Cancer in Ex-Asbestos Cement Workers in Israel, 1953–1992

Theodore H. Tulchinsky, MD, MPH,[1*] Gary M. Ginsberg, DrPH, MSc,[2] Jose Iscovich, MD, MSc,[3] Shihab Shihab, MD, MPH,[4] Alf Fischbein, MD,[5] and Elihu D. Richter, MD, MPH[6]

A cohort of 3,057 male workers employed in an asbestos-cement plant using 90% chrysotile-10% crocidolite, located in Northern Israel, was followed from 1953–1992 for incidence and mortality from cancer. In the years 1978–1992, the cohort had an elevated risk for all malignant neoplasms combined (n = 153, SIR = 117, ns), lung cancer (n = 28, SIR = 135, ns), mesothelioma (n = 21; SIR >5000, p < .0001), unspecified pleural cancer (n = 5; SIR = 278, P < .0001), and liver cancer (n = 7, SIR 290, ns). Risks for colo-rectal (n = 19; SIR = 79, ns), bladder (n = 12, SIR 69) and renal cancers (n = 5, SIR 104) were less than expected. Risk for mesothelioma showed a sharp risk gradient with duration of exposure, increasing from 1 per 625 for those employed less than 2 years to 1 per 4.5 workers employed over 30 years. The ratio of mesothelioma to excess lung cancer cases was 2.9 to 1, or 3.6 to 1, if pleural cases of unspecified origin were included; the pleura to peritoneum ratio of verified mesothelioma cases was 20 to 1. This atypically high ratio of mesothelioma to excess lung cancer cases is suggested to be the combined result of high past asbestos exposures in the workers and their low prior risk for lung cancer, and possibly, relatively early smoking cessation in relation to asbestos exposure. Am. J. Ind. Med. 35:1–8, 1999. *© 1999 Wiley-Liss, Inc.*

KEY WORDS: asbestos; cancer; mesothelioma; asbestos workers; Israel; occupational health

INTRODUCTION

Risks for lung cancer, malignant mesothelioma (hereafter mesothelioma), and certain other cancers are increased in asbestos material production workers [Nicholson and Raffn; 1995; Smith and Wright, 1996; Albin et al.; 1990, Berry, 1994; Hughes et al. 1987]. To assess these risks in Israel, we examined a cohort of ex-asbestos cement production workers from the start of the plant in 1953 through 1992.

In 1978, a follow-up study of this cohort (n = 3,653) reported no excess lung cancer, and only one case of mesothelioma in an ex-worker with less than 2 years of exposure [Djerassi et al., 1970, 1979]. These workers had been exposed to a mixture of chrysotile to crocidolite asbestos in a ratio of 9:1. However, the lapsed time from onset of exposure for the overwhelming majority of workers in the study was less than the expected latency period of 25 years or more associated with most asbestos-related excess cancers. Subsequent mortality studies up to 1984 and 1990 in this group showed excess mesothelioma, lung, and nasopharyngeal cancer rates, with greater excess of mesothelioma than lung cancer [Richter et al., 1984; Baum, 1986; Tuch et al., 1986; Tulchinsky et al., 1992]. A report of cancer incidence for the total populations by region of residence in Israel showed an elevated rate for lung cancer in the

[1]Department of Preventive Health Services, Ministry of Health, Jerusalem, Israel
[2]Department of Technology Assessment, Ministry of Health, Jerusalem
[3]National Cancer Registry, Jerusalem
[4]Acco Public Health Office, Acco
[5]Department of Research and Developmental Health, Sanz Medical Center, Netanya
[6]Department of Environmental and Occupational Health, Hadassah-Hebrew University, Faculty of Medicine, Jerusalem
*Correspondence to: T.H. Tulchinsky, c/o Ministry of Health, 2 Ben Tabai St., POB 1176, Jerusalem, Israel 91010, Fax: 001 972 2 6679 5816; E-mail: dudtedy@matat.health.gov.il.

Contract grant sponsor: Committee on Prevention of Occupational Health and Safety Hazards; Contract grant sponsor: Ministry of Labor and Social Affairs of Israel; Contract grant sponsor: Society for Health and Education in Israel; Contract grant sponsor: Asbestos Worker Injury Association.

Accepted 1 August 1998

© 1999 Wiley-Liss, Inc.

populations of the Acco sub-district, in the Western Galilee, north of Haifa, where the asbestos cement plant is located [Ginsberg and Tulchinsky, 1992].

Environmental sampling in the 1960s and 1970s in the asbestos cement factory showed levels in the plant ranging from 1.5 to 14.0 fibers/cc in storage areas and 0.3–40.0 fibers/cc in processing and molding areas [Richter et al., 1995]. Environmental controls including enclosure, separation, and process exhaust systems, were introduced in the late 1970s with a consequent reduction in asbestos ambient levels in the plant. In 1978, a Threshold Limit Value-Time Weighted Average (TLV-TWA) of 5.0 fibers/cc was mandated by the Ministry of Labor and Social Affairs.[1] In the 1980s, asbestos exposure levels were reported to be generally under levels of 0.4 fibers/cc [Ginsberg and Tulchinsky, 1992; Richter et al., 1995], though above levels of 0.1 fibers/cc [Tulchinsky et al., 1992; Ginsberg and Tulchinsky, 1992], the threshold for detection of asbestos fibers by phase contrast microscopy and the health-based threshold recommended by NIOSH in 1976. The present study extends previous work and reports on cancer risk in relation to onset and duration of exposure for a total cohort of 3,057 male Jewish ex-asbestos workers for lung cancer, mesothelioma, and other cancers. We examine findings on the mesothelioma to excess lung cancer ratio in this cohort and discuss possible interpretations. The findings are of interest in that baseline lung cancer incidence and mortality for males in Israel is less than one-half that of most European and North American countries [Rennert et al., 1988; Coleman et al., 1993; American Cancer Society, 1994; World Health Organization, 1996, 1998].

METHODS

Data Sources

Lists of all persons formerly employed in the asbestos-cement plant were used to define the cohort. The National Population Register was used for calculating population-based risks. The National Death Registry and the population-based National Cancer Registry were used to obtain lists of cases of cancer.

Study Population: Methods

The initial cohort (n = 4,441) was identified by computer listings of ex-workers of the plant provided by the management on request from the Ministry of Health. These lists contained demographic data, which enabled us to assess age, time of onset of employment and duration of exposure.

1. Compilation of Regulations (Kovetz Hatkanim), 4576. Regulations for Work Safety Regarding Asbestos. Ministry of Labor and Social Affairs. Jerusalem: Israel Government Office, January 1984 (in Hebrew).

TABLE I. Distribution by Onset and Duration of Exposure of a Cohort of Male, Jewish Ex-Asbestos Workers (Duration of Exposure, 1946–1992)

Onset	0–2	3–4	5–9	10–19	20–24	25–29	30+	Total
1946–52	2	3	2	21	3	4	1	36
1953–59	174	35	44	75	46	44	15	433
1960–66	820	130	112	77	32	9	0	1,140
1967–73	584	33	31	49	0	0	—	697
1974–80	380	42	44	9	0	—	—	475
1981–92	267	9	0	0	—	—	—	276
Total	2,227	252	233	191	81	57	16	3,057

We were also able to link to case registries. Demographic data on the workers were corroborated with data from the population registry. After this process, 250 (6% of total) persons were excluded because of duplicate or incomplete registrations or having been employed for less than one month. In this study, women office workers (n = 632), generally located away from direct exposure, were not included. Also excluded were non-Jewish male workers (n = 502) because national incidence rates for this group are based on small numbers; moreover, they did not enter the workforce in this factory until the late 1970s and early 1980s. Therefore, the final study cohort consisted of 3,057 Jewish male ex-workers, with 2,419 having at least 1 month of exposure and the remaining 588 whose duration of exposure was uncertain.

Study Population: Exposure Onset and Duration

The work force was analyzed by number of exposed workers, and by onset and duration of exposure. There was a large and sudden expansion of the work force starting in 1960, but even then, there was a high turnover of workers with many employed less than 2 years. The average employment time of a cohort member was only 3.4 years (SD + 6.1 years; range 0.5–33.0) (Table I) . Of the total cohort, 43.1% were employed less than one year, 38.0% for 1–4 years, 7.6% for 5–9 years, 6.2% for 10–19 years, while 5.1% worked for 20 or more years. In 1978, 3.3% of the workers employed at that time were 15–19 years old, 22.7% were 20–29, 28.5% were 30–39, 19.9% were 40–49, 15.4% were 50–59, 3.8% were 60–64, and 6.3% were 65 and over. Approximately 42.3% of the cohort were born in Africa or Asia, 30.8% in Europe or the Americas, and 26.9% in Israel. Some 42% of the total worker population worked on the shop floor in the manufacturing, mixing, or cutting process, and were in direct contact with the asbestos for most of the day.

Outcome Data Sources: Cancer Cases

We used multiple data sources to search for cases and maximize sensitivity and specificity of case finding and confirmation. By computer matching our list of ex-workers with vital records of the Ministry of Interior National Death registry up to 1992, we were able to identify individuals likely to have died of cancer. We then verified causes of death by computer searches of vital records of the Acco Public Health Office for all listed causes of deaths of the ex-workers since 1988. For deaths prior to 1988, manual searches of archival death certificates were carried out. Additional cases were obtained from worker organizations and cases under litigation. Cause of death was confirmed at the Acco Public Health Office.

The study file was linked and cross-matched with the National Cancer Registry File. The Cancer Registry was used to verify suspected cancer cases in our cohort and to provide data on possible new cases of cancers. Israel's National Cancer Registry is based on multiple-systems of identification and verification and follow-up of all cancer cases, including documentation of supportive evidence [Steinitz et al., 1989].

Lung and other cancer cases were considered to be true-positives even when the diagnosis was based on clinical and radiological findings without histological confirmation. Mesothelioma cases were included only if the diagnosis was based on histological examination of tissue removed at autopsy or by biopsy by a registered pathologist. Diagnosis of mesothelioma cases based only on radiology, cytology, or unexpected autopsy findings unconfirmed by histological examination were considered as unconfirmed and recorded under the rubric of ''other cancers.''

Analysis of Data

National, age, regional, sex, and ethnic origin (i.e., born in Africa, Asia, Europe/America, or Israel) specific rates were calculated for cancers at all sites and site-specific cancers (National Cancer Registry data) for the Jewish male population (minus those in the cohort). These rates were applied to the cohort for the years 1978–1992 in order to calculate expected incidence rates.

The expected incidence of lung cancer and mesothelioma for the cohort was calculated comparing rates in our cohort to national and age specific incidence rates for Jewish males minus those in the cohort for the years 1978–1992. Standardized Incidence Ratios (SIR) were calculated by the formula: SIR = O/E, where O = observed incidence in the cohort and E = expected incidence based on the national rates [Ginsberg and Tulchinsky, 1992]. The standard error of the SIR, SE = SIR/O (observed), was used to calculate confidence intervals. Logistic regression analyses were carried out with lung cancer and mesothelioma cases as dependent variables. The independent variables were years of exposure, year of onset of exposure, and age of worker at commencement of employment.

TABLE II. Standardized Incidence Ratios (SIR) for Selected Cancers in a Cohort of Male Jewish Ex-Asbestos Workers, Israel 1978–92*

Malignant neoplasm site	Expected	Observed	SIR	95% confidence interval
Lung	20.7	28	135	85–185
Pleural*	0.2	5	2,777	343–5211
Mesothelioma	0.37	21	5,676	3,242–8,088
Liver	2.4	7	294	76–511
Colo-rectal	24.1	19	79	43–115
Renal	4.8	5	104	13–195
Bladder	18.4	12	65	28–102
Other	61.3	56	90	67–115
All sites	130.6	153	117	99–136

Cases reported originally as mesotheliomas but without histological confirmation.
Expected incidence is based on the Israel National Cancer Registry. Lung Cancer is ICD-9 162). Mesothelioma cases were recorded under Pleural (ICD-9 163) and Peritoneal (ICD-9 158) Cancers.

RESULTS

All Cancers

Table II shows the SIRs for various cancers occurring in this cohort. There was a higher, though not statistically significant (ns), overall standardized incidence rate for all cancer (SIR = 117; 95% CI:99,136).

Lung Cancer

Table II shows elevated lung cancer (ns) incidence in our cohort for the years 1978–1992 (SIR = 135; 95% CI: 85, 185); of the 34 identified cases of lung cancer, 6 were diagnosed prior to 1978. Over time there was a substantial decrease in SIR for lung cancer from 266 (95% CI 109, 394) during 1978–1981, to 251 (95% CI 108, 395) during 1982–1985. Thereafter, it continued to drop to 79 (95% CI 10, 148) during 1986–1989, and then to 17 (95% CI 0, 51) during 1990–1992. Population rates for lung cancer among Israeli males are addressed in the discussion.

The mean ages of diagnosis for lung cancer cases was 62.1 years (SE ± 10.0, range 48–85) and death was 63.6 years (SD ± 9.9, range 48–85). The mean latency period from onset of work to diagnosis was 22.4 years (SD ± 7.1, range 6–36). The mean period of exposure was 14.0 years (SE ± 10.1, range 0.5–30). For persons working 30 years or more, their probability for developing lung cancer was 7.7/100 (Fig. 1).

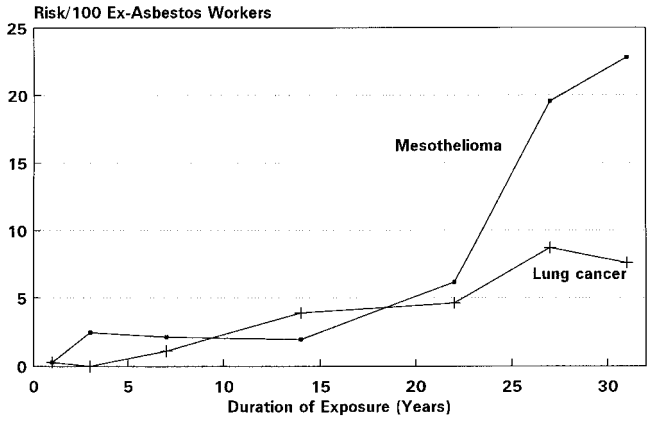

FIGURE 1. Mesothelioma and lung cancer risk by duration of exposure in male, Jewish ex-asbestos workers, Israel, 1958–1992.

Mesothelioma

One case of mesothelioma, possibly attributable to prior exposure in Europe, was identified prior to 1978. Use of multiple data sources resulted in identification of 32 suspect cases of mesothelioma between the years 1978–1992. These data sources include the National Death Registry, the Acco District Health Office (death certificate files), workers' organizations and from cases under litigation. Medical records and pathological reports excluded six cases, leaving 26. Of the 26, 21 had pathological findings from tissue biopsies providing definitive confirmation as malignant mesothelioma, with a pleural/peritoneal ratio of 20:1. Four of the remaining 5 cases had been diagnosed as mesothelioma on the basis of clinical findings and cytology examinations, but lacked pathological verification; one was diagnosed as mesothelioma but died abroad, thus we were unable to ascertain the basis of diagnosis.

The mean age at diagnosis of the 21 confirmed mesothelioma cases in years 1978–1992 was 59.7 years (SE $\pm$ 11.9; range 36–80); and the mean age of death was 60.5 years (SE $\pm$ 11.9, range 36–81). The mean period of exposure was 15.8 years (SE $\pm$ 12.1, range 0.5–30) and mean latency from onset of work to diagnosis was 26.0 years (SE $\pm$ 5.2, range 15–34).

Nationwide, during the years 1953–1992, there were a total of 201 cases of reported mesothelioma, 170 of which were reported between 1978–1992. Of these 170, 122 were males. The expected number of mesothelioma cases in a similar group (size, age, and ethnic origin distribution) of Israeli males for this period of time is 0.37 cases. The SIR for mesothelioma (Table II) in our cohort for the period 1978–1992 is 5,676 ($P < 0.05$; 95% CI 3,242, 8,088). Additional calculations showed that SIR increased from 7,159 (95% CI 143, 14,174; 4 cases) during 1978–1981 and 7,172 during 1982–1985 (95% CI: 883–13,421; 5 cases) to 9,093 (95% CI 2,792, 15,394; 8 cases) during 1986–1989. The rate subsequently fell to 5,142 (95% CI 103, 10,183; 4 cases) during the 1990–1992 period.

Mesothelioma: Within Country Comparisons

The national annual incidence rates of mesothelioma among Jewish Israeli males decreased from 2.4 per million during 1961–1970 to 1.8 per million in 1971–1980, but rose to 4.6 per million in 1981–1992 (Israel Cancer Registry, unpublished data). For the period 1961–1976, the cohort of asbestos-cement workers accounted for none of the 42 confirmed mesothelioma cases reported in Israel. For the years 1978–1984 and 1985–1992, this cohort accounted for 24.2% and 28.8%, respectively, of the national Jewish male mesothelioma incidence rates for all years since 1953; this fraction was 10.4%.

Analysis of geographical variation in mesothelioma incidence showed that the average annual Jewish male mesothelioma rate at the time of diagnosis in the Acco district was 12.1 per million during 1981–1992, compared to 2.1 per million for the male residents of the adjacent Northern Districts. Acco was the only district, or region, in Israel with a significantly increased SIR for mesothelioma.

Other Cancers

Five cancer cases were identified as undefined primary or secondary pleural cancer. They were classified separately (n = 6; SIR = 2,777, 95% CI 343, 5,211). Seven cases of primary liver cancer were also found; this is an increased risk (n = 7; SIR = 294; 95% CI 76, 511). Renal cancer rates (n = 5, SIR = 104, 95% CI 13,195) were not significantly elevated, while the bladder cancer rate was significantly lower than expected (SIR = 65; 95% CI 28, 102). Colorectal cancers rates were also lower than expected, but not significantly so (SIR = 79; 95% CI 43, 115).

Relationship With Exposure

Three persons with mesothelioma were reported to have worked less than 2 years; four worked 3–4 years; and two worked 5–9 years. Ten of the 21 verified cases came from the overwhelming majority of workers who worked less than 20 years. Figure 1 shows a strong gradient between the probability of mesothelioma incidence and the number of years a person was employed in the factory. Mesothelioma occurred in 1 out of 10 workers employed between 25–30 years and 1 in 4.5 workers employed over 30 years, compared with 1 in 625 workers who were employed two years or less. Persons employed between 2–20 years are 3–11 times more likely to develop mesothelioma than persons employed less than 2 years. The risk increases 18-fold in persons employed 20–24 years, to 64-fold in persons employed 25–29 years, and to over 135 times the risk in persons employed 30 or more years.

TABLE III. Risks of Mesothelioma and Lung Cancer per 1,000 Person Years Exposure and Person Years Lapsed Since Exposure in Male, Jewish Ex-Asbestos Workers (1960–1992)*

	Per 1,000 person years exposure	Per 1,000 person years lapsed since first exposure
Mesothelioma (n = 21) (a)	2.01	0.26
Lung cancer (n = 34) (b)	3.2	0.42
Excess lung cancer (n = 7) (c)	0.70	0.09
Ratio (a/b)	0.62	0.62
Ratio (a/c)	2.88	2.88

*Excess = actual number of cases minus the expected number for a cohort of this size of Israeli, Jewish males.

Logistic regression analysis showed highly significant relationships between probability of both lung cancer and mesothelioma and years of exposure (p for both:<0.0001). Age and year of onset of employment, a surrogate for intensity of exposure (since exposures were heavier in earlier years) were found to be non-significant co-variates. Persons who were employed for 20 or more years were 4.6 times as likely to contract lung cancer and 11.3 times more likely to develop mesothelioma than persons employed less than 20 years (risk odds ratios for lung cancer: 4.6; 95% CI 1.9,11.1; for mesothelioma: 11.3; 95% CI 3.9, 32.3).

Mesothelioma/Lung Cancer Ratio

The ratio of confirmed cases of mesothelioma to the total lung cancer cases was 21:34 for the total employment experience of the cohort, and 21:28 just for the years 1978–1992 (Table III). The risks for lung cancer, both per 1,000 person years of exposure and per 1,000 person years lapsed since first exposure, were 1.6 times greater than for mesothelioma over the complete time period 1960–1992.

For the entire employment period (1960–1992), the ratio of mesothelioma/excess lung cancer was 3:1 (21/7 cases) for all cases and 2:1 (16/8 cases) for persons with 10–29 years of exposure.

DISCUSSION

This group of ex-asbestos workers had increased risks (RR) for all cancers (1.17, ns); lung cancer (1.35, ns), mesothelioma (>56, $P < .0001$), pleural cancers of unspecified type (2.8 $p < .001$) and liver cancer (2.9, ns). They did not, however, have an increased RR for cancer of rectum-colon (0.79, ns), bladder (0.69, ns), and kidney (1.04, ns) compared to nationwide rates for years 1978–1992. The very high risk of mesothelioma and moderate increase in lung cancer produced an unusually high mesothelioma/excess lung cancer ratio in this group as compared to other reported cohort studies. In our cohort, if there was a ''healthy worker effect,'' it was not sufficient to result in risks for all cancers combined being less than that seen in the total population.

The cohort was heavily exposed to asbestos on the plant floor with the predominant materials being chrysotile (90%) and crocidolite (10%). In coming years, we can expect the numbers to rise as the full impact of earlier exposures take their toll and later cohorts first employed in the early 1970s emerge into their peak period of risk.

Excess risk for all cancers has been described in other asbestos cement and other worker groups, [Albin et al., 1990; Leigh et al., 1991]. Our data indicated no excess lung cancer; no cases of mesothelioma verified by histology were identified before 1978, presumably because the lapsed period from onset of exposures was too brief. Other studies show a greater risk for lung cancer with more prolonged exposure [McDowall ME, 1984; Raffn et al.; 1989]. The absence of an excess risk for stomach and colorectal cancer in our cohort is at variance with findings from most studies, which have shown that workers exposed to asbestos cement are at increased risk for stomach and colo-rectal cancer [Raffn et al., 1989; 1996]. More prolonged follow-up is needed to determine if the lower than expected risks for colo-rectal cancer found in our cohort persists. In contrast, the high number of cases diagnosed as liver cancer is noteworthy.

The most important finding, however, is the large number of cases of mesothelioma, a specific measure of past exposure to asbestos. Excess mesothelioma risk was related to duration of exposure after 25 years since onset of work on the plant floor. In logistic regression, the duration of exposure completely overshadowed any effect of calendar years of onset of exposure. This absence of an association between years lapsed from onset of exposure to appearance of mesothelioma is puzzling in view of the well-recognized power relationship to years lapsed from onset of exposure [Selikoff et al., 1979]. Some or all of the six pleural cancer cases, though initially excluded because of absence of histological or pathological data, could have been mesotheliomas. This group did not include relatives of workers or persons exposed outside the factory.

The national incidence rate for mesothelioma is 2–4/million in Israel, compared to national figures of up to 11 per million in Denmark [Andersson and Ohlson, 1985; Raffn et al., 1989; 1996] and Australia, where the high rate reflects the focal risks at Wittenoom [Leigh et al., 1991]. The substantial number of cases of mesothelioma (n = 201) occurring in the entire population throughout the country in years 1953–1992, some tenfold the numbers seen in our cohort, reflects risk from other direct, indirect, or community exposures resulting from manufacture, use, or uncontrolled dumping of asbestos products, used throughout the country especially for building materials, plumbing, acoustic insulation, and fireproofing, as well as ship insulation and

brake linings. The fact that some 20% of the more than 200 Israeli victims of mesothelioma were female suggests the need for identifying unrecognized community exposures in non-occupational settings.

Since 1978, mesothelioma risk in our cohort increased rapidly. This was a consequence of exposures starting in the 1950s and the lapsed period from onset of exposure being 26 years (range 15–34 years). In years 1978–1992, the ratio of confirmed cases of mesothelioma to excess cases of lung cancer was 21 to 7 or 3:1; or 3.5 to 1.0 if the previously cited five pleural cases of uncertain status were included, and was found to increase with duration of exposure [Brown and Smither, 1983; Damhuis and van Gelder, 1993]. Almost all (20 out of 21) mesothelioma cases were pleural, (compared to a national pleural to peritoneal ratio of 3.3 to 1).

The 3:1 or possibly 3.5:1 ratio of mesothelioma to excess lung cancer was 6 to 21 times the combined ratios reported among other cohorts [Nicholson and Raffn, 1995]. For those with exposure to ''predominantly amosite, crocidolite and mixed exposure circumstances,'' the ratio of total mesotheliomas to excess lung cancer has been reported as between 0.14 and 0.61 to 1 in studies from various countries. In Finland, the nationwide mesothelioma to lung cancer ratio in asbestos workers from 1964 through 1993 was 0.41:1 [Huuskonen et al., 1995]. Smith and Wright reviewed the ratio of mesothelioma to excess lung cancer in a number of cohorts exposed to various mixes of asbestos, with ratios ranging from 0.19 to 2.28. The pleural mesothelioma/excess lung cancer ratio for exposures to mixed fiber, based on an O/E ratio for lung cancer of 1,722/1,106 and 301 pleural mesotheliomas in 12 studies, was 0.27 [Smith and Wright, 1996]. Other reports of asbestos cement workers reported pleural mesothelioma/excess lung cancer ratios of 0.14 [Raffn et al., 1989], 0.51 [Finkelstein, 1984], and 0.83 [Albin et al., 1990].

There are three suggested explanations, possibly complementary, for the very high mesothelioma to excess lung cancer ratio in this cohort. First, risks for mesothelioma in our cohort could have been especially elevated from high past exposures to chrysotile-crocidolite mixtures. Second, the underlying risk for lung cancer among Israeli men has been low over a long period of time compared to those rates in most European countries, but similar to rates in Sweden [Rennert et al., 1988; Steinitz et al., 1989; World Health Organization, 1996; World Health Organization, European Region, 1998], despite smoking rates not unusual by European standards. Third, smoking cessation alerts among asbestos workers occurred relatively earlier compared to other countries where asbestos exposures began during World War II.

Some comments are necessary on these suggested determinants of the high mesothelioma/excess lung cancer ratio. A lower lung cancer risk—some 1/3 that seen in European countries— together with a 20% estimated contribution of risk from 10% crocidolite, could result in mesothelioma-excess lung cancer ratio in the range of 2.0. A further increase of the ratio could have resulted from reduction in the denominator—lung cancer—as a result of the effect of smoking cessation. There is also the possibility that the mesothelioma rates were higher in our cohort because of greater levels of exposure than in other cohorts of exposed workers. Further, some lung cancer cases may have been under-reported or mis-classified as undefined pleural cancer.

High Past Asbestos Exposures

High levels of exposure were widespread in this asbestos cement plant in early years. Not only were officially reported measurements high, but ex-workers reported that there were times when dust levels were so high that workers ''could not see their hands held at arms length.'' The role of high exposure in increasing the ratio is indicated by the finding that in our cohort, there was the suggestion of a positive relationship between duration of exposure and the size of the mesothelioma/excess lung cancer. Logistic regression analysis showed that earlier year of onset of employment did not modify this relationship. This factor may have elevated the mesothelioma risk in this group compared to asbestos exposed workers in other settings due to presumably higher exposure levels.

Low Lung Cancer Risks in the Male Population

Incidence and mortality of lung cancer in Israeli males are very much lower than in some European countries. Lung cancer incidence in Israel is similar to Swedish rates, less than half reported for Finland, just over 1/3 that of Italy, and 1/4 that of the United Kingdom. Mortality rates from lung cancer in Israeli males are also consistently lower than rates in most European countries in the period 1970–1995 [World Health Organization, 1996; WHO European Region, 1998]. The reasons for this are unknown and remain an intriguing epidemiologic puzzle beyond the scope of this paper. Less smoking is not the explanation, since smoking was more prevalent among Israeli males in the 1980s than in men in the United States, the United Kingdom, and Germany [Rennert et al., 1988]. Urbanization is high in Israel, so that air pollution exposure differences may have an impact.

With lung cancer death rates in Israel 1/3 to 1/4 of those seen in many European countries, and with mesothelioma risk as high or higher, the pleural mesothelioma/lung cancer risk could be twice to three times that seen in similar settings elsewhere. However, Albin et al. [1990], from Sweden, reported a ratio of 0.83, or less than 1/3 the ratio we report, also in a cohort exposed to asbestos cement manufacture, despite a low SMR for lung cancer,14.6, similar to Israel's low rate (16.3). The fact that the mesothelioma/excess lung cancer rate was so much higher in asbestos cement workers in Israel compared to Sweden provides support for the

hypothesis that past asbestos exposures and risks for mesothelioma were much higher in the Israeli cohort. This may account for our high mesothelioma/excess lung cancer by a factor of 2–3.

Smoking Cessation Among Asbestos Workers

Smoking cessation has been promoted in western Europe, the Unites States, and Israel since the late 1970s . In Israel, information on smoking risks and the benefits of cessation was delivered earlier in relation to onset of exposure to asbestos, which occurred later than in Europe. This meant that if these alerts had an effect on smoking cessation, their impact would have been earlier in relation to onset of exposure than in the other countries. Smoking among Israeli men declined from 50% in 1975 to 32% in 1996 [Israel Center for Disease Control, 1997]. However, as no data are available on trends in smoking among the asbestos production workers in this cohort, we are unable to assess the influence of these changes on lung cancer and the mesothelioma/excess lung cancer ratio. It is possible that smoking cessation in this group occurred earlier among the asbestos production workers than among their European counterparts and this could have reduced the lung cancer risk without affecting the mesothelioma risk, accounting for part of the high mesothelioma/excess lung cancer ratio (1.2:1).

Risks of Chrysotile and Amphibole Forms of Asbestos

The World Health Organization has suggested that risks of exposure to chrysotile are lower than risks from other forms of asbestos.[2] A WHO expert group stated in 1996 that: ''Where appropriate control measures have been applied, workplace exposures to chrysotile have been reduced considerably and that the production and processing of chrysotile generally presents less risk for persons involved in mining and manufacturing of friction materials and asbestos cement products. However, other uses of products containing chrysotile may pose health risks...that appropriate control measures should considerably reduce risks of developing asbestosis, lung cancer and mesothelioma...the question of the extent to which mesotheliomas may be attributed to chrysotile verses other contaminating asbestos fibers sometimes present was not resolved by the group.''

Others take issue with the view that chrysotile is less carcinogenic during production and conclude that it is prudent public policy to treat chrysotile asbestos with virtually the same level of concern as the amphibole form of asbestos [Woitowitz, 1991; Smith and Wright, 1996; Stayner et al, 1996]. The Stayner et al. review of the ''Amphibole Theory,'' that chrysotile may be less carcinogenic than amphibole forms of asbestos (crocidolite, amosite, and tremolite), concludes that the evidence does not support this theory. Recent editorials agree that chrysotile is to be regarded as carcinogenic and a public health hazard, so that no changes should be made effecting regulatory approaches restricting its use [Landrigan, 1998; Cullen, 1998]. Risks from mesothelioma were greatly increased in the Israeli cohort of workers exposed to a 90% chrysotile-10% crocidolite mix of asbestos cement fibers. The relatively low risk for lung cancer did not protect members of this cohort from mesothelioma, nor were they spared an increased risk for lung cancer, despite low male population-wide risks for this disease in Israel.

CONCLUSION

We found a high ratio of mesothelioma to excess lung cancer in workers exposed to a 90% chrysotile-10% crocidolite mix of asbestos cement fibers. This high ratio is suggested to have resulted from high past exposures, a low population background risk of lung cancer for Israeli males, and possibly, relatively early onset of smoking cessation. Our findings show that occupational exposure to this mix of predominantly chrysotile asbestos produced increased risk for cancer. These findings and cumulative weight of evidence [Landrigan, 1998; Cullen, 1998] show chrysotile as well as crocidolite to be carcinogenic. Exposure to both types of asbestos fibers should continue to be regarded as a public health hazard in manufacturing and other settings.

ACKNOWLEDGMENTS

This work was carried out in cooperation with the Acco Public Health Office and Bet Loewenstein. We acknowledge the valuable assistance of the staff of the Israel Cancer Registry and editorial assistance of Marla Clayman (Public Health Intern).

REFERENCES

Albin M, Jakobsson K, Attewell R, Johansson L, Welinder H. 1990. Mortality and cancer morbidity in cohorts of asbestos cement workers and referents. Br J Ind Med 47:602–610.

American Cancer Society. 1994. Cancer facts and figures, 1994. Atlanta, GA

Andersson M, Olsen JH. 1985. Trend and distribution of mesothelioma in Denmark. Br J Cancer 51:699–705.

Baum GL. 1986. Public awareness of the problem of asbestos use in Israel. Am J Indust Med 10:445–448.

Berry G. 1994. Mortality and cancer incidence of workers exposed to chrysotile asbestos in the friction-products industry. Ann Occup Hyg 38:539–546.

Browne K, Smither WJ. 1983. Asbestos-related mesothelioma: factors discriminating between pleural and peritoneal sites. Br J Ind Med 40:145–152.

2. Chryostile asbestos evaluated by health experts. World Health Organization press release, September 9, 1996. Not a peer-reviewed publication.

Coleman MP, Esteve J, Damiecki P, Arslan A, Renard H. 1993. Trends in cancer incidence and mortality. Lyon: WHO/International Agency for Research on Cancer Sci Pub. no. 121, pp 311–342.

Cullen M. 1998. Chrysotile asbestos: enough is enough. Lancet 351:1377.

Damhuis RA, van Gelder T. 1993. Malignant mesothelioma in the Rotterdam area, 1987–1989. Eur J Cancer 29A;1478–1479.

Djerassi L, Ilion A, Bar-Nets M. 1970. Follow-up of a population in an asbestos plant. Proc Second National Convention Israel Industrial Medical Association, Zichron Yaakov, Israel, 54–84.

Djerassi L, Kaufman G, Bar-Nets M. 1979. Malignant disease and environmental control in an asbestos cement plant Health Hazards of Asbestos Exposure. Ann NY Acad Sci 330:243–254.

Finkelstein, MM. 1984. Mortality among employees of an Ontario asbestos cement factory. Am Rev Resp Dis 129:754–761.

Ginsberg GM, Tulchinsky TH. 1992. Regional differences in cancer incidence and mortality in Israel: possible leads to occupational causes. Isr J Med Sci 28:534–543.

Hughes JM, Weill H, Hammad YY. 1987. Mortality of workers employed in two asbestos cement manufacturing plants. Br J Ind Med 44:161–174.

Huuskonen MS, Karjalainen A, Tossavainen A, Rantanen J. 1995. Asbestos and cancer in Finland. Med Lav 86:426–434.

Israel Center for Disease Control. 1997. The Health Situation in Israel, 1997. Tel Hashomer, Israel: ICDC, 1998.

Landrigan P. 1998. Asbestos: still a carcinogen. N Engl J Med 338:1618–1619.

Leigh J, Corvalan CF, Grimwood A, Berry G, Ferguson GA, Thompson R. 1991. The incidence of malignant mesothelioma in Australia, 1982–1988. Am J Ind Med 20:643–655.

McDowall ME. 1984. A mortality study of cement workers. Br J Ind Med 41:179–182.

Ministry of Health. 1996. Health in Israel. Jerusalem: Ministry of Health.

Nicholson WJ, Raffn E. 1995. Recent data on cancer due to asbestos in the USA and Denmark, in updating the epidemiology of asbestos disease. Med Lav 86:393–410.

Raffn E, Lynge E, Juel K, Korsgaard B. 1989. Incidence of cancer and mortality among employees in the asbestos cement industry in Denmark. Br J Ind Med 46:90–96.

Raffn E, Villadsen E, Lynge E. 1996. Colorectal cancer in asbestos cement workers in Denmark. Am J Ind Med 30:267–272.

Rennert G, Tamir A, Katz L, Epstein L. 1988. Lung cancer in Israel, 1962–1982: Jews and Arabs. Eur J Epidemiol 4:461–469.

Richter ED, Tulchinsky TH, Goldsmith JR, Yaffe Y. 1984. Asbestos-exposed populations: prevention, care, and compensation. Prev Med 13:286–298.

Richter ED, Berdugo M, Laster R, Westin JB, Fischbein A. 1995. Chrysotile and crocidolite asbestos in Israel: uses, exposures and risks. Med Lav 86:449–456.

Selikoff IJ, Hammond EC, Seidman H. 1979. Mortality experience of insulation workers in the United States and Canada, 1943–1976. Ann NY Acad Sci 3301:91–116.

Smith AH, Wright CC. 1996. Chrysotile asbestos is the main cause of pleural mesothelioma. Am J Ind Med 30:252–266.

Stayner LT, Dankovic DA, Lemen RA. 1996. Occupational exposure to chrysotile asbestos and cancer risk: a review of the amphibole hypothesis. Am J Public Health 86:179–186.

Steinitz R, Parkin DM, Young JL, Bierber CA, Katz L, eds. 1989. Cancer incidence in Jewish migrants to Israel. Lyon: IARC Publications, WHO/International Agency for Research in Cancer, Sci Pub. No. 98.

Tuch H, Tulchinsky TH, Casper M, Knaane H. 1986. Medical screening of former asbestos cement workers in Israel: a pilot program. Am J Ind Med 10:471–478.

Tulchinsky TH, Ginsberg GM, Shihab S, Goldberg E, Laster R. 1992. Mesothelioma mortality among former asbestos-cement workers in Israel 1953–90. Isr J Med Sci 28:543–547.

Wagner JC, Newhouse ML, Corrin B, Rossiter CE, Griffiths DM. 1988. Correlation between fibre content of the lung and disease in east London asbestos factory workers. Br J Ind Med 45:305–308.

Woitowitz HJ. 1991. Chrysotile asbestos and mesothelioma. Am J Ind Med 19:551–553.

World Health Organization. 1996. Highlights on health in Israel. Copenhagen: WHO Regional Office for Europe.

World Health Organization, European Region. 1998. Health for All Data Set, available from WHO Home Page Internet.