A Worrying Increase in the Incidence of Mesothelioma in Israel

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Key words: malignant mesothelioma, pleura, asbestos, incidence, time trend

Abstract

Background: Exposure to asbestos is the main established cause of mesothelioma; the incidence of this tumor is thus often interpreted as an index of past exposure. Asbestos has been widely used in Israel in industry and building, exposing certain population groups to the risk of developing mesothelioma.

Objectives: To analyze the incidence of mesothelioma in Israel during the years 1960–96, and to project its trend for the following years.

Methods: We conducted a population-based study of the incidence of mesothelioma reported to the Israel Cancer Registry during 1960–96. Time trends were analyzed from data on the annual import of asbestos to Israel, which may indicate the magnitude of past exposure. Based on these findings, trends in the incidence of mesothelioma in Israel were projected for the subsequent years.

Results: A total of 327 cases of mesothelioma were reported to the Israel Cancer Registry during the study period. The incidence in Jews was higher than in Arabs (age-standardized incidence rate 2.64 vs. 1.35 per million/year, respectively). Among the Jewish population, Israeli-born males and males born in Europe and America showed the highest incidence (ASR 4.23 and 4.15 per million/year, respectively). Israeli-born males were 20 years younger than Jewish males born elsewhere. The incidence was twice as high among males than females and increased sevenfold from its nadir (1.17 per million/year) in 1978–80 to its peak (8.5 per million/year) in 1993–96. During a similar period the incidence among females increased from 0.33 to 2.56 per million/year. The incidence in both sexes does not appear to level off. The large wave of immigration from the former Soviet Union that began in 1989 only partly accounts for the increased incidence in 1993–96. The time trend in the incidence of mesothelioma in both sexes parallels the use of asbestos in Israel, which peaked in the years 1976–78.

Conclusions: The incidence of mesothelioma in Israel has increased sharply in recent years, unrelated to a wave of immigration from East Europe, and is predicted to continue to rise for another 10–15 years.

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ASR = age-standardized incidence rate

For many years malignant mesothelioma was a rare almost unrecognized tumor that had been described only scarcely. In 1960, Wagner et al. [1] reported a series of South African asbestos miners diagnosed with this type of malignancy. Numerous reports have since convincingly established the causal relationship between asbestos and mesothelioma [2–6]. It has been calculated that the risk is negligible up to 10 years after the first asbestos exposure, very low up to 15 years, but increases thereafter as the third or higher power of time [7]. In recent years a sharp rise in the incidence of mesothelioma has been reported from many countries [8–13]. Mesothelioma rarely occurs without a documented exposure to asbestos [14], or in children [15,16]. It has been suggested that genetic factors may also affect the development of mesothelioma [17].

Asbestos has been widely used in Israel for many years, particularly in the manufacturing of asbestos cement products, thermal insulation, and brake linings. Asbestos cement products were extensively used in buildings for the expanding immigrant population during the 1950s. Previous studies on the incidence of mesothelioma in Israel have shown conflicting trends. Despite the increasing use of asbestos in Israel in the past, the incidence of mesothelioma in Israel in the period 1973–81 was paradoxically reported to be lower than during the antecedent period 1960–72 [18,19]. Although mesothelioma has been a rare tumor in Israel, many medical professionals maintain that the incidence in Israel has been rising lately. In addition, a recent cohort study found a high mesothelioma incidence among previous asbestos cement workers in Israel [20].

In the present study, we analyzed the incidence of mesothelioma in Israel during the period 1960–96. We compared trends in the incidence with data on the annual import of asbestos to Israel. Based on the results of both parameters, we proffer a prediction on the incidence of mesothelioma for the coming years.

Material and Methods

Cases with histologically confirmed mesothelioma were retrieved from the Israel Cancer Registry and included all subjects notified and recorded as mesothelioma by the International Classification of Diseases for Oncology morphology code (ICD-O) 9050-3 [21] during the period 1960–96. The Israel Cancer Registry utilizes a passive notification system whereby identifiers provide quality control and

follow-up based on routine linkage with files of the Population Registry, the National Death Registry and hospital files. The cancer registry data include details of histopathologic diagnosis, anatomic site and stage of the tumor. Cancer registration is considered to be relatively complete, and indices of quality of the registry data are regularly published [22]. Although no active attempt was made to retrieve additional clinical or pathologic data on mesothelioma cases from treating institutions, diagnosis accuracy is assumed to be comparable to other western countries [12].

The study population comprised the total population living in Israel, where each individual has a unique identification number. Demographic data were obtained from the Population Registry [23], using the national population censuses (1972, 1983) and annual estimates stratified by ethnic group, gender and 5 year age groups. The Jewish population comprised 83% of Israeli residents in 1983, and was grouped according to the place of birth into four groups: Israel, Europe and America, Africa, and Asia. Jewish immigrants who came to Israel after 1989 were excluded from all incidence analyses in order to avoid over-presentation of cases diagnosed before immigration from countries once part of the Soviet Union. Non-Jews comprised 17% of Israeli residents in 1983, and were mostly Arab Moslems (14%), Arab Christians (2%), and other minorities.

The direct method of standardization was applied, with Israel's 1983 census population and the world standard population [24] as references. Because of the relatively small number of cases of mesothelioma, the annual age-standardized incidence rate was calculated in 3 year groups starting in 1960. Trend lines were presented as polynomial curves, and statistical significance was calculated with the use of the *t*-test.

The regional medical committee, the National Security Institute, provided the list of mesothelioma cases that were former workers in the asbestos cement plant in Acre. Data on the annual import of raw asbestos to Israel during the period 1960–97 were collected from annual statistical abstracts of Israel foreign commerce and the Central Bureau of Statistics [25], and were presented as the average of 3 year groups.

Results

Temporal changes

A total of 327 cases of mesothelioma in both sexes and in all sites were registered during the period under review. The 3 year age-standardized incidence rates of mesothelioma in both Jewish males and females (including new immigrants) are presented in Figure 1.

The incidence in males decreased in 1960–62 from 1.39 to 1.17 per million/year in 1978–80, rising later to 8.5 per million/year in 1993–96. The incidence in females decreased in 1960–62 from 2.16 to 0.33 per million/year in 1981–83, rising to 2.56 in 1993–96, similar to males. Trend lines for both sexes indicated a continuous increase in mesothelioma incidence with no leveling off.

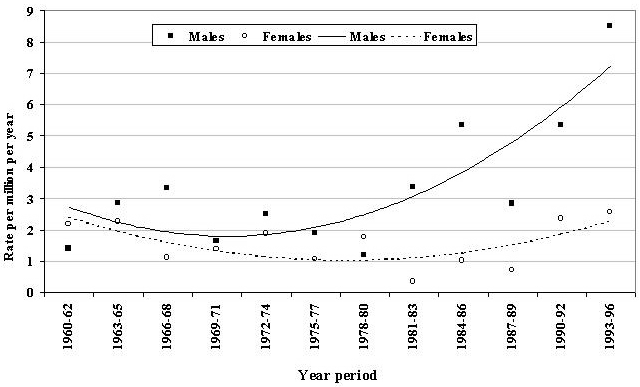

Figure 1. Time trends in age-standardized* incidence of mesothelioma in Jewish males and females in Israel, 1960–96. * To 'World' population.

During the period 1989–96, the Jewish population of Israel increased by 24.3% from 3.72 to 4.62 million, primarily due to a wave of immigration from countries previously belonging to the Soviet Union. The ASR for a selected Jewish population (residing in Israel before 1988 and excluding recent immigrants) during 1989–96 was 3.32 per million/year (males 5.42, females 1.49). The standardized incidence rate ratio for this selected population (excluding immigrants) compared to the total Jewish population (including immigrants) during 1989–96 was 1.12, which was not statistically significant (95% confidence interval 0.74–1.05).

Variation according to ethnicity and country of birth

Of a total of 327 cases, 222 (67.9%) were diagnosed in males vs. 105 cases (32.1%) in females. Only 16 cases of mesothelioma were diagnosed in non-Jews. The ASR in Jews was higher than in non-Jews (2.64 vs. 1.32 per million/year respectively, Chi-square test, $R^2=4.45$, $P=0.035$). The highest incidence of mesothelioma was found among Jewish males (ASR 3.62). The incidence rates of mesothelioma in the Jewish population grouped according to their place of birth are shown in Table 1. The highest incidence was found in Israeli-born males (ASR 4.23 per million/year) and in males born in Europe and America (ASR 4.15). Israeli-born females showed the lowest incidence (ASR 0.65 per million/year). The incidence of mesothelioma in males was higher than in females in all groups compared by place of birth, with the largest ratio (6.5 times) calculated in the Israeli-born population.

The age-specific incidence rate of mesothelioma in the Jewish population increased with age. The rise was particularly sharp above the age of 40 (*t*-test, $R^2=0.88$, $P<0.001$). Eighteen cases were diagnosed below the age 30, including 9 cases aged less than 18 years. The mean age at diagnosis was 58.9 years (males 60.2, females 56). The mean

Table 1. Number of cases and corresponding age-standardized* incidence rates per million/year of mesothelioma in Jews in Israel, by gender and place of birth, 1960–96

Place of birth	Gender**		Total
	Male	Female	
Israel	33 [4.23]	11 [0.65]	44
Europe and America	143 [4.15]	63 [2.34]	206
Africa	16 [1.89]	13 [1.54]	29
Asia	23 [2.24]	9 [0.99]	32
Total	215 [3.62]	96 [1.54]	311

* To 'World' population.

** Number in parentheses denotes ASR per million/year.

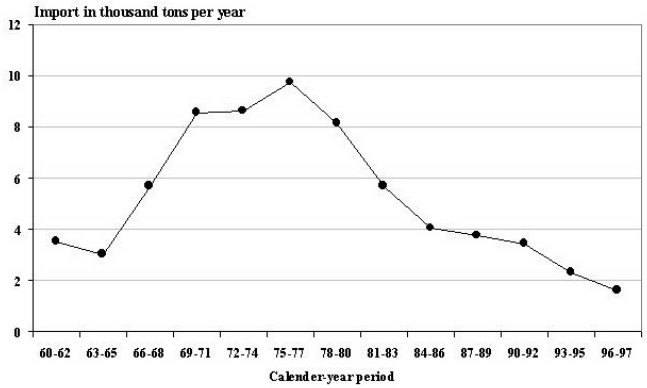

Figure 2. Import of raw asbestos to Israel in thousand tons per year in 3 year periods, 1960–97

age of Israeli-born males was 44.1 compared to 64.8 years in males born in Europe and America. Analysis according to the year of birth showed a peak in number of cases born in the years 1910–29.

Primary anatomic site of diagnosis

The primary anatomic site of diagnosis could be ascertained in 317 of 327 mesothelioma cases (97%). In all, 235 cases (75.1%) were diagnosed in the pleura (and other intrathoracic structures), 78 (24.6%) in the peritoneum, and 4 (1.3%) were intrascrotal. The distribution of mesothelioma cases in the Jewish population according to the primary anatomic site of diagnosis, gender and age (under 30 vs. above 31) is presented in Table 2. In the older age group, the incidence of mesothelioma was significantly higher in males than in females ($P<0.01$), with most tumors diagnosed in the thorax. In contrast, mesothelima is rarely diagnosed below age 30 (total 18 cases, 10 females and 8 males), and has no particular anatomic propensity.

Variations according to geographic district of residence

The incidence of mesothelioma was compared among residents of four mainly urban districts during two consecutive periods, 1979–87 and 1988–96. The incidence in residents of the combined Haifa and Acre district was the highest, and increased from 3.81 to 6.33 per million/year over the two successive year periods. The SIR of mesothelioma for residents in the Acre district, where the largest asbestos cement plant in Israel (Issasbest/Etanit) was located, compared to a selected Jewish population (excluding immigrants after 1989) was 7 and 5.4 in the two periods respectively. Of the 22 mesothelioma cases diagnosed in the Acre district during 1988–96, 16 were former workers of the plant and another 2 were immediate family relatives (wife and daughter) of a former worker. Another two mesothelioma cases in immigrants who had arrived in Israel after 1989 were excluded from the SIR calculation. The ASR in the Jerusalem district increased in 1979–87 from 0.82 to 3.13 per million/year in 1988–96, but remained stable in the Beer Sheva district (1.6 and 1.55 respectively).

Temporal changes in the use of raw asbestos in Israel

Data regarding the 3 year import of raw asbestos to Israel (in thousand tons per year) during the period 1960–96 is presented in Figure 2. The import grew from 3.5 thousand tons per year in 1960–62, peaked to 9.5 in 1975–77, and dropped to 2.15 in 1993–96. About 90% of the import was crysolite and only 10% crocidolite. In 1997 the manufacture of asbestos cement products was discontinued.

Table 2. Number of cases and age-standardized* incidence rates of mesothelioma per million/year in Jews in Israel, by age group, anatomic site and gender, 1960–96

Age group	Site							Total
	Intra-thorax		Peritoneum		Intra-scrotum	All sites [ASR]**		
	M	F	M	F	M	M	F	
≤30years	3	5	4	5	1	8 [0.25]	10 [0.34]	18
≥31 years	163	64	45	24	3	211 [8.25]	88 [3.25]	299
Total	166	69	49	29	4	219	98	317
(%)	235 (74.1)		78 (24.6)		4 (1.3)	317 (100)		

* To 'World' population.

** Number in parentheses denotes age-standardized incidence rate per million/year.

M = male, F = female

Discussion

It is widely accepted that the incidence of mesothelioma is closely related to previous exposure to asbestos [5]. In Israel, where wood is scarce, asbestos was extensively utilized for roofing, wallboard and insulation. Even today, asbestos sheets and roofs remain in many houses, schools and other public buildings in Israel. There is no mining of asbestos in Israel, and the asbestos that is used

SIR = standardized incidence rate ratio

is imported. Levels of the annual import of raw asbestos to Israel have been considered fair indicators of the extent of asbestos use in all industries. The import of asbestos peaked to an average of 9.5 thousand tons per year in 1975–77, and fell subsequently to a minimum average of 2.2 in 1993–96. In addition to the decreasing use of asbestos, occupational regulations at workplaces limiting the permitted air contamination by asbestos fibers to a maximal level of 106 particles/m^2 came into effect during the 1970s. The only brake lining plant in Israel was closed down in 1980, and the asbestos cement plant in the district of Acre (Etanit) closed its asbestos cement manufacturing line in 1997. Much of the damage caused by asbestos may therefore be related to its wide use in previous years.

The highest incidence of mesothelioma in Israel was found among residents of the combined Acre and Haifa districts. The SIR for Jewish residents in the Acre district during the recent period 1988–96 was 5.39. These findings concur with a recent report describing a particularly high incidence of mesothelioma among former workers of the asbestos cement plant [20]. As expected, the majority of mesothelioma cases residing in the Acre district were either former workers in the plant or their family members (two cases).

Despite the rise in the use of asbestos in Israel in 1975–77, a previous population-based study from the Israel Cancer Registry demonstrated an unexplained paradoxical fall in the incidence of mesothelioma during 1973–81 [19] compared with the antecedent period 1960–72 [18]. Our study, extending over a longer period, confirms that observation but fails to indicate its cause. We assume that diagnostic inaccuracy of mesothelioma in a range comparable to that found in other western countries (e.g., 11% in the UK and about 30% in France) [12] could also occur in Israel, particularly during the early study period. However, that kind of error is unlikely to explain the recent rise in the incidence of mesothelioma in Israel.

Considering the relatively long latent period elapsing between the first exposure to asbestos and the diagnosis of mesothelioma (35–40 years) [7], the current increase in incidence of mesothelioma in Israel probably reflects the growing extent of asbestos exposure before it reached its peak in the years 1975–77. Therefore, we may predict that the incidence of mesothelioma will continue to rise, leveling off not before the year 2010. A similar trend of increase in mesothelioma incidence has been reported from other countries [8–12], but not from the USA where the incidence has already reached its peak [13]. In Western Europe, most recent cases of mesothelioma occurred in people who were born after 1940 and had been exposed during the period of extensive asbestos use before the late 1970s [12]. A similar trend may also be expected in Israel, with an increasing incidence among those born in Israel after the 1940s.

A large proportion of the population of Israel, especially in the older age group, consists of immigrants from other countries. The development of mesothelioma in immigrants may reflect exposure to asbestos in their countries of birth. The current rise in mesothelioma incidence in Israel might have been attributed to a wave of immigration starting in 1989 from the former Soviet Union. However, our findings indicate that that wave of immigration only marginally affected the incidence of mesothelioma in Israel during the period 1989–96, and thus cannot explain the recent incidence rise. Furthermore, we have no data on individual asbestos exposure of new immigrants diagnosed with mesothelioma.

The incidence of mesothelioma in the Jewish population was significantly higher than in the Arab population in Israel. This may be due to the fact that Arab society in Israel has traditionally been agricultural, having limited exposure to industrial asbestos. The lower incidence of mesothelioma in Arabs contrasts with the relatively higher incidence of lung cancer in this population compared to the Jewish population. Such an ethnic variation may underscore the importance of asbestos exposure (but not cigarette smoking) to the development of mesothelioma.

The incidence of mesothelioma in Jewish males born in Israel or in Europe and America was higher than in Jewish males born in Africa or Asia. The incidence in Jewish males was consistently higher than in Jewish females, indicating that most mesothelioma in Israel is probably due to occupational rather than environmental exposure. However, the issues of occupation-related mesothelioma and mesothelioma in family members of asbestos workers should be addressed in a separate study, probably of a case-control type.

A unique group comprises cases of mesothelioma diagnosed under the age of 30. This group numbered 18 cases (5.5% of the total number of cases diagnosed in 1960–96). Nine cases were diagnosed under age 18, including a one-year-old baby. Unlike the older group, the sex distribution of mesothelioma cases below age 30 as well as the anatomic distribution of their disease (intrathoracic vs. peritoneal) were similar. As in other childhood cancers, genetic or viral factors probably contribute more to the etiology of mesothelioma in this age group [17].

The sharp increase in the incidence of mesothelioma in Israel reported here indicates that the mesothelioma epidemic already observed in Western Europe [12] may also occur in Israel. Since radical surgery in the very early stages provides the only possible cure for patients with mesothelioma, routine screening may be warranted especially in high risk populations.

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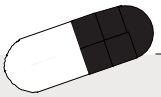
A bad review may spoil your breakfast but you shouldn't allow it to spoil your luch.

Anonymous

Capsule



Ireland's measles outbreak kills two

The Republic of Ireland is suffering its worst measles outbreak for 7 years as a result of the low uptake of the measles, mumps, and rubella (MMR) vaccine. The Irish National Disease Surveillance Centre reported that two children in north Dublin have died.

The centre also said that the disease is starting to spread from Dublin to other parts of the country. Health boards are planning to launch a vaccination campaign in the autumn. Reported cases are now at their highest level since 1993, when 4,328 cases were notified. None of the country's regional health boards has reported vaccination reaching the recommended level of 95%. The average uptake of the vaccine is about 76%, with rates ranging between 68% and 86%. Uptake in the United Kingdom is 88%.

The disease surveillance centre's latest bulletin suggests that the low numbers of MMR vaccinations are the result of parental forgetfulness, apathy, and concerns about side effects. The centre cannot say, however, whether the uptake rate has been influenced by the *Lancet* article published in 1998, which suggested that the MMR vaccine was linked to autism. It only recently started collecting national figures of the vaccination uptake and has no figures before 1999. The article in the *Lancet* has been blamed for reducing the uptake in the United Kingdom from 90.4% to 87.6%.

Parents in Ireland have been influenced by the Best case. The Supreme Court found in 1992 that Kenneth Best, now a severely brain-damaged adult, was affected by being given a dose from a toxic batch of pertussis vaccine.

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