5.0)
260-478	7 / 13	1.3 (0.5-3.5)	5 / 11	1.8 (0.6-5.7)
>478	7 / 18	2.1 (0.8-5.2)	3 / 12	2.8 (0.7-10.6)
		P_{trend} = 0.01		P_{trend} = 0.02
Maximal degreasing frequency across modules (hours/year)				
0	53 / 71	1.1 (0.7-1.7)	39 / 50	1.1 (0.6-1.8)
1-12	19 / 13	0.5 (0.2-1.1)	17 / 10	0.5 (0.2-1.1)
13-35	18 / 17	0.7 (0.4-1.5)	14 / 16	1.1 (0.5-2.2)
36-130	21 / 22	0.8 (0.4-1.5)	19 / 21	0.9 (0.4-1.8)
130-20	16 / 12	0.6 (0.3-1.3)	16 / 9	0.5 (0.2-1.1)
>260	17 / 37	1.7 (0.9-3.2)	10 / 29	2.3 (1.0-5.3)
260-520	9 / 16	1.4 (0.6-3.3)	6 / 13	1.9 (0.6-5.4)
>520	8 / 21	2.1 (0.9-4.9)	4 / 16	3.0 (0.9-9.6)
		P_{trend} = 0.02		P_{trend} = 0.06
Cumulative number of hours spent degreasing				
0	53 / 71	1.1 (0.7-1.7)	39 / 50	1.1 (0.6-1.9)
1-70	19 / 15	0.6 (0.3-1.3)	17 / 12	0.6 (0.3-1.4)
70-216	18 / 13	0.6 (0.3-1.2)	15 / 12	0.6 (0.3-1.5)
217-694	18 / 22	0.9 (0.5-1.9)	16 / 19	1.0 (0.5-2.2)
695-2860	18 / 22	0.9 (0.4-1.7)	16 / 17	0.7 (0.3-1.6)
>2860	18 / 29	1.4 (0.7-2.7)	12 / 25	1.9 (0.9-4.3)
2861-7817	9 / 19	1.8 (0.8-4.3)	8 / 15	1.8 (0.6-5.4)
>7817	9 / 10	1.0 (0.4-2.5)	4 / 10	2.2 (0.6-7.6)
		P_{trend} = 0.18		P_{trend} = 0.04

Abbreviations: Co, controls; Ca, cases; OR, odds ratio; CI, confidence interval; IH, industrial hygienist.

[1] We restricted our analyses to study participants administered a job module during interview (189 cases, 225 controls) and to subjects who were not administered a job module but were assessed by industrial hygienist as probably unexposed to organic solvents in the workplace (180 cases, 213 controls). The remaining study participants (952 cases, 619 controls) were excluded from our analyses due to uncertainty regarding their potential exposure to organic solvents in the workplace.

[2]Odds ratios adjusted for age, sex, study center, ethnicity and education level.