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Preliminary Findings for Pleural Mesothelioma among Women in the Québec Chrysotile Mining Regions

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Introduction. We conducted a descriptive study to compare cases of pleural mesothelioma among female residents of Québec's asbestos mining regions to matched controls for residential, domestic and occupational asbestos exposures.

Methods. We visited hospitals throughout the province of Québec to identify women aged ≥50 yr whose hospital records mentioned any possible mesothelioma between 1970 and 1989. Hospital records and biological materials were reviewed by three expert pathologists to identify individuals who had lived in a mining region in Québec at the time of diagnosis. For each case, 15 controls matched for year (±2) of birth and area of residence were selected from a previously interviewed sample of 817 female asbestos mining area residents alive in 1989. Relatives of the cases were similarly interviewed regarding lifetime occupational and residential histories and cohabitation with asbestos worker(s). Cumulative exposure from each source was estimated in fibers/ml-yr from indirect data.

Results. We identified six 'definite or probable' and four 'possible' pleural mesothelioma cases. All resided in Thetford Mines (none in the town of Asbestos) and were born before 1935. Five cases (50%) worked in the asbestos industry (versus 2.7% of controls; relative risk = 53.8). Nine (90%) had lived with one or more asbestos workers (versus 65% of controls); six (60%) with two or more workers (versus 36% of controls). Mean cumulative exposure (residential, domestic, and occupational combined) was estimated as 226.1 fibers/ml-yr (range 84–525) for cases and 84.1 fibers/ml-yr (range 0–189) for controls, with a plausible 5-fold error on either side.

Keywords: mesothelioma; asbestos; chrysotile; tremolite; amphibole; Québec

INTRODUCTION

The chrysotile mining region of Québec, Canada, has two distinct zones, one of which is centered around the town of Thetford Mines and the other of which is centered around the town of Asbestos. The current work is part of a series of studies aimed at identifying risk factors for asbestos-related disease for women in the Québec chrysotile-mining regions (Camus *et al.*, 1998), and use of these data as a test for existing asbestos risk assessments (Camus *et al.*, 2002). The study described in this preliminary communication aimed at determining the geographic distribution of mesothelioma risk in this area, and at estimating risk as a function of exposure to asbestos.

MATERIALS AND METHODS

Data collection

We identified from hospital records, oncology archives and pathology records all cancers of the pleura or peritoneum diagnosed among women aged ≥50 yr in which the hospital chart made mention of a possible diagnosis of mesothelioma, in hospitals in the populated portion of Québec province.

Cases and validation

In total, 233 potential cases of mesothelioma in women diagnosed 1970–89 were identified throughout

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Table 1. Occupational and domestic exposures of mesothelioma cases and controls

	Cases (%, n = 10)	Controls (%, n = 150)	Relative risk (95% confidence interval)
Occupational exposures			
Worked outside home			
Any job	100	41.7	
Asbestos job	50	2.7	53.8 (6–470)
Domestic exposures			
Never lived with asbestos worker	10	35.3	1.0
1 or 2 workers	50	48.0	3.4 (0.4–30.8)
3 or more workers	40	16.7	9.0 (0.9–87.4)
Cumulative years lived with worker(s)			
1–40	55.6	69.1	3.9 (0.4–35)
>40	44.4	30.9	7.5 (0.8–72)

the province, and for each case the hospital pathology department was contacted and pathology blocks and slides requested. For the present study, only potential *area cases* are considered, defined as all of those first diagnosed between 1 January 1970 and 31 December 1989, living in one of the two mining regions at the date of diagnosis.

For each of the potential cases for whom histological material was available, histological and immunohistochemical materials were circulated blind to two expert pathologists (Drs Andrew Churg and Victor Roggli). Each pathologist issued an opinion as to whether mesothelioma diagnosis was definite, probable, possible or definitely not mesothelioma, or if applicable that material was insufficient for diagnosis. For those cases for which histological materials were not available a probability of diagnosis was assigned on a 10 point scale developed by one of us (B.W.C.). We accepted all cases that were definite, probable or possible mesothelioma as determined by either of the two pathologists or, when pathology material was unavailable, through an algorithm applied to the 10 point rating score (B.W. Case, V. Roggli, A. Churg, M. Camus, J. Siemiatycki, in preparation).

Case-control selection and interviews

Controls were selected from 817 female residents of the mining region interviewed previously in 1989 (Camus *et al.*, 1998). For each identified mesothelioma case, 15 of these controls were chosen, matched as closely as possible for age and area of residence. Controls had previously been interviewed for lifetime residential history, domestic exposure (number of workers with whom they lived and when, and type and duration of work for each), and complete lifetime residential and work histories. The same questionnaire was shortened and administered to obtain similar data on lifetime residential, domestic and occupational histories from proxies for each case. Exposure in fiber-years for both cases and controls was estimated according to the methods described previously (Camus *et al.*, 1998).

RESULTS

Ten pleural mesothelioma cases were identified in this study, all in the Thetford Mines area. Seven had tissue available for review by the two pathologists, and an eighth had been evaluated at the time of diagnosis by other members of the US–Canada mesothelioma panel. Six cases were considered definite or probable mesothelioma and a seventh ‘possible’ by the pathologists. The eighth case had insufficient tissue for diagnosis according to both pathologists (A.C. and V.R.), although available pathology records suggested a high probability of mesothelioma. This case, the case in which both pathologists agreed the diagnosis was ‘possible’, and the two cases for which tissue was unavailable were retained after applying the algorithm we developed. The six definite or probable and four possible cases are grouped together for case-control comparisons.

Cases and controls were similar demographically in most respects. Mean age at diagnosis (years) was 63 yr for both. Cases (mean 23 cigarettes/day) smoked more heavily than controls (13.4) and began smoking earlier, but differences are not statistically significant. Half of cases and 46% of controls were born before 1920; all cases were married or widowed while 18% of controls were single. One hundred percent of cases and 70% of controls were born in the county in which Thetford Mines is located.

Principal results are outlined in Tables 1 and 2. All 10 cases lived for all of the years of their lives (other than the final 20 in one case) in the Thetford Mines area, more specifically in the western part. This is the portion adjacent to the ‘central mines’ known to have the highest tremolite content (McDonald *et al.*, 1997).

Table 2. Estimated cumulative asbestos exposure (fibers/ml-yr) in mesothelioma cases and controls

Type of exposure	Estimated cumulative asbestos exposure (fibers/ml-yr)[a]					
	Cases (n = 10)			Controls (n = 150)		
	Mean	SD	Range	Mean	SD	Range
Occupational						
Among all cases and controls	94.5 (n = 10)	140.0	0.0–390.0	1.1 (n = 150)	8.2	0.0–90.0
Among occupationally exposed	236.3 (n = 5)	118.8	100.0–390.0	41.0 (n = 4)	33.6	15.0–90.0
Domestic						
Among all cases and controls	29.6 (n = 10)	20.3	0.0–55.2	19.9 (n = 150)	20.2	0.0–69.6
Among domestically exposed	32.9 (n = 9)	18.5	2.4–55.2	32.5 (n = 92)	15.9	3.6–69.6
Residential						
(All cases and controls)	102.0 (n = 10)	10.1	82.1–115.0	63.1 (n = 150)	44.8	0.04–122.9
All exposure sources combined						
(All cases and controls)	226.1 (n = 10)	146.7	84.5–525.6	84.1 (n = 150)	58.7	0.0–190.0

[a]As estimated by methods described by Camus *et al.* (1998).

Domestic exposures in nine of the 10 cases were in part related to work by household members in one or more of the central mines, but no attempt was made to compare these in a quantitative fashion to the (also very frequent) domestic exposures in the control population (Table 1). Estimated cumulative exposures for occupational, domestic and residential sources are outlined in Table 2, calculated as described in Camus *et al.* (1998). Figures shown in the table are the ‘best estimates’ as determined by the methods developed by one of us (M.C.) in association with the expert panel.

DISCUSSION AND CONCLUSIONS

The first striking finding was that 10 identified cases had lived in Thetford Mines and none in Asbestos. The chrysotile mining region of Québec is divided geologically into two distinct geological zones with respect to tremolite content; the large, open-pit Jeffrey mine at Asbestos having less tremolite (Williams-Jones *et al.*, 2001) and a group of mines near the central portion of the Thetford Mines area having the highest levels (McDonald *et al.*, 1997). Lung-retained fiber among those *without* occupational exposure has confirmed that those who lived in Thetford Mines had elevated lung tremolite content from ambient air (Case and Sébastien 1989; Case, 1991), while those who lived in or near the town of Asbestos did not (Case and Sébastien, 1987).

The case-control study was susceptible to errors both in the diagnosis of mesothelioma and in the exposure assessment, and to bias. We used a conservative case definition which included all *possible* cases. This may have attenuated case-control differences (Rogers *et al.*, 1991). The retrospective assessment of exposure was particularly challenging. The expert panel involved in determining the parameters for this assessment had access to multiple data sources, but actual fiber measurements in the different environments assessed (neighborhood, domestic, occupational) were few and relatively recent (Camus *et al.*, 1998). Nevertheless, we believe that exposure estimates are accurate within the bounds stated (i.e. a 5-fold possible error in either direction).

One possible source of bias in the case-control comparisons is related to the sampling strategy used for controls. Namely, for the study from which controls were derived, subjects were stratified to over-represent residents from rural areas surrounding the mining towns. This could have led to overestimating the residential exposure differences between cases and controls. Nevertheless, as may be seen in Table 2, exposure estimates for controls—and for the entire population from which controls were drawn—were for the most part non-trivial (63.1 ± 44.8 fibers/ml-yr cumulative exposure for controls, with a range of 0.04–122.9 fibers/ml-yr).

The case-control comparison demonstrated the particularly high risk associated with having worked in the asbestos industry. Two cases worked as cobbers prior to World War II; this work was done by hand. Three additional cases were women who worked in a single unventilated asbestos bag fabrication and repair shop (Case *et al.*, 1990; and A. Dufresne, personal communication) in the period immediately following World War II. Bags were made of burlap, and came from locations both within and outside Thetford Mines. Lung-retained fiber analysis [fibers >5 µm/µg dry lung; aspect ratio >3:1; assessed by analytical transmission electron microscopy (Case and Sébastien, 1987)] had been performed for two of these three cases, and for a third woman who died from lung cancer and asbestosis who worked in the same facility during the same years (Case *et al.*, 1990). In the two mesothelioma cases lung levels of tremolite were 5.0 and 29.9 fibers/µg and chrysotile 2.9 and 7.5 fibers/µg, respectively. In one of the two lung tissue also contained crocidolite (1.4 fibers/µg) and amosite (1.1 fibers/µg). For the woman with lung cancer and asbestosis who worked in the same facility, lung tissue contained 45 chrysotile fibers/µg dry lung, 36 tremolite fibers/µg and 8.4 amosite fibers/µg (fibers >5 µm). Tissue for lung burden analysis was not available for any of the other mesothelioma cases.

In summary, all cases of pleural mesothelioma—whether definite, probable or possible—were found in Thetford Mines, and all lived close to the central mines. Further, all of the cases had incurred very high cumulative exposures, including half as workers in the industry and all but one as relatives of one or more workers in the industry. Additional data refinement and statistical analyses are in progress.

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