Occupational Exposures and Non-Hodgkin's Lymphoma in Southern Sweden

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In a case-control study based on 859 consecutive non-Hodgkin's lymphoma (NHL) cases identified through a tumor registry between 1990 and 1998, the authors collected demographic, occupational, exposure, and education information. Exposures were identified through self-report, reported occupational history, and the use of a job-exposure matrix. Conditional logistic regression analyses of the 859 cases and 1,310 controls showed increased risks in workers exposed to gasoline (odds ratio [OR] 1.46; 95% confidence interval [CI] 1.04, 2.05), aliphatic or alicyclic hydrocarbons (OR 1.75; CI 1.03, 2.99), aromatic hydrocarbons (OR 1.45; CI 1.13, 1.86), and solvents for more than five years (OR 1.59; CI 1.11, 2.28), as well as automobile mechanics (OR 1.82; CI 1.18, 2.81) and painters (OR 1.77; CI 1.13, 2.76). Exposures to pesticides and farming were not associated with increased risk. Prior radiotherapy was associated with increased risk (OR 2.84; CI 1.85, 4.37). Concordance between analyses based on self-reported exposures, occupations, and the job-exposure matrix supported the links between organic solvents and prior radiotherapy and NHL but did not support associations between farming or pesticides and NHL. *Key words*: lymphoma, non-Hodgkin's; occupational exposure; risk factors; solvents; hydrocarbons; pesticides; radiotherapy.

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The incidence of non-Hodgkin's lymphoma (NHL), a heterogeneous group of lymphoproliferative neoplasms, has been increasing in virtually all world registries with adequate numbers of cases over the past 50 years.[1–5] In the United States, for example, the age-standardized incidence among white men was 6.9 per 100,000 person-years in 1947–1950 and 17.4 in 1984–1988[6] and the trend continues.[7] 53,400 new cases of NHL and 23,400 deaths from NHL are expected in the United States for 2003.[8] In Sweden, NHL is the second fastest growing cancer.[9]

The increasing incidence of NHL has placed a premium on the identification of causative risk factors for NHL. Numerous studies have investigated the interactions between immunologic factors and oncogenic viruses, in particular the Ebstein–Barr virus, in the etiology of NHL.[10] Other studies have focussed on occupational and environmental exposures and have implicated a variety of substances (e.g., solvents, pesticides) and occupations (e.g., farmers, meat handlers), but have often yielded conflicting results. Most case–control studies have focussed on a certain reported exposure (e.g., to phenoxy herbicides) or occupation (e.g., veterinarian) without cross-referencing data from both reported exposures and occupations (e.g., exposure to oil products and automobile mechanic). Furthermore, most of the significant odds ratios have been in the range of 1.5 to 3, and the impacts of these exposures combined with those of immunologic and infectious lymphoma risk factors do not explain the increased incidence of NHL, even when misclassifications, improved diagnosis, and the acquired immunodeficiency syndrome (AIDS) epidemic are taken into account.[6,11,12]

Over the past decade we obtained demographic, occupational, exposure, and education information from a large number of patients with NHL identified through the comprehensive South Swedish Regional Tumor Registry, as well as from gender-, age- and parish-matched controls. The resulting database has allowed us to re-examine the relationships between putative occupational and non-occupational exposures and NHL, to cross-reference the impacts of exposure and occupation, and to search for unidentified risk factors for NHL.

POPULATION AND METHODS

Using the South Swedish Regional Tumor Registry, 1,414 consecutive cases of pathology-confirmed NHL occurring in patients who were over 18 years of age at diagnosis were identified between 1990 and 1998. The diagnoses are usually reconfirmed at the pathology department of Lund University before the patients undergo therapy. The diagnostic codes were 200 and 202 according to the International Classification of Diseases, Injuries, and Causes of Death, seventh revision (ICD 7).[13] The primary physicians of these patients were

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contacted first; 119 recommended against their patients' participation in the study, while 46 failed to respond. With the consent of the remaining physicians, standardized questionnaires were mailed to 1,249 lymphoma patients. Of these, 925 (74%) returned completed questionnaires, while 219 refused to participate in the study. The remaining 105 patients were either dead (n = 85), misclassified (n = 14), or unreachable (n = 6).

Gender-, age- and parish-matched individuals were concurrently identified using the Swedish unique-person identification number and sent the same questionnaires. Most parishes in Southern Sweden consist of fewer than 3,000 inhabitants (Dr. Olsson, personal communication). The goal was to obtain information from two matched individuals for each NHL case. A total of 2,820 matched-individuals were sent questionnaires; 1,943 (69%) returned completed questionnaires. Based on information from the 2,868 individuals from whom we obtained questionnaires, we excluded lymphoma patients when matched control information was lacking (n = 66) and controls when the case information was lacking (n = 622). While the matching process strove to select controls with the same age as the cases, the ages of 11 controls differed from the ages of their associated cases by more than three years, and these controls were excluded. The remaining 2,169 individuals consisted of 859 cases and 1,310 controls.

The questionnaire requested information regarding demographics, education, and smoking, as well as occupations and exposures. It inquired specifically whether the respondent had ever been employed in the following 25 occupations: textile industry, oil industry, chemical industry, rubber industry, dye industry, mining, printing, farming, battery manufacturing, automobile mechanic, gas station attendant, film manufacturing, silver plating, plumber, painter, varnishing, welding, ship building, furniture industry, stonemasonry, car manufacturing, smithwork, gardening, forestry, and professional fishing. In additional, respondents were prompted to list all of their occupations (up to 8); these lists of occupations were used to generate the job-exposure matrix variables (see below). All occupations were coded according to the Nordic Occupational Classification.[14] The questionnaire further inquired about 16 specific exposures (nickel, asbestos, solvents, gasoline, other oil products, woodproofing, insecticides or pesticides, herbicides, herbicides against brushwood, herbicides against weeds, dye, fertilizers, cadmium, zinc, welding smoke, and radiation or radioactivity) and the lengths of time exposed. Respondents were also asked which animals they were or had been exposed to at home and which animals (including farm animals) they had been exposed to outside the home. When only one box was provided in the questionnaire to answer a binary question, the absence of a check mark was interpreted as a negative answer.

We generated 11 additional exposure variables using FINJEM, a job-exposure matrix[15]: 1) occupational inhalatory exposures to aliphatic hydrocarbon solvents (white spirit, solvent naphtha, hexane, etc.), alicyclic hydrocarbon solvents (turpentine), or gasoline; 2) occupational inhalatory exposures to aromatic hydrocarbon solvents (benzene, toluene, xylene, styrene, etc); 3) occupational, inhalatory exposures to aliphatic chlorinated hydrocarbon solvents (trichloroethanes, trichloroethylene, perchloroethylene, chloroform, methylene chloride, etc.); 4) occupational inhalatory exposures to organic solvents other than those defined in the three previous variables (e.g., alcohols, ketones, esters, glycol ethers, etc.); 5) occupational inhalatory exposures to particulate or volatile polycyclic aromatic hydrocarbon (PAH) compounds, including 2-ring PAHs (naphthalene), 3-ring PAHs (phenanthrene, anthracene, carbazole, fluorene), and 4-n-ring PAHs (e.g., pyrene, benzo(a)pyrene, chrysene, benzo(ghi)perylene); 6) occupational inhalatory exposures to diesel engine exhaust, including exposures to nitrogen dioxide (NO_2), other nitrous oxides (NO_X), carbon monoxide (CO), volatile and semivolatile hydrocarbons, inorganic and organic lead compounds, and particulate PAHs; 7) occupational inhalatory exposures to engine exhaust from leaded or unleaded gasoline, including exposures to carbon monoxide (CO), nitrogen dioxide (NO_2), other nitrous oxides (NO_X), volatile and semivolatile hydrocarbons, inorganic and organic lead compounds; 8) occupational inhalatory or dermal exposures to pesticides (including fungicides, herbicides, and insecticides); 9) occupational inhalatory exposures to dust from living animals (cows, horses, cats, dogs, reindeer, etc.), or hairs of animals (raw wool, furs of minks, foxes, etc.); 10) exposures to ionizing radiation; 11) exposured to low-frequency magnetic fields.

FINJEM links occupations with exposures during three separate time periods and includes information about the mean level of exposure and probability of exposure. We used FINJEM's 1960–1984 time period. We estimated group exposure for each occupation by multiplying the proportion of individuals in a given profession exposed to a given agent by the mean level of exposure. Exposure level units were parts per mil (ppm) for the solvents, micrograms per cubic meter ($\mu g/m^3$) for polycyclic aromatic hydrocarbons, milligrams per cubic meter (mg/m^3) for engine exhaust and exposure to animal-borne dusts, milli Sivert (mSv) for ionizing radiation, and micro Tesla (μT) for exposure to low frequency magnetic fields. FINJEM utilizes a numerical index for pesticide exposure. A lower group exposure threshold of 0.01 units was used for all variables. For most exposures, (e.g., exposure to aromatic hydrocarbons) we also generated additional variables corresponding to increasing group exposure levels in order determine whether a higher degree of exposure correlated with an increased risk of NHL.

TABLE 1. Case and Control Demographics, South Sweden non-Hodgkin's Lymphoma, 1990–1998

	Cases and Controls		Cases	Controls
Individuals	2,169	(100%)	859	1,310
Men	1,214	(56%)	478	736
Age				
Mean, men and women	61.9 years		62.0 years	61.8 years
Mean, men	61.8 years		61.7 years	61.9 years
Mean, women	62.0 years		62.4 years	61.7 years
< 40 years	150	(6.9%)	59	91
40–49 years	171	(7.9%)	66	105
50–59 years	449	(20.7%)	177	272
60–69 years	664	(30.6%)	263	401
70–80 years	722	(33.3%)	288	434
> 80 years	13	(0.6%)	6	7

Conditional logistic regression analyses were carried out using the Statistical Package for the Social Sciences (SPSS,) version 10.0.

RESULTS

Table 1 illustrates the breakdown by age and gender of the 2,169 individuals (859 cases and 1,310 controls) included in this study. Of the study population, 56% were men, and the mean age for men and for women was 62 years. Over 98% of the controls were within one year of age of their matched cases. Tables 2–7 illustrate the odds ratios (ORs) for NHL and the associated 95% confidence intervals (CIs) of various exposures and occupations.

Exposures to gasoline (OR 1.92; CI 1.20, 3.08), solvents (OR 1.59; CI 1.11, 2.28), and other oil products (OR 1.54; 1.01, 2.36) for more than five years were associated with increased risks of NHL (Table 2). The occupations of automobile mechanic (OR 1.82; CI 1.18, 2.81) and painter (OR 1.77; CI 1.13, 2.76) were also related to increased NHL risks. Job-related exposures to aliphatic and alicyclic hydrocarbons (OR 1.75, CI 1.03, 2.99), aromatic hydrocarbons (OR 1.45; CI 1.13, 1.86), and other organic solvents apart from chlorinated hydrocarbon solvents (OR 1.41; CI 1.11, 1.80) were as well, and increasing degrees of exposures to aromatic hydrocarbons appeared to confer an increasing risk of NHL (Table 3).

On the other hand, there were no significant associations between an increased risk of NHL and the self-reported exposures to insecticides or pesticides (OR 0.76; CI 0.43, 1.33), herbicides (OR 0.95, CI 0.66, 1.38), fertilizers (OR 0.92; CI 0.66, 1.28), or farm animals (OR 0.75; CI 0.63, 0.90) (Table 4). Nor was there an association between NHL and the occupations of farming (OR 0.86; CI 0.67, 1.09) or forestry (OR 0.97; CI 0.69, 1.38) or the matrix-derived exposures to animal dust (OR 0.83; CI 0.62, 1.12) or pesticides (OR 1.16; CI 0.55, 2.49).

Our analyses revealed a significant association between NHL and radiotherapy (OR 2.84; CI 1.85, 4.37), which was preserved even when radiotherapy within ten years of NHL diagnosis was excluded (OR 2.07; CI 1.24, 3.44) (Table 5). Matrix-derived exposure to ionizing radiation was not associated with a significantly increased NHL risk (OR 1.27; CI 0.61, 2.64), possibly due to a very small sample size (a total of 22 exposed cases and controls). Self-reported occupational exposures to radiation or radioactive substances showed no association with NHL risk.

TABLE 2. Exposure to Hydrocarbons: Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Non-Hodgkin's Lymphoma, South Sweden 1990–1998

	Exposed Cases/ Controls	OR	CI
Self-reported exposures			
Gasoline	78/89	1.46	1.04, 2.05
Gasoline ≥ 5 vs < 5 years	45/44	1.92	1.20, 3.08
Solvents	138/178	1.20	0.93,1.54
Solvents ≥ 5 vs < 5 years	72/74	1.59	1.11, 2.28
Other oil products	89/103	1.41	1.02, 1.95
Other oil products ≥ 5 vs < 5 years	53/55	1.54	1.01, 2.36
Self-reported occupations			
Automobile mechanic	52/50	1.82	1.18, 2.81
Painting	46/38	1.77	1.13, 2.76
Gas station attendant	27/28	1.62	0.92, 2.83
Varnishing	31/30	1.52	0.91, 2.54
Printing industry	30/31	1.48	0.87, 2.52
Rubber industry	31/38	1.26	0.75, 2.11
Oil industry	14/22	0.94	0.46, 1.89
Matrix-derived exposures*			
Aliphatic or alicyclic hydrocarbon solvents	32/27	1.75	1.03, 2.99
Aromatic hydrocarbon solvents	140/153	1.45	1.13, 1.86
Chlorinated hydrocarbon solvents	56/62	1.38	0.94, 2.01
Other organic solvents	43/34	1.88	1.18, 2.99
Polycyclic aromatic hydrocarbons	31/46	1.08	0.67, 1.74

* The exposure threshold used was 0.01 parts per mil (ppm).

TABLE 3. Multivariable Logistic Regressions of Matrix-derived Exposures* to Hydrocarbons: Odds Ratios (OR) and 95% Confidence Intervals (CI) for Non-Hodgkin's Lymphoma, South Sweden, 1990–1998

	Cases/ Controls	OR	CI
Aliphatic or alicyclic hydrocarbon solvents			
No exposure (reference)	827/1283	1.00	
Medium exposure	22/23	1.42	0.77, 2.60
High exposure	10/1	15.66	1.98, 123.67
Aromatic hydrocarbon solvents			
No exposure (reference)	719/1157	1.00	
Low exposure	103/122	1.35	1.02, 1.79
Medium exposure	22/19	1.72	0.91, 3.25
High exposure	15/12	1.95	0.90, 4.21
Chlorinated hydrocarbon solvents			
No exposure (reference)	803/1248	1.00	
Low exposure	52/45	1.70	1.13, 2.57
Medium exposure	4/17	0.40	0.13, 1.22
Other organic solvents			
No exposure (reference)	816/1276	1.00	
Low exposure	6/1	7.58	0.90, 63.94
Medium exposure	36/30	1.77	1.07, 2.94
High exposure	1/3	0.67	0.07, 6.41
Polycyclic aromatic hydrocarbons			
No exposure (reference)	828/1264	1.00	
Low exposure	20/31	1.00	0.57, 1.77
Medium exposure	7/11	1.07	0.39, 2.98
High exposure	4/4	1.84	0.40, 8.58

*The exposure threshold used was 0.01 parts per mil (ppm). Low = ppm 0.01–0.99; medium = ppm 1.0–9.9; high = ppm ≥ 10.

The occupation of welder (OR 1.42; CI 1.01, 1.99) and exposure to low-frequency magnetic fields (OR 1.24; CI 1.01, 1.54) were associated with increased risks of NHL of borderline significance, but exposures to welding fumes (OR 0.98; CI 0.73, 1.30), diesel engine exhaust (OR 1.16; CI 0.82, 1.63), and gasoline engine exhaust (OR 1.07; CI 0;78, 1.47) were not (Table 5). Our analyses failed to demonstrate a significant association between smoking and NHL risk. University education was associated with lower NHL risk (OR 0.73; CI 0.56, 0.95), while gymnasium education was associated with an increased risk (OR 1.41; CI 1.06, 1.87) (Table 7). Household pets and marital status showed no association with altered NHL risk.

DISCUSSION

We examined the associations between occupational exposures and NHL in three different ways: through

TABLE 4. Farming Exposures: Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Non-Hodgkin's Lymphoma, South Sweden, 1990–1998

	Exposed Cases/ Controls	OR	CI
Self-reported exposures			
Insecticides or pesticides	20/40	0.76	0.43, 1.33
Insecticides or pesticides ≥ 5 vs < 5 years	9/14	0.97	0.41, 2.29
Herbicides	52/86	0.95	0.66, 1.38
Herbicides ≥ 5 vs < 5 years	14/25	0.94	0.48, 1.86
Herbicides against brushwood	10/30	0.49	0.23, 1.02
Herbicides against weeds	44/69	1.04	0.69, 1.58
Fertilizers	79/124	0.92	0.66, 1.28
Fertilizers ≥ 5 vs < 5 years	28/53	0.71	0.41, 1.22
Exposure to farm animals	307/555	0.75	0.63, 0.90
Cow or horse	119/209	0.82	0.64, 1.07
Sheep or goat	16/36	0.64	0.35, 1.17
Chicken	89/160	0.83	0.62, 1.11
Pig	82/160	0.74	0.55, 1.00
Self-reported occupations			
Farming	166/281	0.86	0.67, 1.09
Gardening	74/112	0.97	0.71, 1.32
Forestry	71/113	0.97	0.69, 1.38
Matrix-derived exposures*			
Animal dust	97/173	0.83	0.62, 1.12
Pesticides	12/16	1.16	0.55, 2.49

*The exposure threshold used for animal dust and pesticides was 0.01 mg/m^3.

self-reported exposures, through occupational histories, and through a job-exposure matrix.[15] Each method suffers from shortcomings. Self-reported exposure may suffer from recall bias or ignorance of the fact that the exposure occurred. Cases may also report exposures more completely than controls, resulting in differential misclassification of exposures. Self-reporting of occupational histories is unlikely to be significantly affected by recall bias, but occupations do not consistently determine exposures. The job-exposure matrix links occupations to a fixed list of exposures, but is uninformative as to other occupational exposures and non-occupational (e.g., recreational) exposures. The strength of the job-exposure matrix approach is that the cases and controls are analyzed based on their occupational histories in exactly the same manner and therefore differential misclassification bias is unlikely. The fact that these three methods do not share the same shortcomings allows each one to support (or detract from) the results of the other two.

While FINJEM is based on Finnish data, the similarities in technologic levels, working conditions, and eco-

TABLE 5. Specific Exposures: Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Non-Hodgkin's Lymphoma, South Sweden, 1990–1998

	Exposed Cases/Controls	OR	CI
Self-reported exposures			
Radiotherapy	62/37	2.84	1.85, 4.37
Radiotherapy ex 10 years pre Dx	36/31	2.07	1.24, 3.44
Radioactivity/radiation	26/39	1.04	0.62, 1.74
Radioactivity/radiation ≥ 5 vs < 5 years	13/18	1.11	0.52, 2.37
Welding fumes	101/158	0.98	0.73, 1.30
Welding fumes ≥ 5 vs < 5 years	49/69	0.96	0.62, 1.47
Ever vs never smoked	501/734	1.12	0.92, 1.35
Self-reported occupations			
Welding	73/81	1.42	1.01, 1.99
Matrix-derived exposures			
Ionizing radiation*	14/18	1.27	0.61, 2.64
No exposure (reference)	845/1,292	1.00	
Low exposure	8/15	0.90	0.37, 2.18
High exposure	6/3	2.98	0.73, 12.14
Low-frequency magnetic fields†	224/295	1.24	1.01, 1.54
No exposure (reference)	635/1,015	1.00	
Low exposure	199/265	1.22	0.98, 1.52
High exposure	25/30	1.50	0.85, 2.65
Diesel engine exhaust‡	64/86	1.16	0.82, 1.63
No exposure (reference)	795/1,224	1.00	
Low exposure	9/7	2.34	0.82, 6.70
High exposure	55/79	1.07	0.75, 1.54
Gasoline engine exhaust§	74/107	1.07	0.78, 1.47
No exposure (reference)	785/1,203	1.00	
Low exposure	14/17	1.25	0.61, 2.56
Medium exposure	51/83	0.96	0.67, 1.40
High exposure	9/7	1.68	0.62, 4.57

*The exposure threshold used for ionizing radiation was 0.01 milli Sivert (mSv). Low = 0.01– 0.09 mSv; high ≥ 0.1 mSv.
†The exposure threshold used for low-frequency magnetic fields was 0.01 micro Tesla (μT). Low = 0.01– 0.99 μT; high ≥ 1.0 μT.
‡The exposure threshold used for diesel engine exhaust was 0.01 mg/m^3 nitrogen dioxide. Low = 0.01– 0.09 mg/m^3; high ≥ 0.1 mg/m^3.
§The exposure threshold used for gasoline engine exhaust was 0.01 mg/m^3 carbon monoxide. Low = 0.01– 0.99 mg/m^3; medium = 1.0– 9.9 mg/m^3; high ≥ 10 mg/m^3.

nomic structures between Sweden and Finland, as well as the narrow job descriptions used, justify FINJEM's application to Swedish data. We chose the 1960–1984 FINJEM time period because of evidence suggesting that chronicity of exposure may be important.[16]

Exposures to Organic Solvents

Each of the three methods employed revealed an association between exposures to organic solvents and an increased risk of NHL. We also found an association between exposures to gasoline and other oil products and an increased risk of NHL. Gasoline contains mainly aliphatic and aromatic hydrocarbons, including benzene at around 2% by volume,[17] and it may be that the solvent or solvent-like components of oil products mediate their lymphogenicity.

Organic solvents are a heterogeneous group of chemicals, including aliphatic and alicyclic hydrocarbons (e.g., white spirit, hexane, turpentine), aromatic hydrocarbons (e.g., benzene, toluene, xylene, styrene), chlorinated hydrocarbons (e.g., trichloroethylene, trichloroethanes), and other compounds (e.g., alcohols, ketones, esters, glycol ethers). An animal study revealed an association between benzene exposure and lymphoma in rats and mice.[18] About half of the epidemiologic studies published between 1979 and 1997 that examined the link between NHL and exposures to solvents reported a significant association.[19] In particular, a case–control study from Southern Sweden based on consecutive NHL cases diagnosed between 1978 and 1981 demonstrated an OR for NHL of 3.3 in association with solvent exposure.[20] Some specific agents have been identified—e.g. trichloroethylene[21,22]—but the occupational use of multiple solvents concurrently (e.g., toluene, xylene, white spirits, Stoddard solvent) has hampered the incrimination of individual agents.[23].

Painters may be exposed to solvents,[23] which may mediate the increased risk of NHL found in a number of studies.[24–28] A segment of rubber industry workers may be exposed to styrene as a solvent. Our analyses did not show an association between employment in

TABLE 6. Other Exposures: Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Non-Hodgkin's Lymphoma, South Sweden, 1990–1998

	Exposed Cases/ Controls	OR	CI
Self-reported exposures			
Wood proofing	29/36	1.17	0.71, 1.92
Wood proofing ≥ 5 vs < 5 years	11/11	1.37	0.59, 3.20
Dyes	51/65	1.19	0.81, 1.75
Dyes ≥ 5 vs < 5 years	23/29	1.12	0.64, 1.96
Silica	17/26	1.04	0.55, 1.97
Silica ≥ 5 vs < 5 years	8/10	1.28	0.48, 3.39
Asbestos	84/136	0.95	0.71, 1.27
Asbestos ≥ 5 vs < 5 years	36/52	1.03	0.66, 1.60
Cadmium	9/17	0.84	0.37, 1.91
Cadmium ≥ 5 vs < 5 years	6/7	1.24	0.41, 3.75
Zinc	19/35	0.85	0.48, 1.50
Zinc ≥ 5 vs < 5 years	9/14	1.07	0.46, 2.48
Nickel	17/26	1.04	0.55, 1.97
Nickel ≥ 5 vs < 5 years	8/10	1.34	0.51, 3.54
Self-reported occupations			
Furniture industry	23/25	1.38	0.77, 2.44
Dye industry	13/19	1.02	0.49, 2.12
Textile industry	77/99	1.22	0.88, 1.69
Chemical industry	41/72	0.87	0.58, 1.30
Mining industry	13/11	2.00	0.89, 4.50
Plumbing	21/29	1.08	0.60, 1.94
Ship building	14/27	0.74	0.37, 1.48
Stonemasonry	14/16	1.39	0.67, 2.87
Car manufacturing	5/18	0.40	0.14, 1.12
Smithwork	28/50	0.91	0.55, 1.50
Professional fishing	7/7	1.54	0.50, 4.69
Battery manufacturing	5/7	0.94	0.30, 3.02
Film manufacturing	2/2	2.00	0.28, 14.20
Silver plating	3/3	1.79	0.36, 8.97

the rubber industry and NHL, and our results are consistent with a pooled estimate from reported studies that did not show an excess risk of hematologic malignancies among rubber plant workers.[23]

There was no association between a self-reported occupation in the oil industry and NHL. This may be due to the fact that only a portion of oil industry employees comes into contact with oil products. While some studies show an association between employment in the petroleum industry and NHL,[29,30] a cohort study of over 300,000 petroleum workers failed to show an excess of NHL cases,[31] while a review of 24 studies showed mostly no association.[32]

Farming Exposures

Some studies have reported an association between adult NHL and gardening, farming, or exposure to animals,[33–37] while other studies have not confirmed such an association.[38–41] The putative increased risk of NHL among farmers has been attributed in part to exposures to pesticides (insecticides, herbicides, or fungicides), which some studies have found to be associated

TABLE 7. Education and Home Exposures: Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Non-Hodgkin's Lymphoma, South Sweden, 1990–1998

	Exposed Cases/ Controls	OR	CI
Education			
Gymnasium vs other	132/158	1.41	1.06, 1.87
University vs other	111/218	0.73	0.56, 0.95
Marital status			
Single	62/110	0.80	0.56, 1.14
Married/common law	625/961	1.00	0.81, 1.23
Divorced	65/83	1.19	0.84, 1.68
Widow/widower	104/152	1.02	0.76, 1.38
Household pets			
Dog	490/773	0.91	0.76, 1.08
Cat	436/694	0.93	0.78, 1.12
Rodent	92/142	1.02	0.75, 1.37
Caged bird	158/227	1.12	0.88, 1.42
Exotic pet*	43/63	1.06	0.70, 1.62

*E.g., monkey, spider, fish, lizard, etc.

with an increased risk of adult NHL.[38,42–47] In particular, a recent Swedish study reported increased NHL risks with exposures to herbicides, pesticides, and fungicides.[48] Other studies, however, have not demonstrated such an association.[49–56] Some studies have found an absence of increased risk of NHL with farming yet an increased risk of NHL with exposure to herbicides or cows,[38,57] while other studies have focussed on the controversies themselves.[58–60]

Our analyses reveal no increased risk of NHL with the self-reported occupations of farmer, gardener, or forester; with the self-reported exposures to pesticides or farm animals; or with the matrix-derived exposure to pesticides or animal dust. In fact, some of those exposures appeared to be protective against NHL, e.g., exposure to farm animals. Due to the climatic conditions in Scandinavia, pesticides are used only at certain times during the year and at relatively low levels. In fact, the group exposure level to pesticides among farmers was below the 0.01 unit threshold used in this study, explaining the discrepancy beween the number of individuals self-reporting pesticide exposures (20 cases, 40 controls) and the number of individuals exposed to pesticides according to FINJEM (12 cases, 16 controls).

Other Exposures

Our analyses found an association between prior radiotherapy and an increased risk of NHL. Seven percent of the cases had received radiotherapy, compared with 3% of the controls, numbers consistent with those found in a 1990 review of the relationship between irradiation and cancer risk (6% NHL cases, 3% controls) in which radiotherapy was confirmed in the medical records.[61] These results suggest that radiotherapy may be causally involved in the development of NHL. An alternative possibility is that the primary cancer necessitating radiotherapy is responsible for the increased NHL risk. Few studies have reported an association between radiation and NHL.[62–64] However, an association between radiotherapy of a primary cancer and the subsequent development of NHL has previously been reported.[65] A review of the relationship between irradiation and cancer risk[61] found that 75% of the localized NHLs were within previously irradiated areas, supporting a causal link between irradiation and NHL.

Only a limited number of previous studies support an association between welding and NHL.[27,28] The lack of association between exposure to welding smoke and an increased risk of NHL casts doubt on the strength of the association between the occupation of welder and an increased risk of NHL. As for smoking, cohort and case–control studies have shown conflicting evidence in regard to a potential association between smoking and an increased risk of NHL.[66]

The majority of previous studies report no association between magnetic-field exposure and lymphoma.[67–74] We were unable to examine this relationship using any method other than the job-exposure matrix, which revealed an increased NHL risk of borderline significance.

Exposure to vehicle exhaust emissions has been proposed as the culprit for the increased NHL incidence over the past 50 years.[17] Engine exhaust contains benzene as well as many other compounds.[17] Our analyses did not reveal an association between NHL and gasoline engine exhaust or diesel engine exhaust, nor did they suggest a dose–response association.

Some studies have shown an association between wood-related occupations,[36,75,76] while others have not.[41] Our analyses failed to show an association between either woodproofing, employment in the furniture industry, or wood dust exposure and NHL. Other result pairs (e.g., exposure to dyes, dye industry employment; exposure to asbestos, ship-buidling employment; exposure to minerals, mining industry employment) have not suggested associations with increased NHL incidence.

Education and Exposures at Home

Until the 1970s, Swedish secondary education consisted of two main options: gymnasium, which prepared mainly for manual labor, and university, which prepared for non-manual jobs. Our data reveal an association between gymnasium education and an increased incidence of NHL, while university education was associated with a decreased risk. The associations between secondary education and NHL may result from subsequent professional exposures rather than from different exposures during the education years. Other studies have failed to reveal an association between education and non-Hodgkin's lymphoma, but educational systems differ between countries.

Our analyses, based on self-reported exposure, occupation, and the use of a job-exposure matrix, support the hypothesis that exposures to organic solvents confer an increased risk of NHL. They also suggest that prior radiotherapy is a risk factor for NHL. However, our study provides no support for the association between farming exposures and NHL, and in particular no evidence that pesticide exposure, at the levels occurring in Southern Sweden, confers an increased risk of NHL. In this study, we did not identify exposures to specific chemicals (e.g., trichloroethylene solvents, organophosphorus insecticides) but instead focussed on exposures to classes of compounds, such as hydrocarbons and pesticides. These limitations may have biased our results towards the null hypothesis. Nevertheless, this bias should have affected all the compound classes we examined, making it unlikely that, e.g., herbicides are more lymphogenic that solvents.

The additional variables created for the use of the job-exposure matrix may have compounded the phenomenon of "multiple comparisons" whereby significant yet spurious associations are generated due to the number of comparisons alone. Corrections were not applied for multiple significance testing due to the confirmatory and hypothesis-generating nature of this study. Nevertheless, the phenomenon of multiple comparisons cannot explain the concordant findings derived through self-reported exposure, occupation, and the use of the job-exposure matrix.

In addition, we did not subdivide the NHLs according to subtype or site, and were consequently unable to seek associations between exposures and lymphoma subtypes. However, this study has the advantage of being able to be juxtaposed against the results of other studies using either no NHL classification system or different classifications without having to address the prickly issue of misclassification. Finally, the study suffers from the lack of duration-of-employment information, which would have allowed for the calculation of cumulative exposures.

In conclusion, this study adds further evidence to the hypothesis that organic solvents are associated with an increased risk of NHL and suggests that public health policymakers should strive to reduce solvent exposures among, e.g., automobile mechanics. Conversely, the study provides some degree of reassurance to farmers working under the conditions prevailing in Southern Sweden, although it does not exclude the possibility that certain pesticides, under certain conditions, are lymphogenic. Finally, the study does not identify any new NHL risk factors that might explain the worldwide increase in NHL incidence.

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