Editorial

Cancer cluster investigation: toward a more rational approach

Judith A. Leech, MD, FRCPC

The report by Dr. Murray M. Finkelstein on his examination of mortality among employees at two Ontario automotive parts factories (pages 125 to 130 of this issue) raises a number of questions that have little to do with the potential health risks from exposure to asbestos fibres.

The study was undertaken by the Health Studies Service of the Ontario Ministry of Labour at the request of concerned employees. Since the plant had been closed in 1980 and a number of deaths had occurred by the time of the investigation the reader surmises that the employees' concern was about a perceived increase in the incidence of cancer. The workers suggested not only the study and the outcome of interest but also the putative agent, asbestos.

However, two similar studies involving larger numbers of workers had previously shown conflicting results;[1,2] therefore, what was the realistic expectation of demonstrating meaningful results in this workplace? Indeed, perhaps fewer than 100 people at any one time were thought to have been exposed to asbestos. Given the results of previous studies of known asbestos exposure, likely at higher doses, few excess deaths from cancer could be expected in so small a sample. For example, among Quebec miners and millers of chrysotile asbestos the rate of death from respiratory cancer was a maximum of 32 per 1000 people for the highest dust levels (800 million particles/ft^3 per year) and 10 per 1000 people for the lowest dust levels (10 million particles/ft^3 per year).[3]

If there were excess mortality no certainty of exposure or measure of possible confounding variables was available. Hence, no causal relation could reasonably be suggested regardless of the results. The investigative team went to a great deal of time and effort for what may have been an unanswerable question in this instance.

Will the employees be satisfied with the uncertainty of the answer they have received? From the cohort analysis an apparent increase in the risk of laryngeal carcinoma (i.e., four deaths among men who did not work with asbestos) was found, and from the case-control analysis no relation between laryngeal or lung cancer and the length of employment was demonstrated. If the excess number of deaths from laryngeal cancer is "real", the next logical step for employees is to ask what indeed the etiologic culprit was and whether compensation is justifiable.

With the ever growing public concern about environmental hazards, particularly carcinogens, increasing demands will be made by exposed people to assess the risk not only in the workplace but also in and around the home. Whether it be children's proximity to high-power lines or "sick-building" complaints, the informed consumer has come to demand a sophisticated level of epidemiologic expertise to answer such questions. But from the point of view of common sense and cost containment a decision must first be made as to whether a study is plausible and possible in a given population.[4,5]

In the usual academic milieu, if a research study is doomed to "fail" because of a tiny sample size a sensible granting agency would not fund the project, no matter how interesting. No more readily should an investigative study of occupational risk be undertaken at the expense of the public purse if the question was raised by exposed individuals rather than researchers.

These issues were addressed at a recent symposium on the clustering of health events, held in February 1989 by the US Centers for Disease Control (CDC), Atlanta, and several states have implemented policies to handle possible cluster reports. In Wisconsin, for example, 149 requests for investigations have been received since 1978, 60%

Reprint requests to: Dr. Judith A. Leech, Division of Respirology, Ottawa Civic Hospital, 1053 Carling Ave., Ottawa, Ont. K1Y 4E9

of them between 1985 and 1988;[6] 110 of the requests were regarding suspected excesses in the number of cases of cancer. Therefore, Wisconsin has developed the following cluster investigation protocol.

- Circumscribe the cluster (descriptively or visually). Determine such information as the number of cases, the type of disease, the age and sex of the people and their addresses.
- Assess the biologic plausibility. Look at the case specificity and evidence in the literature.
- Using the available and appropriate data resources (e.g., death certificates, birth certificates, cancer registry, hospital discharge survey and medical records) locate all cases relevant to the investigation.
- Examine potential exposures. This can involve looking at water quality, air quality and landfill reports.
- Assess the risk of the exposed population, as compared with the reference population. Information on the reference population can be obtained from such sources as SEER (Survey, Epidemiology and End Results — a program of the National Cancer Institute [NCI]), NCI maps, CDC birth defect registry, vital statistics reports, census data and state population data.
- Statistically analyse disease rates. Possible methods include age-adjusted analysis of incidence rates, use of standard mortality ratios (SMRs), relative risk calculation and Poisson regression analysis. The policy is to not reveal rates if the observed number of cases is *less than five.*
- Determine overall cluster significance. Look at the geographic pattern, evidence of exposure, biologic plausibility and statistical significance all together. Decide if further work should be considered. [Since this protocol has been in place no extensive studies have been undertaken.]
- Report results to the informant, local public health agencies, public officials and the media and at public meetings.

A two-stage protocol has been in use in Missouri since 1984 to review reports of excess numbers of cases of cancer.[7] Of 85 reports examined in the first stage to identify problems and evaluate risks, only 3 led to full-scale, second-stage investigation. However, the existence of the protocol has resulted in the development of a cancer surveillance system and congenital defect registry.

Finkelstein has expertly performed a number of the above steps and functions, but the result remains unsatisfactory to the reader, and probably to the employee group at risk, because it cannot answer the posed question with sufficient power. If a policy for dealing with random variation ("noise") or elevated SMRs in small samples were in place such studies could be stopped at an earlier stage with at least an equal degree of satisfaction, or dissatisfaction, among exposed workers.

The development and implementation of provincial policies on investigation of reported clusters, particularly of cancer, is a task whose time has come in Canada. Even if exposed groups, such as a union or a community, wished to fund the investigation an independent review to determine plausibility and feasibility would be optimal, as would peer review of the study design and the results if a complete investigation were undertaken.

References

1. Berry G, Newhouse ML: Mortality of workers manufacturing friction materials using asbestos. *Br J Ind Med* 1983; 40: 1-7
2. McDonald AD, Fry JS, Wooley AJ et al: Dust exposure and mortality in an American chrysotile asbestos friction products plant. *Br J Ind Med* 1984; 41: 151-157
3. Becklake MR: Asbestos-related diseases of the lung and other organs: their epidemiology and implications for clinical practice. *Am Rev Respir Dis* 1976; 114: 187-227
4. Schulte PA, Ehrenberg RL, Singal H: Investigation of occupational cancer clusters: theory and practice. *Am J Public Health* 1987; 77: 52-56
5. Rothman KJ: Clustering of disease [E]. Ibid: 13-15
6. Fiore BJ, Hanrahan LP, Anderson HA: State health department response to disease cluster reports: a protocol for investigation. Presented at the National Conference on Clustering of Health Events, Atlanta, February 1989
7. Devier JR, Brownson RC, Bagby JR et al: Development of a public health response to cancer clusters in Missouri. Presented at the National Conference on Clustering of Health Events, Atlanta, February 1989

Remedies

We must deal with luck as with health: enjoy it when it is good, be patient when it is bad, and resort to extreme remedies only in extreme need.

— Duc François de La Rochefoucauld (1613-1680)