

Occupational exposure to organic solvents and Hodgkin's disease in men

A case-referent study

by Håkan Olsson, MD, Lars Brandt, MD¹

OLSSON H, BRANDT L. Occupational exposure to organic solvents and Hodgkin's disease in men: A case-referent study. *Scand j work environ health* 6 (1980) 302—305. A standardized personal interview schedule was used to study occupational exposure to organic solvents among 25 men aged 20—65 a with Hodgkin's disease and 50 referents matched for sex, age and residence. When exposure was defined as the handling of organic solvents every workday for at least 1 a within the 10-a period immediately preceding the interview, 12 of the Hodgkin's disease patients (48 %) and six referents (12 %) were occupationally exposed with a relative risk of 6.6 ($p = 0.0005$). For 9 of the 12 exposed Hodgkin's disease patients exposure to aromatic solvents was verified, and such exposure may well have occurred for the remaining three patients also. It was concluded that exposure to organic solvents may constitute an occupational risk with regard to Hodgkin's disease.

Key terms: aromatic solvents, occupational hazard.

Results of epidemiologic studies suggest that occupational exposure to chemicals may be of etiologic importance for the development of Hodgkin's disease in men (4, 8, 9, 10, 11, 12). Among possible chemical agents, benzene has been pointed out as an occupational hazard with regard to malignant lymphoma, including Hodgkin's disease (2, 12). In the present report we present results from a case-referent study which indicate that exposure to other organic solvents may also be relevant to the development of Hodgkin's disease.

Hospital, Lund, with a recent diagnosis of Hodgkin's disease and aged 20—65 a were studied. All the patients were diagnosed in 1978 and 1979. Because exposure to occupational hazards rarely starts until the age of 20, younger patients were excluded from the study. It was also considered possible that the oldest patients might have difficulties to recall occupational exposure, and we therefore decided to exclude patients over the age of 65 from the study. Only one of the men admitted to our department with Hodgkin's disease during 1978—1979 was older than 65 a of age.

Subjects and methods

Patients

Twenty-five men admitted consecutively to the Department of Oncology, University

Referents

For each patient two referents were selected from the computerized Swedish population register. The referents were matched for sex and residence, and the two men closest in age to each respective Hodgkin's disease patient were selected. A letter was sent to the referents to inform them about the aim and organization of the investigation.

¹ Department of Oncology, University Hospital, Lund, Sweden.

Reprint requests to: Dr Håkan Olsson, Department of Oncology, University Hospital, S-221 85 Lund, Sweden.

Interviews

One investigator (HO) personally interviewed all the patients and referents. A questionnaire was drawn up and followed in order to standardize the interviews. The following interview schedule was used:

1. Occupations from school age up to the date of the interview were recorded. The period for each occupation and the name and address of the employer were registered.

2. A description was obtained of the various tasks during an average workday in each occupational period.

3. When handling chemicals was spontaneously mentioned as a work task, the interviewee was asked to define the chemicals used. He was also asked whether the handling of chemicals was sporadic or occurred every workday.

If the composition of the chemicals used was unknown, the employer and/or the manufacturer was contacted by letter for more information.

In addition to questions regarding occupation, those interviewed were asked about smoking and drinking habits.

No patient or referent refused to be interviewed. All the subjects were interviewed on one occasion except for one referent who was interviewed twice. One of the patients was an immigrant, and his occupational history was obtained through an interpreter.

Definition of exposure

Occupational exposure was defined as the handling of organic solvents every workday for at least 1 a within the closest 10-a period preceding the interview. In addition daily exposure for at least 1 a more than 10 a before diagnosis was recorded for the patients and referents.

Results

According to our definition 12 out of the 25 Hodgkin's disease patients (48 %) had been occupationally exposed to organic solvents. Six of the 50 referents (12 %) had been exposed (table 1). The relative

risk, calculated according to Miettinen (7), was 6.6 ($p = 0.0005$) with a 95 % confidence interval of 1.8–23.8. When the observation period was extended beyond the closest 10-a period, the same 12 patients (48 %) had been exposed, and 8 referents (16 %) had been exposed daily for at least 1 a.

The chemicals used by the exposed patients and referents are given in table 2. For nine of the patients exposure to aromatic hydrocarbons was recorded (patients 1–9). For the remaining three patients (patients 10–12) exposure to aromatic solvents could neither be confirmed nor precluded because the solvents used were only labeled by code.

The duration of exposure varied between 1.5–35 a with a median duration of 8 a (table 2). The time from the start of exposure to the diagnosis of Hodgkin's disease, ie, the latency period, was 4–35 a (median 10.5 a). For 8 of the 12 exposed patients the latency period was ≤ 15 a.

No differences in smoking or drinking habits were detected between the patients and referents.

Discussion

Our results are in agreement with other reports indicating that exposure to chemical agents may be of importance for the development of Hodgkin's disease in man (8, 9, 10, 11, 12). They suggest that organic solvents constitute a group of chemicals that are especially hazardous in this respect.

Although the personal interviews with the patients and referents were standardized, it was considered possible that the patients might be more motivated than the

Table 1. Exposure in triplets of patients and controls.

	Both referents exposed	One referent exposed	No referent exposed
Patient exposed	—	3	9
Patient not exposed	—	3	10

Table 2. Exposure of patients and referents to organic solvents. The numbers given to patients and referents are used for description in the text and do not indicate matched triplets.

Number	Age (a)	Occupation	Solvents	Duration of exposure (a)
<i>Patients</i>				
1	36	Chemist	Xylene, trichloroethylene	14
2	46	Wood fiber worker	Toluene, xylene, styrene, phenol	15
3	51	Painter	Toluene, various coded paints and solvents	35
4	27	Chemist, varnish research	Toluene, xylene, hexane, tetrahydro-naphthalene, ethyl acetate, cyclohexane, white spirit ^a	4
5	27	Electrician, cleaning transformers.	Toluene, hexane, trichloroethylene, trichloroethane, glycol ether	5
6	48	Plastics worker	Styrene, cellulose acetate	9
7	36	Printer	Toluene, coded solvents	20
8	56	Painter	Toluene, xylene, various coded solvents	7
9	45	Repair and cleaning of typewriters	Trichloroethylene, white spirit ^a	29
10	21	Painter	Various coded paints and solvents, cellulose glues	1.5
11	39	Fuel production for model air crafts	Various coded solvents, methanol	5
12	59	Chemical process worker	Various coded solvents, ethanol	7
<i>Referents</i>				
1	46	Pharmacist	Various solvents, other chemicals	26
2	45	Woodworker, making wooden shoes	Acetone, various glues	3
3	36	Shipyard worker	Toluene, various coded paints and solvents	10
4	29	Painter	Toluene, various coded paints and solvents	6
5	28	Printer	Toluene, various coded solvents	12.5
6	23	Photographer	Hydroquinone, p-aminophenol	1

^a May contain ≤ 17 % aromatic hydrocarbons.

referents to answer questions and to recall exposure. To reduce this bias, we required a period of 1 a of daily handling solvents to define exposure. Moreover, we considered that all those interviewed should be able to recall such a long period if it had occurred during the last 10 a. Admittedly, exposure to solvents for shorter periods than 1 a might be of importance for the development of Hodgkin's disease, and exposure to solvents may therefore be of an even greater etiologic importance for Hodgkin's disease than is indicated by our results.

Vianna & Polan (12) suggested that occupational exposure to benzene will in-

crease the risk of Hodgkin's disease, but they also stated that exposure to other organic solvents might be of some importance. Exposure to benzene was not recorded for any of our patients. Because many of the solvents used were only designated by codes or had commercial names, we were sometimes unable to determine their composition. In Sweden benzene became a classified poison in 1972, and it is therefore unlikely that in recent years benzene was added to commercial solvents.

The occupational handling of various aromatic solvents was documented for 9 of the 12 exposed Hodgkin's disease pa-

tients but may well have occurred for all of them. Commercially available aromatics may contain benzene as an impurity (5), and it is possible that exposure to at least small amounts of benzene was common. It cannot therefore be established whether several aromatic solvents are hazardous with regard to Hodgkin's disease or whether the oncogenic effect of these solvents is due to benzene as an impurity. In either case exposure to commercial aromatic solvents may constitute an occupational risk with regard to Hodgkin's disease.

In addition to the handling of aromatic hydrocarbons, the handling of other organic solvents was common in the group of exposed patients. It is possible therefore that exposure to organic solvents may be relevant for the development of Hodgkin's disease, irrespective of the chemical configuration.

The median duration of exposure to solvents was 8 a for the Hodgkin's disease patients. In patients with acute myeloid leukemia following exposure to benzene, the corresponding time was an average of 10 a (1) and for six Hodgkin's disease patients exposed to benzene the mean duration of exposure was 11 a (2). A relatively short period of exposure to oncogenic chemicals may therefore be sufficient to promote the development of malignancy in hemopoietic or lymphoid tissue. The median latency period, ie, the time from the start of occupational exposure to the diagnosis of Hodgkin's disease, was also relatively short, 10.5 a. For two-thirds of the patients the latency period was ≤ 15 a.

For the present study men of working age, ie, 20–65 a of age, were selected. In Sweden one-third of the men with Hodgkin's disease in this age group are 20–34 a old at diagnosis and two-thirds are 35–64 a (3). For Hodgkin's disease there is a bimodal age incidence curve with one peak between 25–30 a of age and a second increase beginning at about the age of 35 a. It has been proposed that this phenomenon may indicate differences in etiology between Hodgkin's disease in younger and older age groups (6). Of our 12 Hodgkin's disease patients exposed to

solvents, three were 20–34 a old and nine were 35 a or over. Thus it is possible that exposure to organic solvents may promote the development of Hodgkin's disease irrespective of other, still unknown, etiologic factors.

Acknowledgments

We wish to thank T Möller, MD, and B Gullberg, PhD, of the Tumor Registry for Southern Sweden for their assistance with the selection of the referents and their valuable statistical advice.

This work was supported by grants from the Swedish Cancer Society.

References

1. Aksoy M, Erdem S, Dincol G. Types of leukemia in chronic benzene poisoning: A study in thirty-four patients. *Acta haematol* 55 (1976) 65–72.
2. Aksoy M, Erdem S, Dincol K, Hepyükse T, Dincol G. Chronic exposure to benzene as a possible contributory etiologic factor in Hodgkins disease. *Blut* 28 (1974) 293–298.
3. Cancer Registry, National Board of Health and Welfare. Cancer incidence in Sweden 1973. Stockholm 1979.
4. Greene MH, Hoover RW, Eck RL, Fraumeni JF. Cancer mortality among printing plant workers. *Environ res* 20 (1979) 66–73.
5. Hunter D. The diseases of occupations. The English Universities Press Ltd, London 1969, p 507.
6. MacMahon B. Epidemiology of Hodgkin's disease. *Cancer res* 26 (1966) 1189–1200.
7. Miettinen OS. Estimation of relative risk from individually matched series. *Biometrics* 29 (1970) 75–86.
8. Olin R. Leukaemia and Hodgkin's disease among Swedish chemistry graduates. *Lancet* 2 (1976) 916.
9. Olin R. The hazards of a chemical laboratory environment — A study of the mortality in two cohorts of Swedish chemists. *Am ind hyg assoc j* 39 (1978) 557–562.
10. Olin R, Ahlbom A. The cancer mortality among Swedish chemists graduated during three decades: A comparison with the general population and with a cohort of architects. *Environ res* (1980) 154–161.
11. Olsson H, Brandt L. Occupational handling of chemicals preceding Hodgkin's disease in men. *Br med j* 2 (1979) 580–581.
12. Vianna NJ, Polan A. Lymphomas and occupational benzene exposure. *Lancet* 1 (1979) 1394–1395.