

Epidemiologic surveillance of mesothelioma in Canada

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Summary: The number of fatal malignant mesotheliomas was ascertained for the period 1960-70 by contacting all pathologists in Canada. The annual incidence was steady between 1966 and 1970 at 1.4 per million population. Of 71 cases registered in 1968-70 and not previously reported, 66% were pleural, 24% peritoneal and the remainder in both sites; 45% of tumours were in women. The diagnosis of mesothelioma was approved by the Canadian Mesothelioma Panel in 59%. Sixty-nine cases were successfully investigated epidemiologically. A history of definite or probable occupational asbestos exposure was found in 30% of male cases compared with 11% of controls, but in none of the female cases or controls. However, among cases, four women and one man had had domestic exposure to dusty clothing of an asbestos worker. Most of the excess occupational exposure was in the manufacture of asbestos products or insulation and little in mining or milling. No case other than those occupationally or domestically exposed had lived within 20 miles of asbestos mines or mills.

Résumé: *Surveillance épidémiologique du mésothéliome au Canada*

Une enquête menée auprès de tous les pathologistes canadiens a permis d'établir le nombre de mésothéliomes malins ayant eu une issue fatale durant la période 1960-70. La fréquence annuelle des cas, régulière de 1966 à 1970, s'établissait à 1.4 cas par million. Des 71 cas enregistrés de 1968 à 1970 et qui n'avaient pas été rapportés, 66% étaient localisés à la plèvre, 24% au péritoine et les autres à ces deux sièges; 45% des tumeurs touchaient les femmes. Dans 59% des cas, le diagnostic de mésothéliome a été approuvé par le Colloque Canadien sur le mésothéliome. Au point de vue épidémiologique, on a pu étudier 69 cas avec succès. Des antécédents évidents ou probables de contacts professionnels avec l'asbeste ont été trouvés chez 30% des cas chez l'homme, et chez 11% des témoins. Aucun cas semblable n'a été décelé dans les cas féminins ou chez les témoins. Cependant, on a trouvé quatre femmes et un homme qui avaient été en contact avec la poussière d'asbeste en brossant les habits d'un travailleur de l'asbeste. La majorité des cas de contact professionnel excessif survenaient chez des ouvriers travaillant à la fabrication de produits d'asbeste ou à l'isolation. On trouvait peu de cas chez les mineurs et chez ceux affectés au broyage. En dehors des cas venus en contact avec l'asbeste, soit sur le plan professionnel soit sur le plan domestique, aucun des sujets n'avait vécu dans un rayon de 20 milles des mines ou des manufactures.

Fibrotic and malignant diseases of the lung and pleura are hazards faced by those who work with asbestos, but in recent years it has been suggested that malignant mesothelial tumours may occur in the general population as a result of a lesser degree of exposure. The greatly increased production and use of asbestos and the long latent period between history of first exposure to asbestos and detection of these tumours have caused concern.

A survey of mesothelioma in Canada was begun in 1968 and is continuing. It has two aspects — epidemiologic and pathological. The objectives are to determine: (a) whether the incidence of mesothelioma is increasing, (b) what proportion of these tumours are related to exposure to asbestos at work, by residence near asbestos mines and mills, or in the home from dusty clothing of persons working with asbestos; (c) the nature and timing of the exposures; (d) the criteria of pathological diagnosis; and (e) whether pathological features are related to evidence of exposure.

A controlled epidemiological study of 165 fatal cases reported by pathologists across Canada from the beginning of 1960 to mid-1968 has been published.¹ The overall rate of occurrence in Canada was one per million persons per annum, but the annual number of cases rose from 1960 to 1966 probably owing mainly to better records and identification of the tumour during the later years. Two thirds of the cases were in men. An association with definite or probable occupational exposure to asbestos was clearly demonstrated, but only 20% of male cases and one female case had any such contact. Most of the exposure in these cases was to manufacturing processes and the industrial application of asbestos rather than to mining or milling. There was also a small excess of possible domestic exposure. No association was found with lesser degrees of occupational exposure or residence in asbestos mining areas. Tobacco consumption was similar to that of controls with secondary lung cancer and substantially less than that of a series of primary lung cancer patients.

Pathological findings, based mainly on the same series but also including some information about cases recorded from mid-1968 to the end of 1970, have been reported.² The Mesothelioma Panel of the Canadian Tumour Reference Centre was in favour of the diagnosis of mesothelioma in 54% of cases registered between 1960 and 1968, uncertain in 10%, and against it in 36%. In cases in which the Panel favoured the diagnosis of mesothelioma, exposure to asbestos was slightly more frequent.¹ However, when classified histologically, about 10% of epithelial and mesenchymal tumours were associated with asbestos exposure

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whereas nearly half the mixed or biphasic tumours had such a history.³

The purpose of this paper is to report cases in which the diagnosis was established from mid-1968 to the end of 1970 with special reference to (a) the incidence trend for mesothelioma in Canada and (b) whether the epidemiological conclusions derived from the earlier study (1960-1968) were confirmed by further independently collected evidence.

Methods

All primary malignant tumours of the pleura and peritoneum diagnosed between June 1968 and the end of 1970 by pathologists across Canada were recorded during 1971. The methods used were those described in a previous report.¹ All members of the Canadian Association of Pathologists and physicians certified as specialists in pathology in Quebec were asked individually whether or not they had seen any such case. After a reply had been received from each of the 453 pathologists listed, a visit was made to those who answered in the affirmative. Information was obtained about every fatal case which the pathologist considered "on balance" was such a tumour. At the same time another patient who had pulmonary metastases from an extrathoracic primary tumour was selected as a control from the autopsy or biopsy records of the same hospital. Controls were matched for sex, and as closely as possible for age and date of death. Field workers (usually public health nurses) sought relatives and friends of the deceased persons without knowing which were mesothelioma cases and which were controls, and completed a detailed standard questionnaire on occupational, residential and smoking history. The coding of these records was also carried out "blind".

Material from each tumour and gross autopsy or clinical findings, but not an occupational history, were submitted to the Canadian Tumour Reference Centre. Sets of slides and copies of reports were sent to each of the six members of the Mesothelioma Panel who gave their opinions on whether they considered the diagnosis was definite, probable, possible, unlikely or incorrect. If a panel member chose "possible" he was further asked whether he tended to be in favour of or against the diagnosis. The opinion of each pathologist was then classed as "in favour", "uncertain" or "against" and the majority view taken as the Panel diagnosis. Finally, cases accepted by the panel were classified by one member³ as one of three histological types — epithelial, mesenchymal and biphasic or mixed.

Table I—Distribution by age of cases and matched controls

Age (years)	Men		Women	
	Cases	Controls	Cases	Controls
20-29	0 (—)	0 (—)	2 (2)	0 (—)
30-39	3 (2)	2 (2)	4 (4)	4 (4)
40-49	6 (5)	6 (6)	4 (4)	5 (5)
50-59	12 (12)	12 (11)	6 (6)	5 (5)
60-69	8 (8)	10 (10)	6 (6)	8 (8)
70-79	7 (7)	5 (5)	7 (7)	8 (8)
80-89	2 (2)	3 (3)	3 (3)	2 (2)
90-99	1 (1)	1 (1)		
Total	39 (37)	39 (38)	32 (32)	32 (32)
Mean	58.7	59.2	58.9	59.0
Standard deviation	13.9	13.2	18.2	15.2

The number successfully investigated epidemiologically is given in parentheses.

Findings

In all, 71 cases of mesothelioma were recorded in which death had occurred during the period from July 1968 to the end of 1970: 47 (66%) were pleural tumours, 17 (24%) peritoneal and 7 (10%) both pleural and peritoneal; 39 (55%) were in men and 32 (45%) in women. The age distribution of cases and of controls is shown in Table I. In all but two male cases and one male control, relatives

Table II—Distribution of reported cases by year of death and province (1960-1970)

	Ontario	Quebec	Other provinces	Canada
1960	0	6	9	15
1961	1	6	3	10
1962	4	4	5	13
1963	9	3	7	19
1964	6	8	3	17
1965	7	7	5	19
1966	8	14	9	31
1967	6	13	6	25
1968	7	18	7	32
1969	12	7	6	25
1970	9	16	5	30
	69	102	65	236
Annual incidence per million population 1966-70	1.2	2.3	0.9	1.4
Reviewed by pathology panel	57	80	47	194
Accepted as mesothelioma	71%	42%	57%	55%

Table III—Occupational exposure of men to certain materials*

	Cases (37 men)	Controls (38 men)
Asbestos	11	4
Cement	6 (1)	10 (1)
Copper	5 (1)	10 (1)
Fibreglass	5 (4)	0 (0)
Nickel	2 (1)	2 (0)
Rubber	1 (0)	4 (0)
Wood	6 (3)	11 (1)

*Definite or probable exposure to the substance named in dust or vapour form. The number of men who were also exposed to asbestos is given in parentheses.

Table IV—Distribution of cases and controls according to occupational exposure to asbestos

Exposure to asbestos	Men		Women	
	Cases	Controls	Cases	Controls
Definite	7	0	0	0
Probable	4	4	0	0
Possible	16 (43.2)	22 (57.9)	4 (12.5)	3 (9.4)
Unlikely	10 (27.0)	12 (31.6)	28 (87.5)	29 (90.6)
All	37	38	32	32

Figures in parentheses represent percentages

or friends were interviewed and questionnaires completed.

The 71 cases were reviewed by the Mesothelioma Panel of the Canadian Tumour Reference Centre. In 42 (59%) the Panel was in favour of the diagnosis, in 5 (7%) uncertain and in 24 (34%) against it. The Panel accepted about the same proportions of male and female cases and of pleural and peritoneal tumours.

Table II shows the annual number of cases reported in Canada during the period 1960-1970. The number has fluctuated little since 1966 when it was observed to have levelled off.¹ The mean annual incidence per million population since 1966 was 1.4. In Quebec the incidence was considerably higher than in Ontario and in the other provinces. However, in a much lower proportion of Quebec cases the diagnosis was accepted by the Panel, so it is doubtful whether there was any real difference between Quebec and the rest of Canada.

Definite or probable occupational exposure to asbestos and certain other materials in dust or vapour form is shown for men in Table III. Eleven men with mesothelioma had worked with asbestos compared with four controls but, except for fibreglass, other exposures were more frequent in controls than in cases. Four of the five cases with fibreglass exposure had also been exposed to asbestos.

Of the 11 male cases exposure to asbestos was definite in seven and probable in four, whereas in all four controls exposure was probable (Table IV). None of the 32 female cases had been occupationally exposed to asbestos but four had been exposed at home, two to a father and two to a husband who worked with asbestos and brought home dusty clothing (Table V). Only one female control had such an exposure. One male case had been domestically exposed. In all, probable or definite direct or indirect occupational exposure was reported in men in 29.7% of cases and in 10.5% of controls; in women there was no instance of either such degree of occupational exposure but it was possible in 12.5% of cases and in 9.4% of controls. The types of occupation are shown in Table V. Manufacture of asbestos products or insulation work was recorded in nine cases but in no control, mining or milling in three

cases and in no control, and other occupations in four cases and five controls. In both men and women there was little difference between cases and controls in the proportion possibly exposed to asbestos. There were no instances of men exposed at home to the dusty clothing of persons possibly working with asbestos, but in five women — four cases and one control — there had been such exposure.

Apart from persons themselves occupationally or domestically exposed, no case had lived within 20 miles of asbestos mines or mills. Smoking histories of men with mesothelioma closely resembled those of controls (Table VI). Women with mesothelial tumours were less frequently non-smokers than were controls.

Three of the 11 men with definite or probable exposure had worked with asbestos for only one year or less. The intervals between exposure and death were 26, 26 and 33 years. One man died from mesothelioma at 91 years of age and was reported to have worked in asbestos mines between the ages of 15 and 24 years. If this exposure was responsible for his death the latent period was probably over 70 years. The interval between first exposure and death for the remaining seven men lay between 19 and 61 years.

Discussion and conclusions

As in the previous series (1960-1968) two thirds of the mesothelial tumours recorded were pleural, one quarter peritoneal and the remainder in both sites. A somewhat larger proportion of cases, however, were in women — 45% compared with 35% for the previous series — and the Mesothelioma Panel approved the diagnosis in a higher proportion of female cases than previously (59% of 32 compared with 35% of 37). However, the numbers were small and this difference may have been a chance occurrence. There was no indication that the possible relative increase in female cases was associated with an increase in asbestos exposure.

Overall, the Panel accepted as mesotheliomas about the same proportion of cases as previously (59% compared with 54%). There was therefore nothing to suggest that pathologists were reporting cases differently, and the steady number of cases of mesothelioma reported annually since 1966 gives no indication of a change in incidence. However, the survey would need to be extended for at least several years to confirm this conclusion.

The occupational histories of both cases and controls revealed more frequent exposure than in the previous series to asbestos and the other materials investigated except wood. The shorter interval between death of the subject and interview of the relatives may have contributed to a fuller occupational history, but for reasons unknown a higher proportion of male cases and controls were from urban industrialized areas.

Table VI—Average daily number of cigarettes smoked

Cigarettes per day	Men		Women	
	Cases	Controls	Cases	Controls
Nil	7 (19.4)	8 (21.1)	14 (45.2)	22 (68.8)
10 or less	6 (16.7)	4 (10.5)	5 (16.1)	5 (15.6)
11-29	18 (50.0)	17 (44.7)	8 (25.8)	3 (9.4)
30 or more	5 (13.9)	9 (23.7)	4 (12.9)	2 (6.3)
Total	36*	38	31*	32

*Excluding 1 man and 1 woman whose smoking histories were not recorded
Figures in parentheses represent percentages

Table V—Types of occupation in which there was definite or probable asbestos exposure

Type of occupation	Men				Women			
	Occupational		Domestic		Occupational		Domestic	
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Mining and milling	1	—	1 (father)	—	—	—	1 (father)	—
Asbestos products manufacture	4	—	—	—	—	—	—	—
Insulation work	2	—	—	—	—	—	3 (1 father, 2 husbands)	—
Other occupations	4	4	—	—	—	—	—	1 (husband)

However, the main findings from this 1968-70 survey of cases were very similar to those from the earlier period, 1960-67. The excess of definite or probable exposure to asbestos in male cases compared with controls was much the same — 19% compared with 17%. The occupations mainly implicated were, again, manufacture of asbestos products and insulation; mining or milling was mentioned in only a small proportion of cases. There was more evidence than in the previous survey that exposure in the home of children and wives to dust from the clothing of asbestos workers was related to mesothelioma but no association with either lesser degrees of occupational exposure or living near asbestos mines and mills.

The cigarette-smoking histories of male cases closely resembled those of controls, as in the previous survey, but this time there was a difference in those of women. Overall, it remained clear that smoking is not an important factor. The total number of male cases in 1960-70 with asbestos exposure was 31. Of these, 13 (42%) smoked more than 10 cigarettes daily compared with 52 (40%) of 132 controls. Therefore there was no evidence that cigarette smoking potentiates asbestos exposure in the production of mesothelioma.

Our findings suggest that asbestos exposure is associated with a relatively small proportion of the tumours that Canadian pathologists call mesotheliomas, and there is no

reason to think that they differ in their diagnostic criteria from pathologists elsewhere.³ The observation that mixed or biphasic tumours were more often associated with asbestos exposure than were epithelial or mesenchymal tumours suggests that it may be possible to specify criteria of asbestos-associated mesotheliomas. This finding, together with studies of the type of fibre found in the lungs of persons with mesothelioma, should help to elucidate the relationships between fibre type, dose and perhaps additional occupational carcinogens, and mesothelioma.

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I am progeny

I am gleam.
I am response.
I am sweet-talk.
I am embrace.
I am passion.
I am content.

I am sperm.
I am egg.
I am eggsperm.
I am spermegg.
I grow.

I am phylogeny.
I am hollow sphere.
I am fish.
I float.
I evolve.
I grow.
I am whole.

I am ontogeny.
I am pressured.
I descend.
I escape.
I am detached.
I am free.

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