CORRESPONDENCE

Hexachlorophene exposure in a young patient with soft tissue sarcoma

Sir,—We read with concern the correspondence from Hardell (1992; 49:743) who speculates on a causal relation between exposure to dioxin in hexachlorophene and the development of soft tissue sarcoma in a patient 17 years later. The author seems to be unaware of several considerations that would be relevant to the scientific establishment of a cause and effect relation in this case. Firstly, dioxin has not been shown to be carcinogenic in humans. Secondly, the daily dose of dioxin to which the patient may have been exposed was unknown, and based on the level alleged to be present in hexachlorophene, would be miniscule. The concept of dose-response, which is fundamental to medicine, has never been shown to be inappropriate for chemical carcinogenesis. Thirdly, other possible exposures (chemical or otherwise) before, concurrent with, or subsequent to the exposures to hexachlorophene were not considered. The possibility of an idiopathic aetiology was also not mentioned. Although it is important accurately to assess the carcinogenic risk of chemicals, this goal is not advanced when unsupportable speculation is published in medical journals. Unfortunately, Hardell's letter may be cited in the future as supportive of a cause and effect relation for dioxin and cancer that is not scientifically justified by the information presented. Finally, to propose such an unsupported relation is to reinforce falsely the common chemophobia that all human illness and disease are the result of exposure to "toxic chemicals".

MARK J REASOR

West Virginia University Health Sciences
Center, Morgantown,
WV 26506-9223, USA

MARK R MONTGOMERY

Veterans Administration Medical Center
and University of South Florida,
Tampa, FL 33612, USA

Author's reply:

We have published case reports on soft tissue sarcoma¹ and non-Hodgkin's lymphoma² in patients exposed to hexachlorophene. We believe that these clinical observations are of interest due to the contamination of dioxins, including 2,3,7,8-TCDD (TCDD), in hexachlorophene.^{3,4}

In previous case-control studies we found an association between soft tissue sarcoma⁵⁻⁸ and malignant lymphoma, including non-Hodgkin's lymphoma,^{9,10} and exposure to phenoxy herbicides or chlorophenols, which are chemically related to hexachlorophene. Two recent studies have verified an association between exposure to phenoxyacetic acids, chlorophenols, or TCDD and soft tissue sarcoma.^{11,12} A carcinogenic effect by exposure to TCDD—that is, an effect on all cancer sites combined, has been shown in three cohorts.^{11,13,14} In a meta-analysis of our four case-control studies of soft tissue sarcoma a dose-dependent increased risk for soft tissue sarcoma was associated with exposure to TCDD and other dioxins, assessed as exposure to phenoxy herbicides or chlorophenols contaminated with TCDD and other isomers.¹⁵

Also, TCDD is carcinogenic in animals^{16,17} as is hexa-CDD, including an increased incidence of soft tissue sarcoma.^{18,19}

- 1 Hardell L. Hexachlorophene exposure in a young patient with soft tissue sarcoma. *Br J Ind Med* 1992;49:743.
- 2 Hardell L, Eriksson M. Non-Hodgkin lymphoma and previous exposure to hexachlorophene: A case report. *J Occup Med* 1992;34:849-50.
- 3 IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Some halogenated hydrocarbons. 1979;20:241-57.
- 4 Hagenmeier H. Determination of 2,3,7,8-tetrachlorodibenzo-p-dioxin in commercial chlorophenols and related products. *Fresenius Z Anal Chem* 1986;325:603-6.
- 5 Hardell L, Sandström A. Case-control study: soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. *Br J Cancer* 1979;39:711-7.
- 6 Eriksson M, Hardell L, Berg NO, Möller T, Axelsson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. *Br*

J Ind Med 1981;38:27-33.

- 7 Hardell L, Eriksson M. The association between soft-tissue sarcomas and exposure to phenoxyacetic acids: a new case-referent study. *Cancer* 1988;62:652-6.
- 8 Eriksson M, Hardell L, Adami HO. Exposure to dioxins as a risk factor for soft-tissue sarcoma: a population-based case-control study. *J Natl Cancer Inst* 1990;82:486-90.
- 9 Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. *Br J Cancer* 1981;43:169-76.
- 10 Hardell L, Bengtsson NO. Epidemiological study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. *Br J Cancer* 1983;48:217-25.
- 11 Fingerhut MA, Halperin WE, Marlow DA, et al. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *N Engl J Med* 1991;324:212-18.
- 12 Saracci R, Kogevinas M, Bertazzi PA, et al. Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 1991;338:1027-32.
- 13 Zober A, Messerer P, Huber P. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *Int Arch Occup Environ Health* 1990;62:139-57.
- 14 Manz A, Berger J, Dwyer JH, Flesch-Janys D, Nagel S, Waltsgott H. Cancer mortality among workers in chemical plant contaminated with dioxin. *Lancet* 1991;338:959-64.
- 15 Hardell L, Eriksson M, Axelsson O, Fredriksson M. Dioxin and mortality from cancer. *N Engl J Med* 1991;324:1810.
- 16 Kociba RJ, Keyes DG, Beyer JE, et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicol Appl Pharmacol* 1978;46:279-303.
- 17 Pitot HC, Goldsworthy T, Campbell HA, Poland A. Quantitative evaluation of the promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. *Cancer Res* 1980;40:3616-20.
- 18 National Toxicology Program. *Carcinogenesis testing program Bioassay of a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxins for possible carcinogenicity (gavage study)*. National Cancer Institute carcinogenesis technical report series No 198. Washington DC: Government Printing Office, 1980. (DHHS publication No (NIH) 80-1754).
- 19 National Toxicology Program. *Toxicology and carcinogenesis studies of two pentachlorophenol technical-grade mixtures in B6C3F₁ mice*. National Cancer Institute carcinogenesis technical report series No 349. Washington DC: Government Printing Office, 1989. (DHHS publication No (NIH) 89-2804.)