

# Letters to the Editor

## Breast Cancer and Ethylene Oxide Exposure

From LORRAINE J LUCAS AND M JANE TETA

Sir—The recent investigation by Norman *et al.*<sup>1</sup> examines cancer incidence among 1132 employees with potential exposure to ethylene oxide in a medical sterilant plant, whose workers were reported in a prior study to have elevated cytogenetic changes. The authors appropriately point out the limitations of the data and interpret the findings of an excess breast cancer incidence based on 12 of 28 total cancer cases with due caution.

There are several interesting features of this population suggesting the potential for increased awareness and early detection bias as an explanation for the nearly twofold excess of breast cancer observed in this population:

- 1) The study participants were the subject of the earlier investigation, the results of which were widely communicated both at the worksite and in the community.
- 2) The study population was placed under active medical surveillance.
- 3) The study population resided in the Buffalo, NY area during the period of intense concern surrounding Love Canal about chemically-related health effects.
- 4) Ten of the 12 breast cancer cases were identified by the time of the first update in 1985.
- 5) The time from first potential for exposure to diagnosis of breast cancer was less than 11 years for all 12 cases.

A possible explanation for the number of breast cancer cases detected in the first year of surveillance may be attributable to early case-finding. With more extensive breast cancer screening, smaller tumors that would not have become manifest until a later time are detected much earlier, thereby creating a temporary increase in incidence rates.<sup>2</sup>

Norman *et al.* note that 2 of the 12 cases worked only 2 months at the site, but they do not present complete

data by duration of exposure or time from first exposure nor analyses by these factors. Data presented in an unpublished prior analysis of the findings for this cohort through 1985, indicate that 5 of the 10 cases worked one year or less at the worksite during the period of ethylene oxide use.<sup>3</sup> Though there appears to be an association with both brief duration of exposure and limited time from first exposure, there does not appear to be an increased risk with duration of exposure nor with increased 'latency', as would be expected if ethylene oxide were a causative factor.

In the absence of quantitative historical exposure data, the authors use 'temporary' versus 'regular' employment as a surrogate index for low and high exposure based on: 1) the median duration of employment for regular female employees being greater than that for temporary employees and 2) documented leaks of ethylene oxide at the plant suggested that exposure could have been widespread within the plant. The authors appear to have used type of employment as a proxy for duration of employment, though this information was apparently available. We believe an examination of the 12 observed breast cancer cases by duration of employment and time from presumed exposure to detection would have provided a more appropriate exposure measure and a better indication as to the likelihood of a work-related association.

In light of the absence of an elevated breast cancer risk observed in the numerous other studies of ethylene oxide workers,<sup>4</sup> which include NIOSH's mortality study<sup>5</sup> with over 9000 women (42 observed breast cancer deaths versus 49.6 expected), we concur with Norman *et al.* that this excess must be considered in the context of the numerous limitations of this investigation.

### REFERENCES

- <sup>1</sup> Norman S, Berlin J, Soper K *et al.* Cancer incidence in a group of workers potentially exposed to ethylene oxide. *Int J Epidemiol* 1995; **24**: 276–84.
- <sup>2</sup> Kelsey J, Hildreth N. Cancer of the Breast. In: *Breast and Gynecologic Cancer Epidemiology*. Boca Raton: CRC Press, 1983, pp. 5–50.

<sup>3</sup> Unpublished report. A preliminary report of cancer incidence in a group of workers exposed to ethylene oxide. Clinical Epidemiology Unit, University of Pennsylvania, School of Medicine, April 25, 1986.

<sup>4</sup> Shore R, Gardner M, Pannett B *et al.* Ethylene oxide: An assess-

ment of the epidemiological evidence on carcinogenicity. *Br J Ind Med* 1993; 50: 917–97.

<sup>5</sup> Steenland K, Stayner L, Griefe A *et al.* Mortality among workers exposed to ethylene oxide. *N Engl J Med* 1991; 324: 1402–07.

## Authors' Response

From SANDRA A NORMAN, JESSE A BERLIN, KEITH A SOPER, BRUCE F MIDDENDORF AND PAUL D STOLLEY

Sir—As Lucas and Teta state, the results of our study of cancer incidence in a group of workers potentially exposed to ethylene oxide have been reported and interpreted with due caution. We, too, were concerned about the issue of increased awareness and early detection. Thus, as stated in the article, in addition to comparisons of observed numbers of cases to those expected using the National Cancer Institute's SEER data, we also compared the number of breast cancers observed to those expected based on cancer incidence rates in Western New York, where the plant was located. Love Canal is also located in the eight-county area encompassed by the Western New York Tumor Registry. If heightened concern about cancer risk in the area from publicity about Love Canal resulted in more screening and early detection of breast cancer, breast cancer incidence rates in Western New York should have been higher than the SEER rates. This was not the case, as is stated in the article. We also noted in the article that none of the 12 breast cancer cases was discovered by screening carried out by the Health Appraisal Project.

Lucas and Teta suggest that using duration of employment and time from first exposure as stratifying

variables would have provided more useful information concerning the likelihood of a work-related association. We agree that ideally this type of analysis is preferable for very large studies. However, stratification on multiple levels related to duration of employment and/or latency could have resulted in serious loss of sensitivity due to the small size of our cohort. Nor is multivariate modelling an attractive alternative to stratification in these data due to the small number of cases. Further, because there was not consistent monitoring of exposure, and because there were some intermittent leaks of ethylene oxide at the plant, it is not clear that the factors suggested by Lucas and Teta would much improve the rough measures of potential exposure in our paper. The regular employees worked at the plant for a considerably longer time, on average, than the temporary employees. Also, results for analyses assuming latency periods of 2–5 years were similar to those that did not include a latency period.

For cancers like breast cancer, for which survival is relatively high, incidence studies, although difficult, are especially relevant. Mortality studies alone will not suffice unless there is sufficient follow-up to include development of cancer after exposure and then death. Nevertheless, we agree that, given the inconsistency of findings in the literature, the relationship between ethylene oxide exposure and breast cancer risk is still not known.

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