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Radiographic Asbestosis Is Not a Prerequisite for Asbestos-Associated Lung Cancer in Ontario Asbestos–Cement Workers

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In recent years, controversy has developed about whether pre-existing asbestosis is a prerequisite for the diagnosis of asbestos-related lung cancer. This paper presents the results of a prospective study, in a cohort of Ontario asbestos–cement workers, of lung cancer in relation to radiographs obtained 20 and 25 years from first exposure to asbestos. Radiographs were interpreted by a single NIOSH-certified "B" reader, and asbestosis was defined to mean an ILO code of 1/0 or greater. There were 143 subjects (123 without asbestosis, 20 with asbestosis), with a radiograph available for interpretation at 20 years from first exposure or later. The lung cancer standardized mortality ratio (SMR) among men without asbestosis at 20 years latency was 5.53 (95%CI: 2.9–9.7). There were 128 subjects (114 without asbestosis, 14 with asbestosis) with a radiograph available for interpretation at 25 years from first exposure or later. The lung cancer SMR among men without asbestosis at 25 years latency was 5.81 (95%CI 2.7–11). The results of this study are consistent with those of epidemiologic studies of asbestos-exposed populations in a variety of exposure situations. These studies have demonstrated that lung cancer risk is elevated in the presence of radiographic asbestosis, but they have also shown that lung cancer risk may be elevated in the absence of radiographic asbestosis. Am. J. Ind. Med. 32:341–348, 1997.

KEY WORDS: epidemiology; cohort study; asbestosis; lung cancer; SMR

INTRODUCTION

In recent years a considerable controversy has developed about whether pre-existing asbestosis is a prerequisite for the diagnosis of asbestos-related lung cancer [Jones et al., 1996; Egilman and Reinert, 1996]. As discussed by Abraham [1994] the controversy "does not originate in science, but in litigation" and the acceptance of one position or the other can make a large difference in the outcome of litigation. This paper presents new data that address this issue.

In 1948 an American multinational corporation opened a factory for the manufacture of asbestos–cement products in Scarborough, Ontario. This was the same corporation that owned the Louisiana asbestos–cement plants studied by Hughes and Weill [1991]. In 1984, a colleague and I published a study of radiographic abnormalities in a longitudinal investigation of 181 production workers from this plant [Finkelstein and Vingilis, 1984]. With follow-up to 1980, it was observed that men with radiographic abnormalities had higher lung cancer mortality rates than men with normal radiographs. Because a "best evidence" classification of cause of death was used, no comparisons were made to the mortality experience of the general population and it was not possible to say whether the lung cancer risk of workers without asbestosis was increased in relation to members of the general population. Since information from this population is directly relevant to the question of asbestosis as a precursor to lung cancer, I have updated the mortality experience of the workers in this cohort to the end of 1985 and have compared their mortality experience to that of the general population of Ontario. A clear and unambiguous finding is that lung cancer mortality was significantly increased among workers without asbestosis on their radiographs.

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METHODS

The Factory and Exposure

The workers in this cohort were employed at a factory that manufactured asbestos–cement pipe and board from chrysotile and crocidolite asbestos, silica, and cement. Cumulative exposures to asbestos were calculated using a model that extrapolated measurements made by the personal membrane filter, a method that came into use 21 years after the plant opened in 1948 [Finkelstein, 1984]. Estimates of exposure to the silica component of the dust cloud are not available. Eighteen-year cumulative exposures were calculated by summing annual exposures during the 18 years from first exposure; later accumulations were generally well less than 10% of the 18-year totals.

The Study Population and Follow-up

The study cohort consists of production workers hired prior to 1960, who were employed for 9 years or more, and who worked for at least 12 months in asbestos exposure. There were 186 men who were eligible for inclusion. At least one radiograph was available for interpretation for 151 men; these are the subjects of the present study. Mortality in the cohort was ascertained to the end of 1985 by record linkage to the Canadian Mortality Database at Statistics Canada.

The Radiographs and Their Interpretation

While employed, workers received annual chest radiographs as part of their routine medical surveillance by the Occupational Chest Disease Service of the Ontario Ministry of Labour, and most of these films were available. Many long-service employees returned for ongoing surveillance after separation, and others who had filed claims with the Workers' Compensation Board were also followed by the Chest Service. In 1980, former workers who had not had a recent radiograph were invited to return for an examination, and we sought radiographs of deceased workers from hospitals.

Radiographs (posteroanterior projections) were interpreted by a single National Institute for Occupational Safety and Health (NIOSH)-certified "B" reader using the 1971 ILO Classification of Radiographs of the Pneumoconioses as reference standard. Film quality was somewhat variable (most films had been obtained during routine surveys), but it was believed that reasonably consistent interpretations could be made. File folders were retrieved and stacked in unordered sequence. Individual files were examined in known temporal order. To avoid coding many normal films, the files were usually scanned quickly to find the earliest abnormal film, and this film and later ones taken at approximately 5-year intervals (determined by film quality) were coded. Radiographs were interpreted without knowledge of the worker's cumulative exposure category, the last year he had worked in asbestos exposure, or his smoking habit.

Smoking Information

Beginning in the early 1970s, pulmonary function technicians obtained smoking information at the annual examinations. Missing information was sought by interview and from physicians' records. Men were classified as never smokers, as ex-smokers if they had given up cigarettes within 10 years of first exposure, or as current smokers if they smoked cigarettes beyond 10 years from first exposure.

Statistical Analysis

The radiographic abnormalities selected for analysis were small irregular opacities and bilateral pleural thickening, both associated with asbestos exposure. Radiographic asbestosis was defined as the presence on the radiograph of small irregular opacities, ILO category 1/0 or more. It was previously reported that asbestosis was a progressive disorder in this cohort [Finkelstein and Vingilis, 1984]. I thus selected three evaluation times: 20 years; 25 years, 30 years from first exposure as times at which to classify the workers with respect to asbestosis and to begin mortality follow-up. Comparison was made to the mortality experience of the general population of Ontario using the person-years computer program [Coleman et al., 1986]. Confidence intervals (95%CI) were computed assuming a Poisson distribution for the numbers of observed deaths. Cox proportional hazards regression analysis was used to examine risk while controlling for confounders [SPSS, 1994].

RESULTS

The 1984 [Finkelstein and Vingilis, 1984] study demonstrated that the risk of developing radiographic asbestosis depended on the time from first exposure and on the cumulative exposure to asbestos. The time of assessment is thus important, since a worker without asbestosis at 20 years may have progressed to clinical asbestosis at 25 years from first exposure.

Mortality in Relation to Radiographic Asbestosis (Small Opacities ≥ 1/0)

Mortality in Relation to Radiographic Coding at 20 Years from First Exposure

There were 143 subjects (123 without asbestosis, 20 with asbestosis) with a radiograph available for interpretation at 20 years from first exposure or later. Table I shows the standardized mortality ratios (SMRs). All Cause mortality

TABLE I. Standardized Mortality Ratios in Relation to Latency and Radiographic Asbestosis: Asbestosis = ILO ≥1/0

		20 years latency				25 years latency				30 years latency			
Cause of death	Asbestosis	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
All causes	No	45	22.2	2.02	1.47–2.70	36	14.8	2.43	1.70–3.36	1	2.25	0.44	0.01–2.45
	Yes	15	4.4	3.43	1.92–5.66	9	2.24	4.01	1.83–7.61	11	2.66	4.13	2.06–7.39
All malignancies	No	28	6.03	4.65	3.09–6.72	23	4.23	5.44	2.68–6.35	0	0.68	0	—
	Yes	5	1.14	4.39	1.42–10.2	3	0.61	4.92	1.01–14.4	6	0.75	7.99	2.93–17.4
Digestive cancer ICD 150–159	No	8	1.84	4.34	—	7	1.27	5.50	—	0	0.20	0	—
	Yes	1	0.36	2.76	—	1	0.19	5.32	—	3	0.23	13.20	—
Lung cancer	No	12	2.17	5.53	2.86–9.66	9	1.55	5.81	2.66–11.0	0	0.25	0	0–8
	Yes	4	0.40	9.96	2.71–25.5	2	0.22	9.20	1.11–33	2	0.27	7.46	0.90–27
Pleural mesothelioma	No	3	—	—	—	2	—	—	—	0	—	—	—
	Yes	0	—	—	—	0	—	—	—	1	—	—	—
Circulatory disease	No	8	11.0	0.73	0.3–1.4	7	7.26	0.96	0.4–2.0	1	1.08	0.93	0.02–5.2
	Yes	5	2.30	2.18	0.7–5.1	3	1.16	2.59	0.5–7.6	2	1.33	1.50	0.2–5.4
Respiratory disease	No	3	1.28	2.35	0.5–6.9	2	0.89	2.26	0.3–8.2	0	0.14	0	—
	Yes	4	0.29	13.80	3.76–55	3	0.16	19.30	4.0–56	1	0.19	5.20	0.1–29
Pneumoconiosis	No	1	0.06	18.00	—	0	0.04	0	—	0	0.01	0	—
	Yes	2	0.01	—	—	1	0.01	—	—	1	0.01	—	—

was significantly increased among both groups: 3.43 among the men with asbestosis, and 2.02 among the men without asbestosis. Mortality from digestive cancer (including peritoneal mesothelioma) was significantly elevated in both groups. Overall, there were three carcinomas of the stomach, one of the rectum, four peritoneal mesotheliomas, and one gastrointestinal carcinoma with uncertain primary.

With respect to lung cancer, the lung cancer SMR among men without asbestosis at 20 years latency was substantially and significantly elevated at 5.53. The lung cancer SMR among the men with asbestosis was almost twice as high but, because of the small sample size, the confidence intervals overlapped, and there was no significant difference between the two groups of workers.

Workers with asbestosis had an increased SMR for circulatory disease, but the increase was not significant. Both groups of workers had increased mortality from respiratory disease, including pneumoconiosis.

Mortality in relation to radiographic coding at 25 years from first exposure

There were 128 subjects (114 without asbestosis, 14 with asbestosis) with a radiograph available for interpretation at 25 years from first exposure or later. Table I shows the SMRs. All cause mortality was significantly increased among both groups: 4.01 among the men with asbestosis and 2.43 among the men without asbestosis. With respect to lung cancer, the lung cancer SMR among men without asbestosis at 25 years latency was significantly elevated at 5.81. The lung cancer SMR among the men with asbestosis was almost twice as high, but, because of the small sample size, the confidence intervals overlapped, and there was no significant difference between the two groups of workers. Workers with asbestosis had an increased SMR for circulatory disease, but the increase was not significant. Both groups of workers had increased mortality from respiratory disease.

Mortality in relation to radiographic coding at 30 years from first exposure

There were only 33 subjects (15 without asbestosis, 18 with asbestosis) who were still alive and had sufficient time from first exposure to have a radiograph available for interpretation at 30 years from first exposure or later. Table I shows the SMRs. All cause mortality was significantly increased among the men with asbestosis, but there was only one death, versus 2.25 expected among the men without asbestosis. There were two deaths from lung cancer, both among men with asbestosis. The number of subjects was so small that the SMR, 7.46, among men with asbestosis was not statistically significant.

Investigations of Other Factors Potentially Associated With Lung Cancer Mortality

Cumulative exposure

Workers were divided among the five exposure categories used in the 1984 asbestosis paper [Finkelstein and Vingilis,

TABLE II. Lung Cancer Standardized Mortality Ratios in Relation to Cumulative Exposure: Follow-up from 20 Years After First Exposure

Cumulative exposure	Obs	Exp	SMR (95%C.I.)
<50 f-y/ml[a]	2	0.35	5.76 (0.7–21)
50–99 f-y/ml	5	0.91	5.51 (1.8–12.9)
100–149 f-y/ml	7	0.73	9.60 (3.9–20)
150–199 f-y/ml	3	0.44	6.87 (1.4–20)
≥200 f-y/ml	3	0.33	9.06 (1.9–26)

[a]f-y/ml = fiber-years/ml.

1984]. The results for lung cancer are presented in Table II. There is the suggestion of increasing lung cancer SMRs with increasing cumulative exposure, but the confidence intervals are very wide, and there are no significant differences among the exposure groups. In this small group of men, the influence of competing causes of death such as mesothelioma, gastrointestinal cancer and asbestosis has a substantial influence on the observed mortality rates for lung cancer. Figure 1 shows the mortality rates for lung cancer, as well as for "all asbestos diseases" in relation to exposure. The pattern for "all asbestos diseases" is more monotonic than is the one for lung cancer.

Smoking

Beginning in the early 1970s, pulmonary function technicians obtained smoking information at the annual examinations. Missing information was sought by interview and from physicians' records. Men were classified as never smokers, as ex-smokers if they had given up cigarettes within 10 years of first exposure, or as current smokers if they smoked cigarettes later than 10 years from first exposure. For analysis here, the former and current smokers were combined. The only deaths from respiratory disease occurred among the smokers (Obs = 7, Exp = 1.32, SMR = 5.32). However, three men who reported that they had never smoked died of lung cancer, and there was no difference in lung cancer SMRs between the smokers (Obs: 14, Exp: 2.18, SMR: 6.44) and nonsmokers (Obs = 3, Exp = 0.49, SMR = 6.18).

Multivariable analysis

Cox regression analyses were performed in order to examine the simultaneous effects of all the lung cancer risk factors. It must be emphasized that the Cox analyses provide only internal comparisons, and do not permit comparison with the general population. Analyses were conducted using the asbestosis classifications at 20 and 25 years latency. The results essentially reproduce the relationships in the SMR calculations shown previously. Of the four variables considered: age, asbestosis, smoking, and cumulative exposure, only age was significantly associated with lung cancer risk. For asbestosis as a risk factor, the relative risk for lung cancer for men with asbestosis, compared to men without, was 1.4 ($P = 0.58$). This compares with a ratio of 1.8 for the SMRs for lung cancer in Table I.

Time-dependent Cox analysis

The probability of development of radiographic asbestosis increases with time from first exposure. This issue was addressed previously by examining risk in relation to three evaluation times at 20, 25, and 30 years from first exposure. Another approach is to follow the cohort through time and to take note of the time at which asbestosis is diagnosed. This approach was carried out with a time-dependent analysis. Of the four variables considered: age, asbestosis, smoking, and cumulative exposure, only age was significantly associated with lung cancer risk. For asbestosis as a risk factor, the relative risk for lung cancer for men with asbestosis, compared to men without, was 2.3 ($P = 0.15$; 1-tailed $P = 0.07$). This compares with a ratio of 1.8 for the SMRs for lung cancer in Table I.

Pleural thickening

There were only three workers at each of 20, 25, and 30 years latency who had pleural thickening as the only

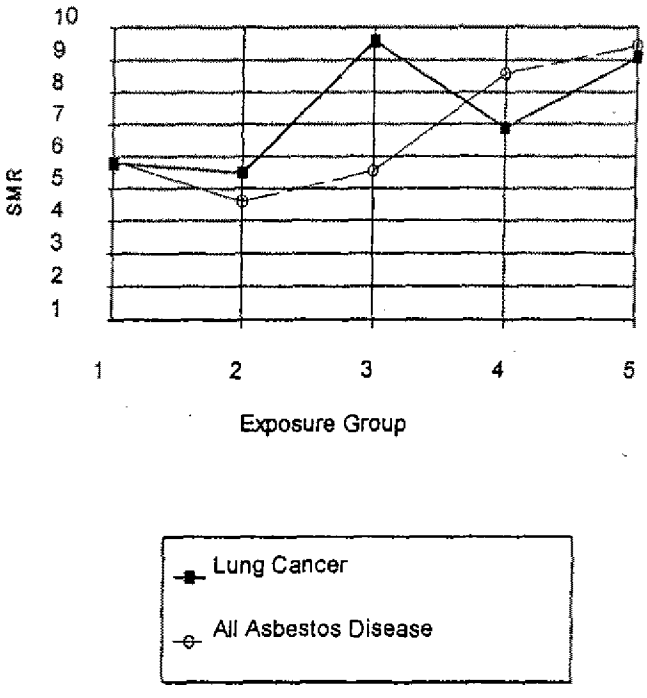

FIGURE 1. SMRs for lung cancer and all asbestos-ssociated disease in relation to estimates of 18-year cumulative exposure. Group 1: <50 f-y/ml; group 2: 50–99 f-y/ml; group 3: 100–149 f-y/ml; group 4: 150–199 f-y/ml; group 5: ≥200 f-y/ml (f-y/ml = fiber-years/ml).

radiographic abnormality. All three workers survived to the end of follow-up.

DISCUSSION

There has been substantial controversy in recent years as to whether asbestosis is a prerequisite for the development of asbestos-related lung cancer. Much weight has been given in these discussions to the results of Hughes and Weill [1991] from a study at a New Orleans asbestos–cement manufacturer. Hughes and Weill used the results from a 1969 radiographic survey of the workforce as input to a prospective study of mortality. By coincidence, in 1984 I had published the results of a prospective study of the relationship between asbestosis and mortality among Ontario employees of the same multinational corporation [Finkelstein and Vingilis, 1984]. The present analysis updates the mortality experience to the end of 1985 and carries out comparisons with the general population of Ontario.

Several important characteristics of radiographic asbestosis must be borne in mind. First, asbestosis is a disorder that usually takes 15 or more years to become evident and which often progresses in severity. Second, the probability of developing asbestosis is related to the amount of asbestos dust inhaled. Third, workers who smoke have a higher probability of being diagnosed with asbestosis than workers who do not smoke [Finkelstein and Vingilis, 1984]. These factors are consistent in the prediction that workers without asbestosis will have a lower lung cancer risk than will workers with asbestosis, since workers without asbestosis will, on average, have inhaled less dust and have smoked less than workers with asbestosis. The question at issue is whether workers exposed to asbestos, but without asbestosis, might have a risk of lung cancer increased above the baseline risk in the general population.

In this study, radiographic asbestosis was defined to mean an ILO code for small irregular opacities of 1/0 or more. The radiographs in this study were interpreted by a single NIOSH-certified "B" reader (Dr. J. Vingilis). Workers without asbestosis were found to have an increased risk of lung cancer, but might the reader have coded as normal those films that other readers would have coded ILO category 1/0 or more? One piece of evidence that the radiographic coding was valid and consistent is the dose-response relationship observed between the risk of asbestosis and estimates of cumulative exposure [Finkelstein and Vingilis, 1984]. In addition, Table 5 of the 1984 paper [Finkelstein and Vingilis, 1984] shows a comparison of the radiographic codes and histologic findings for 26 workers from the cohort. The pathologic interpretations were made by a number of local pathologists without any uniform protocol for grading the specimens. In general, the opinions of the radiologist and the pathologists were in reasonable agreement with respect to the presence or absence of asbestosis but, in a number of instances, the pathologists reported histologic asbestosis while the radiologist did not code radiographic asbestosis. Kipen and colleagues [1987] reported on pathologic–radiologic comparisons in 138 lung cancer cases from the American insulation workers study. All 138 cases had histological evidence of parenchymal fibrosis, but in 25 (18%) there was no radiographic evidence of fibrosis. There was no significant difference between Vingilis and Kipen and colleagues with respect to the proportion of subjects who had histologic asbestosis but whose radiographs were coded $<1/0$.

Analysis of the Ontario data shows that asbestos–cement workers without radiographic asbestosis had a significantly increased risk of lung cancer in comparison to men in the general population. An advantage of this study over those which use cross-sectional data is that the employees of the plant were under annual surveillance by the Occupational Chest Disease Service of the Ontario Ministry of Labour, so that temporal changes in their chest x-ray status could be assessed. Increased lung cancer risk among workers without asbestosis was apparent in relation to classifications of the radiographs at 20 and 25 years from first exposure to asbestos. There were no lung cancer deaths observed among workers without asbestosis at 30 years latency, but the number of surviving workers was so few that only 0.25 deaths were expected. The 95% confidence interval on the lung cancer SMR at 30 years latency ranged from 0 to 8.0.

Surprisingly, we found no relation between lung cancer risk and smoking habit. Three of 20 men with lung cancer reported that they had never smoked. I suspect that these men were misclassified as never-smokers. In any event, the lung cancer risk in the cohort was so large that any misclassification of smoking habits will not alter the conclusions about lung cancer risk in comparison with the general population. A higher prevalence of smoking among blue collar workers might be expected to increase the lung cancer SMR by only about 20% [Finkelstein et al., 1987].

Figure 1 shows that lung cancer risk tended to increase with exposure, but there was no significant relation between estimates of cumulative exposure and lung cancer risk in this cohort. This is probably related to the small population size (which resulted in wide confidence intervals on the estimates of SMR) and the effects of "competition" from other asbestos-related causes of death.

How do the results of this study of Ontario asbestos–cement workers compare with those of Hughes and Weill from New Orleans? There are some difficulties in making the comparison. Hughes and Weill included two New Orleans plants in their studies. Plant 1 was housed in a single building and manufactured building products; Plant 2 consisted of four separate buildings, each manufacturing different products, including asbestos–cement pipe. The lung cancer risk in these two New Orleans plants was very different, being twice as high in Plant 2 as it was in Plant 1

TABLE III. Comparison of New Orleans and Ontario Studies of Asbestos–Cement Workers

	Ontario plant				New Orleans plant (all latencies)			
Latency (Ontario)	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
I. Small Opacities ≥1/0								
20 yr	4	0.40	9.96	2.7–25	9	2.1	4.32	1.98–8.2
25 yr	2	0.22	9.20	1.11–33	—	—	—	—
30 yr	2	0.27	7.46	0.90–27	—	—	—	—
II. No radiographic asbestosis								
20 yr	12	2.17	5.53	2.86–9.96	16	13.3	1.20	0.69–1.95
25 yr	9	1.55	5.81	2.66–11	—	—	—	—
Total (no asbestosis):								
Ontario (20 yr) and New Orleans					28	15.5	1.81	1.20–2.61
Total (no asbestosis):								
Ontario (25 yr) and New Orleans					25	14.9	1.68	1.09–2.48

[Hughes et al., 1987]. Despite these differences in lung cancer mortality rates , Hughes and Weill [1991] combined the populations for their analysis of asbestosis and mortality. They indicate [Hughes and Weill, 1991: pg 231) that all the excess mortality occurred in the second plant, but they do not specifically tell us about the relationship between asbestosis and mortality at the second plant. We are thus presented with a mixture of two workforces, one with an increased risk of lung cancer and the other without. The Ontario facility was similar to Plant 2, comprising a number of buildings for the manufacture of different asbestos–cement products, including pipe, in addition to rockwool and fibreglass insulations. Ideally, one would want to compare the Ontario workers with those from Plant 2 in New Orleans, but this is not possible with the data presented by Hughes and Weill.

Table III compares the results of the Ontario and New Orleans asbestos–cement studies. For workers with asbestosis, that is, among men with small opacities of ≥1/0, the lung cancer rates in both plants were very high. The rates were higher in Ontario, but the confidence intervals overlap, and there is no significant difference between New Orleans and Ontario for workers with small opacities ≥ 1/0. Now, what about workers without asbestosis? As shown in Table III, lung cancer mortality was high and significantly increased among the Ontario workers. Mortality was increased among the New Orleans workers without asbestosis, but not significantly so. In the last rows of the Table, I have combined the lung cancer experience of the New Orleans and Ontario asbestos–cement workers without asbestosis. We see that the combined SMRs are significantly greater than 1.0 even when the experience of the New Orleans Plant 1 workers was included. We can thus conclude that lung cancer risk was significantly increased among asbestos–cement workers, in the combined populations, who did not have radiographic asbestosis.

The finding of increased lung cancer risk among asbestos–cement workers without radiographic asbestosis is consistent with epidemiologic findings in other settings. In fact, epidemiologic studies show that lung cancer risk may be increased among workers with, and without, radiographic asbestosis, and among workers with, and without, histologic asbestosis. The major studies are discussed below.

Liddell and McDonald [1980] studied mortality, during 1967–1975, in a cohort of 4559 Quebec chrysotile miners and millers, in relation to the coding of the most recent radiograph obtained before 1967. There were 119 deaths from lung cancer, as compared to an expectation of 67. Among workers with small opacities ≥0/1, the lung cancer SMR was 3.1 (33 observed; 10.6 expected). See the Appendix for the details of a computation that demonstrates that among workers without small opacities the lung cancer SMR was 1.51 (95%CI: 1.21–1.87).

Hillerdal [1994] conducted a prospective cohort study of 1,596 men from the general population of Uppsala, Sweden, who were found to have pleural plaques on their radiographs. Interviews revealed that 95% of the subjects had a history of exposure to asbestos. During follow-up from 1963 to 1985, the lung cancer SMR was 2.3 for men with parenchymal asbestosis, category 1/0 or more. The lung cancer SMR was also significantly increased for men with asbestos exposure but with ILO code <1/0, that is, without parenchymal asbestosis (SMR = 1.4; 95%CI = 1.04–1.97).

deKlerk and colleagues [1996] reported on the risk factors for lung cancer in a case-control study among Australian crocidolite miners. In a logistic regression model, both radiographic asbestosis (Category 1/0 or more) and cumulative exposure to asbestos fibers were significantly

associated with lung cancer risk. This suggests that lung cancer risk increased with cumulative exposure even among miners without asbestosis, so that some cases of lung cancer attributable to asbestos exposure must have occurred among the miners without asbestosis.

The epidemiologic studies are consistent in their estimates of the additional risk attributable to asbestosis. In the Ontario study, the time-dependent Cox analysis found a relative risk of 2.3 for men with asbestosis in comparison to men without radiographic asbestosis. In the study conducted by Hillerdal [1994], the relative risk was 1.6. In the chrysotile study reported by Liddell and McDonald [1980], the relative risk for miners with small opacities ≥ 0/1 compared to men without small opacities was 2. Among Australian crocidolite miners [deKlerk et al., 1996], the relative risk for miners with opacities of ≥1/0 was 2.5. Compared to workers without radiographic asbestosis, workers with small opacities have a risk of lung cancer that is increased 1.5- to 2.5-fold, but asbestos-exposed workers without radiographic asbestosis have a risk of lung cancer increased above that among members of the population without asbestos exposure.

The only study of histologic asbestosis and lung cancer risk in humans is the case-control study conducted by Sluis-Cremer and Bezuidenhout [1989] among South African amphibole miners. They found that among miners with even slight histologic asbestosis, the relative risk of lung cancer was increased 4.5-fold. However, similar to the study conducted by deKlerk et al. [1996] in Australia, both the asbestosis term, and an exposure term (years of exposure) were each significant in a logistic regression model. This again suggests that lung cancer risk increased with exposure, even among men without histologic asbestosis. The authors fitted additional regression models using cumulative exposure (f-y/ml) and residence-time-weighted exposure as the exposure metrics. In neither of those models was the exposure term significant. A reasonable interpretation is that the conversion of particle counts to fibers was so crude that the exposure measures bore little relation to lung dose.

CONCLUSIONS

Epidemiologic studies of asbestos-exposed populations in a variety of exposure situations have demonstrated that lung cancer risk is elevated in the presence of radiographic asbestosis, but they have also shown that lung cancer risk may be elevated in the absence of radiographic asbestosis. These studies of North American asbestos–cement workers, Quebec chrysotile miners and millers, Australian crocidolite miners, and Swedish citizens demonstrate clearly that radiographic asbestosis is not a prerequisite for asbestos-associated lung cancer. In addition, the study of Sluis-Cremer and Bezuidenhout [1989] found that lung cancer risk is significantly elevated in the presence of even slight histologic asbestosis, but also that lung cancer risk may be increased in the absence of histologic asbestosis.

Data published in the last decade demonstrate that the statement "radiographic asbestosis is a prerequisite for asbestos-attributable lung cancer" is logically untenable. The reasoning is as follows:

1. Histologic asbestosis may be present when the radiograph is normal. Kipen and colleagues [1987] found that mild, moderate, and severe histologic asbestosis could occur in the presence of a normal radiograph. Based on his extensive experience in South Africa, Sluis-Cremer [1989, p. 540] wrote "slight asbestosis is commonly, and moderate asbestosis occasionally, undetected radiologically."
2. Histologic asbestosis is a marker for increased lung cancer risk. Sluis-Cremer and Bezuidenhout [1989] found that, in comparison to miners without histologic asbestosis, miners with histologic asbestosis had an increased risk of lung cancer of fourfold or greater.
3. It follows that lung cancer risk may be increased among asbestos-exposed workers even in the presence of a normal radiograph.

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APPENDIX: CALCULATION OF THE SMR FOR MINERS WITHOUT SMALL OPACITIES IN THE STUDY OF LIDDELL AND MCDONALD [1980]

In the total cohort, there were 119 lung cancer deaths and 67 expected. The SMR was thus 1.77 and there were 52 excess lung cancer deaths. On page 266, the authors state that among 118 cases for which data were available, there were 33 lung cancer deaths among workers with small opacities. There were thus 118 - 33 = 85 lung cancer deaths among workers without small opacities. Table V of the paper cited above shows that among workers with completely normal films, there were 49 lung cancer deaths and the SMR was 1.08. Therefore, the number expected was 45.4. Table VI of the paper cited above shows that the relative risk for men with small opacities in comparison to men with normal films was 2.88. Now relative risk = SMR_1 / SMR_2 = Obs/Exp/1.08 = 33/Exp/1.08 and the number of expected deaths for men with small opacities was 10.6. Now, the total expected was 67, while the numbers expected for miners with normal films was 45.4 and for men with small opacities was 10.6. Therefore, the number expected for men with all other abnormalities was 67 - 45.4 - 10.6 = 11. Therefore, the number of lung cancer deaths expected among all men without small opacities was 45.4 + 11 = 56.4. The lung cancer SMR for miners without small opacities was thus Obs/Exp = 85/56.4 = 1.52 (95%CI: 1.21–1.87).