

Occupational Medicine Clinical Update

Dedicated to the prevention of occupational illness and injuries, and promoting the well-being of all workers

This Issue:

- Case Studies in Lymphoma
- Chromosomal Changes in Lymphoma

Coming Issues:

- Proving Causation
- Limits of Epidemiology



Occupational Health Clinics for Ontario Workers Inc, Samia-Lambton

Lymphoma II— Case Studies

This month's newsletter will be a little interactive. We give you the case, you try to guess the possible exposure that may have contributed "significantly to the patient developing a lymphoma."

Case 1 - Foundry Worker

The worker had been employed at a foundry for 15 years where he had over 50 chemical exposures including toluene, silica dust, asbestos, and metals and their fumes. He then was a painter for ten years. At the age of 65, he developed non-Hodgkin's lymphoma (NHL). Where is the potential culprit?

- A) Toluene in the paint thinner
- B) Silica dust in the foundry
- C) Asbestos
- D) Metals
- E) Paint

Case 2 - Lumberyard Worker / Firefighter

This man was 16 when he began working part-time at a lumber yard. He worked there a

total of 24 years. Concurrently he also worked as a firefighter for a total of 20 years. At the age of 42, he developed a NHL with multiple complications including CNS involvement and died within two years of initial diagnosis. His exposures:

- A) Wood
- B) Smoke
- C) Heat and heavy rubber boots

Case 3 - Farmer and Family

A 52-year-old farmer (also a smoker) developed NHL, as did his wife, his sister and his brother's wife. All had an extensive history of agricultural work and grew up on farms. Contributors?

- A) Lifestyle factors
- B) Familial tendency toward hematologic malignancy
- C) Exposure to pesticides
- D) Livestock

(Answers on page 2)

Chromosomal Abnormalities in Lymphocytes of Workers

Chromosomal abnormalities are used to diagnose, treat and prognosticate in lymphomas. There are various mutations associated with specific types of lymphoid malignancies (see table).

Many studies have demonstrated that workers exposed to organic solvents (benzene, toluene, trichloroethylene, etc) and other petroleum products have increased frequencies of chromosomal aberrations in their lymphocytes, compared to non-exposed. Lymphocytes, in particular, have been shown to be the most sensitive hematological cell type to benzene exposure. Reduced levels of peripheral lymphocytes have been observed at exposure levels as low as 10 p.p.m.

It is possible that molecular genetics may one day be able to use these chromosomal 'fingerprints' to determine the cause of a person's NHL.

References

Brandt L, Kristoffersson U, Olsson H, Mitelman F. 1989. Relation between occupational exposure to organic solvents and chromosome aberrations in non-Hodgkin's lymphoma. *Eur J Haematol* 42(3):298-302.

Diagnosis	Chromosomal Abnormality
Precursor B-cell acute lymphoblastic lymphoma/leukemia	Translocation (12;21) commonly TEL1 and AML1 genes
Precursor T-cell acute lymphoblastic lymphoma/leukemia	Diverse translocations, TAL1 gene commonly rearranged
Small lymphocytic lymphoma/ Chronic lymphocytic leukemia	Trisomy 12, deletions 11q23
Follicular lymphoma	Translocations (14;18)
Diffuse large B-cell lymphoma	Translocations (14;18) and others
Burkitt lymphoma	Translocations (8;14), (2;8) or (8;22)
Multiple myeloma	Translocations (4;14)

Cotran RS, Kumar V, Collins T. 1999. *Robbins pathologic basis of disease. Sixth Edition. Philadelphia: Saunders Company, 1425p.*

Hayes RB. 2001. Benzene and lymphohematopoietic malignancies in humans. *American Journal of Industrial Medicine. 40:117-126.*

OHCOV

Occupational Health Clinics for Ontario Workers Inc,
Sarnia-Lambton

171 Kendall Street
Point Edward, Ontario
N7V 4G6

Phone: 519-337-4627
Fax: 519-337-9442
Email: sarnia@ohcow.on.ca
WEBSITE: WWW.OHCOV.ON.CA

Edited by:
Warren Teel, M.D.

Medical Staff:
Abe Reinhartz, M.D. areinhartz@ohcow.on.ca
Jim Mackenzie, M.D. jmackenzie@ohcow.on.ca
Warren Teel, M.D. wteel@ohcow.on.ca

(Answers to Cases from page 1)

Case 1 - Foundry Worker

Answers - likely A, B, C, D.

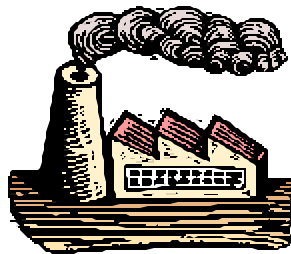
Silica dust and asbestos have been studied to a limited degree in the setting of NHL and the evidence for a causal relationship is weak-to-moderate. Working with metals (which may be a surrogate marker for exposure to metal fumes, metal cutting fluids or solvents) has been shown, in the few case-control studies done, to have very high associations with NHL.

Paint and painting as an occupation has had weakly positive or negative associations with NHL in case-control studies and in a large cohort analysis showed no significant excess. Painters do, however, have elevated rates of lung and bladder cancers.

The strongest association is with benzene. No, benzene wasn't on the list. The interesting part is that in the era this worker was working with the solvent toluene, it was contaminated up to 25% with benzene.

Benzene is a known 'leukemogen', proven on the weight of 100 years of study to cause a wide range of leukemias. The ubiquity of this chemical as a superb solvent and building block for so many other chemicals has resulted in massive global exposure in workplaces and hence, the most readily studied of the solvents.

The evidence for benzene causing NHL has been accumulating in case-control studies for decades. However, the most definitive data has come from a cohort study of 74,848 benzene-exposed workers in China [Hayes et al, 1997]. They demonstrated not only a strongly positive association but also a dose-response relationship. Moreover, this study demonstrated benzene was associated with a broad range of other hematological malignancies.



Lymphoma's have been found to be remarkably unrelated to the usual lifestyle factors associated with many other cancers

Case 2—Lumberyard Worker / Firefighter



The correct answer is A and B. Wood dust has been shown fairly consistently to be associated with both Hodgkin's and non-Hodgkin's lymphoma. This appears to be a surrogate marker for herbicides and fungicides used on lumber and wood products and, particularly, wood preservatives. The most noteworthy of these is pentachlorophenol [Hardell, 1994], which has been shown to have very high associations with NHL (and other cancers).

Firefighters have been shown to be at high risk for numerous malignancies including NHL, leukemia, multiple myeloma, brain and bladder cancers [Golden, 1995]. Firefighting supervisors have also been shown to be at particularly, high risk of NHL. This may be a reflection of their not using PPE yet having significant exposures to products of combustion and hazardous materials encountered in industrial and agricultural fires.

No, heat and rubber boots haven't been studied.

Case 3 - Farmers Family

Farmers and agricultural workers, in general, have been shown fairly consistently to have excess rates of lymphomas and leukemias. It appears that pesticides are playing a major role. This husband and wife recall going into the fields within hours of spraying to pick crops. This practice is discouraged today due to the known risks of hematologic malignancies as well as other toxic effects of pesticides.



There has been only a weak tendency for families to have increased rates of lymphomas. Interestingly, these studies have never controlled for occupational or environmental exposures.

Although this farmer did not have livestock there have been studies looking at this exposure and NHL. Significant elevations have not been observed. Interestingly, however, workers in the meat industry (butchers, abattoir workers, and meat-cutters/wrappers) have been shown to suffer large excesses of a variety of hematologic malignancies [Metayer, 1998]. The hypothesis is that these cancers may be related to exposure to oncogenic viruses.

Lifestyle factors such as diet, smoking and obesity have been studied for their potential impact on NHL's. Somewhat surprisingly, the associations found have been weak to non-existent. This is what makes lymphoma particularly interesting since it is rampantly on the rise globally, and lifestyle factors do not appear to play a significant role.

References

Golden AL, Markowitz SB, Landrigan PJ. 1995. The risk of cancer in firefighters. *Occup Med. Oct-Dec;10(4):803-20.*

Hardell L, Eriksson M, Degerman A. 1994. Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma. *Cancer Res. May 1;54(9):2386-9.*

Hayes RB, Yin SN, Dosemeci M, Li GL, Wacholder S, Travis LB, Li CY, Rothman N, Hoover RN, Linet MS. 1997. Benzene and the dose-related incidence of hematologic neoplasms in China. *Chinese Academy of Preventive Medicine--National Cancer Institute Benzene Study Group. J Natl Cancer Inst. 89(14):1065-1071.*

Metayer C, Johnson ES, Rice JC. 1998. Nested case-control study of tumors of the hemopoietic and lymphatic systems among workers in the meat industry. *Am J Epidemiol. Apr 15;147(8):727-38.*