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Environmental asbestos exposure and malignant pleural mesothelioma

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Asbestos-related benign and malignant pleural diseases are endemic in some rural parts of central Turkey because of environmental exposure to asbestos fibres. We report here epidemiological data on 113 patients with diffuse malignant pleural mesothelioma (DMPM) diagnosed in our clinic in Eskişehir, located in central Turkey.

Of the 113 patients, 59 were men and 54 women (male:female ratio=1). Ninety-seven patients (86%) had non-occupational asbestos exposure; all were living in villages. Their mean age was 56 years. As the patients had been exposed to asbestos from birth, the latency period was equivalent to the age of the patients. Twenty-eight patients (29%) had lived in villages their entire lives. The other 69 (71%) had been born in a village but migrated to the city or had given up white-soil usage for various reasons. The mean exposure time was 55 years for those with a long exposure period and 25 years for those with a short exposure period, but there was no significant difference between the age of the disease appearance for both groups (55 and 56 years, respectively). Thus, the latency time of mesothelioma due to environmental exposure to asbestos was longer than that due to occupational exposure, but independent of the length of exposure. Soil samples from 67 villages were analysed, comprising a population of 10 120 villagers. Tremolite and some other types of asbestos were found.

In conclusion, DMPM in our region is due to mainly to environmental exposure to asbestos. The risk is substantial as a large proportion of the villagers are exposed. After smoking, asbestos exposure is one of the most serious health hazards in our rural population.

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Introduction

Asbestos exposure is the most important cause of diffuse malignant pleural mesothelioma (DMPM) (1–4). Soil mixtures containing asbestos can be found in certain parts of the world. This soil is known in Anatolia as '*aktoprak*' (white soil) or '*çorak*', and deposits are common. The villagers in these mainly agricultural regions use this soil as a whitewash or plaster material (white stucco) for walls, for insulating and waterproofing floors and roofs of houses, for baby powder and also in pottery (1,5–7) .

Similar deposits and uses of the soil have been reported from other countries, such as Geece, Cyprus and New Caledonia. The white soil has been shown to contain tremolite asbestos and pleural lesions, parenchymal asbestosis and malignant mesothelioma occur in these regions (1,8–12).

Our clinic is a department of the Medical School of Osmangazi University in Eskişehir, Turkey (Fig. 1). The Eskişehir district is located in the central part of Anatolia. The total population is 641 057, with 163 621 living in a total of 403 villages. Patients are mostly admitted from Eskişehir and from nearby rural areas of two neighbouring cities, Kütahya and Bilecik. The whole area has a population of about 1.2 million and no occupational relation to asbestos exposure. However, many patients with diffuse malignant pleural mesothelioma or other asbestos-related chest diseases are admitted to our clinic each year from these regions.

In our rural region the use of white soil was very widespread before the 1970s, but decreased during the 1980s. Nowadays it has been largely replaced with lime whitewash and plaster, although white soil is still in partial use in some villages.

In this paper, we report the epidemiological data of DMPM patients diagnosed in our clinic over the period

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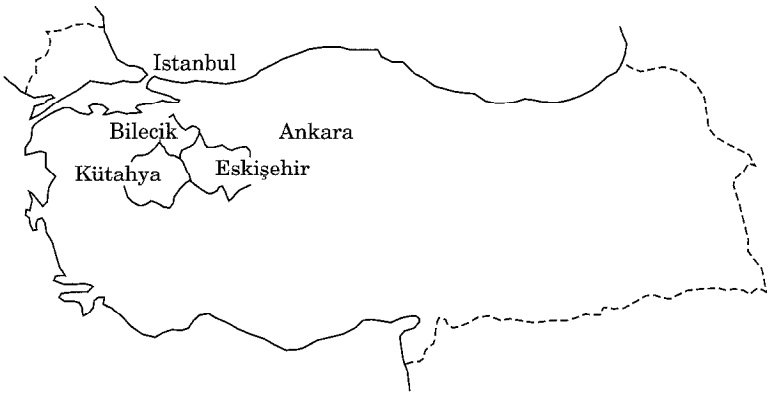

FIG. 1. Map of the Eskişehir region in Turkey.

from May 1989 to December 1997. If these epidemiological results are significantly original this report will provide a reference point for subsequent studies concerning the role of non-occupational asbestos exposure, thus adding to existing knowledge of DMPM epidemiology.

Methods

PATIENTS

The study was performed prospectively. All consecutive patients with DMPM confirmed by histopathological diagnosis were included. Following conclusive diagnosis, epidemiological data, such as age, sex, profession, period of residence in rural area, place of occupation, white soil or '*çorak*' exposure, habits, contact with other mineral and chemical substances, previous illness and cigarette smoking, were determined from the patient and noted on a protocol specifically designed for this study. The study included 113 DMPM patients from May 1989 to December 1997.

CONFIRMATION OF ENVIRONMENTAL EXPOSURE

In view of the high percentage of villagers among the patients, the fact that most of them had used white soil and that previous studies had established the white soil of this region to be contaminated with tremolite or a tremolite–chrysotile combination (1,6,13), we decided to go to some of the villages concerned and conduct a mineral analysis of the white soil. Of the 403 villages of Eskişehir, we were able to acquire data via a questionnaire from 196. We learned that white soil had been used in 140 villages, and was still being used in 126. By random sampling, we chose 67 of these villages, from some of which we were receiving patients, and collected white soil samples from them. A mineral analysis of these samples was carried out using X-ray diffraction (XRD), mostly at the Gebze Institute of Higher Technology (İstanbul) and partly at the National Institute of Mineral Research (Ankara).

X-RAY DIFFRACTION PATTERN OF THE WHITE SOIL SAMPLES

The chemical compositions of the white soil samples were determined using a Rigaku (Tokyo, Japan) RINT 2000 X-ray diffractometer with an ultima+wide angle goniometer operating at 40 kV and 40 mA. XRD was used to examine the sample by employing CuKα monochromatic radiation (λ=1·5418 Å).

Each white soil sample was ground to a particle size of $<50\,\mu$m in an agate mortar with an agate pestle. The powder was pressed into the sample holder and particles were provided as randomly oriented. The specimens were scanned at a speed of $2°\,\text{min}^{-1}$, using a scanning step of 0·01 degrees and the XRD pattern was examined. Fig. 2 shows the XRD pattern of a white soil sample.

As λ is known and the value of θ producing reflection can be determined, the crystal d-spacing for each intensity peak of the XRD pattern is found using Bragg's Law ($d_i=\lambda/2\text{Sin}\theta_i$) (Table 1), where d_i and θ_i are the crystal d-spacing and the angle of the reflected ray of the ith peak, respectively.

The values of the crystal d-spacing were compared to a computer search program of a powder diffraction file, supplied by the Rigaku Corporation of Japan, to identify the chemical composition of the sample (Fig. 3).

STATISTICAL ANALYSIS

The differences between the mean ages and between the exposure durations of the subgroups were calculated according to the Student's t-test. A two-sided t-test was used at the 5% significance level.

Results

Of the 113 DMPM patients, 59 were men and 54 women. Twelve patients had no known exposure to asbestos, and four had occupational exposure. One hundred patients (88%) had lived in a rural area all their lives or for a long time (mean 25 yrs). Villagers living in these regions are

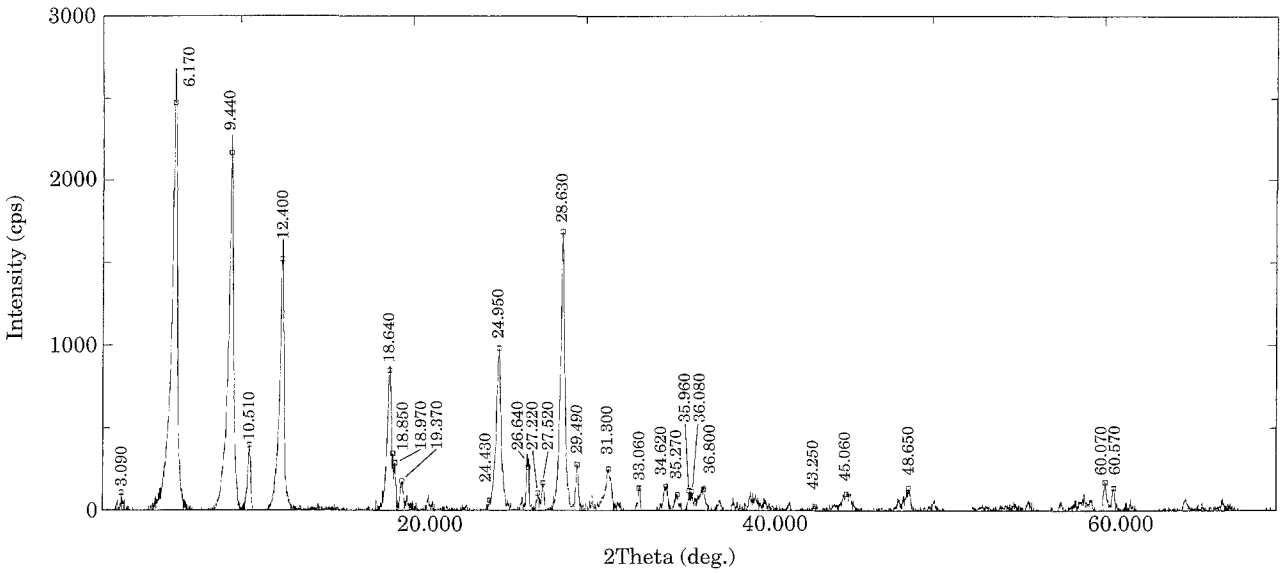

FIG. 2. X-ray diffraction pattern of a white-soil sample.

engaged in agriculture. Ninety-seven (86%) patients had white-soil exposure; all were living in villages, with white-soil deposits surrounding their houses, which they had been using mostly for whitewashing the walls of their houses and for insulation on the roofs.

In the present study, we found that white soil is still being used in 126 villages which have a total population of 121 950 (according to the population census in 1995). We found tremolite or other types of asbestos fibre contamination in a total of 41 white soil samples (61%) collected from 67 randomly sampled villages. A total of 10 120 people are still living in these villages.

Mineral analysis of these white-soil samples identified contamination with tremolite; tremolite–chrysotile complex, or various combinations of actinolite, anthophyllite, or chrysotile. Other minerals detected in white-soil samples are talc, feldspar, quartz, dolomite, calcite, chlorite, and mica.

There were three villages (with a total population of about 1548), with four patients each; one village with three patients; and three villages with two patients each. Two of the patients were husband and wife. In a village from which four patients had presented, white-soil samples were contaminated with tremolite and chrysotile fibres. In the second village with four patients only tremolite contamination was found, while in the third, interestingly, anthophyllite and chrysotile were also found (Figs 2 and 3). The white-soil sample from the village in which three patients had presented was contaminated only by tremolite fibres.

An interesting observation was that no asbestos fibres were found in any samples from soil used as baby powder or in pottery-making. Asbestos was only present in soil used as plaster and/or paint and as roof insulation.

On consideration of the mineral analysis results for the samples of white soil used, and of mineral analysis results established in earlier studies in this region, it was seen that our white-soil exposed patients were in contact with asbestos fibres. Therefore, 97 patients had non-occupational exposure to asbestos due to the use of white soil.

Of the 97 patients with non-occupational asbestos exposure, 50 were men and 47 were women. Twenty-five patients were farmers, 16 labourers (no asbestos exposure), eight officers, two drivers and 46 were house-wives. The mean age was 57·5 years for men, 54·0 for women, and 55·8 years for all patients. The age difference between men and women was not statistically significant. The age distribution at diagnosis, which is also the latency time as the patients were exposed from birth, can be seen in Fig. 4.

A large proportion of the patients (36%) were in the 60–69 years age group and 30% were 50–59, 11 patients (11%) were aged under 40 years and eight (8%) were 70 years or over. The youngest patient was diagnosed at age 26.

Twenty-eight patients (29%) had lived in villages their entire lives and thus formed the 'continuous exposure group'. The other 69 patients (71%) had been born in a village but migrated to the city or given up white-soil usage for various reasons, and formed the 'partial exposure group' (Table 2).

As can be seen, the mean exposure was 25 years for the 'partial exposure' group and 55 years for the 'continuous exposure' group, a significant difference ($P<0·001$). The mean age for disease onset for the 'continuous exposure' patients was numerically lower than that for the 'partial exposure' patients, but the difference was not statistically significant ($P>0·05$).

Of the 97 patients with environmental exposure to asbestos, 39 had epithelial cell type DMPM, 18 had mixed type and 14 had sarcomatous type. Pathologists did not report a cell type for 26 patients of the 97. Table 3 shows details of the patients' asbestos exposure periods and ages in relation to the cell-type classifications/distinctions.

TABLE 1. Crystal *d*-spacings and relative line intensities for each peak of the X-ray diffraction pattern and matching lists for the same white soil sample

Matching list No.	Card No.	R.F.	Observed peak no./intensity (I/Io)																										
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
			51	00	88	17	62	35	14	12	8	3	40	11	5	7	69	12	11	6	7	4	5	5	6	2	5	6	8	6
1	29-1493	302			100					20	60						90				20			30						
2	24-0506	256		67			100	43		7	22		53	5			4		9		19	27			25		16		14	30
3	25-0645	172									50	80									40	20	50		65	40				
4	43-0662	155									40	80									20	30			80	60			30	65
5	45-1343	146				57					3	28		10		55		000	11	4	17	3	11		5		3	1	7	2

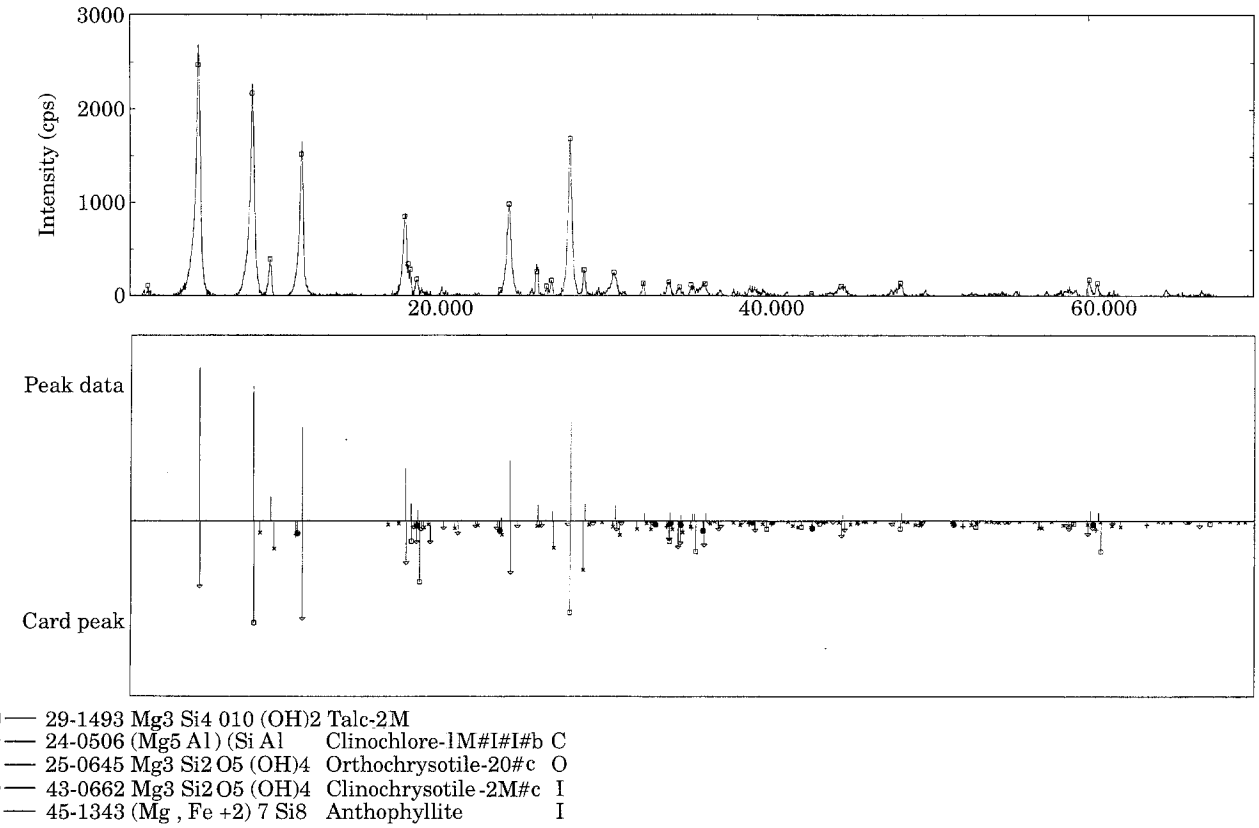

FIG. 3. X-ray diffraction pattern of the white-soil sample from Fig. 2, comparing peaks with the computer program of a powder diffraction file.

The mean exposure periods of patients for each cell type, epithelial, mixed and sarcomatous, were $36{\cdot}6 \pm 18{\cdot}2$, $29{\cdot}9 \pm 19{\cdot}2$ and $34{\cdot}5 \pm 22{\cdot}6$ years, respectively. There were no significant differences in mean exposure period between patients of different cell type groups; epithelial–mixed ($P>0{\cdot}05$), epithelial–sarcomatous ($P>0{\cdot}05$), and mixed–sarcomatous ($P>0{\cdot}05$).

Of the 113 patients, 49 were smokers (43%). Forty-six of the 59 men (78%) were smokers, but only three of the 54 women (6%).

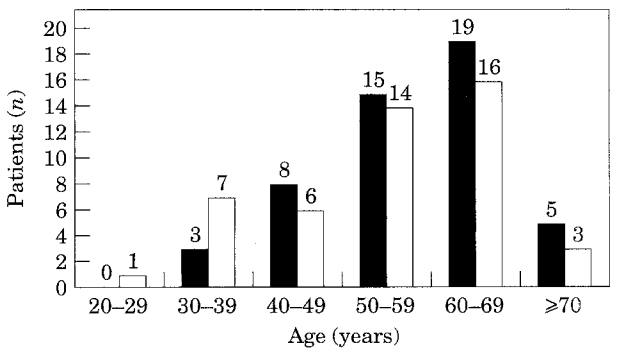

FIG. 4. Age distribution, in decades, of the 97 patients environmentally exposed to asbestos (■, men; □, women).

Discussion

Of the 113 patients diagnosed at our clinic as DMPM, 86% had a history of non-occupational asbestos exposure due to the use of white soil in their villages. Earlier studies conducted in the province of Eskişehir have demonstrated asbestos contamination in some white-soil samples (1,6,13). In the present study, 10 120 people were found to reside in villages determined to have asbestos-contaminated white soil. If the other, less accessible, villages, which we were unable to survey, are taken into account, the size of the population exposed to white soil may be far greater.

In our patient series from Eskişehir, three villages, which had a total population of 1548, had a high number of mesotheliomas; each provided four patients. Interestingly, two of the patients were husband and wife. The high rate of DMPM in these villages may be related to the concentration of dust to which inhabitants are exposed. Another interesting finding was the presence of anthophyllite and chrysotile in samples taken from one of the villages with four patients. Some previous studies have failed to demonstrate a strong aetiological link between anthophyllite and/or chrysotile exposure and malignant mesothelioma, as with tremolite or other amphiboles.

The present study has confirmed that DMPM in our region is due mainly to environmental exposure to asbestos.

TABLE 2. Mean ages and exposure duration of environmental asbestos exposure of patients, according to period type, with consideration of patient sex

Exposure period	Sex	Patients (*n*)	Exposure duration (years)	Mean age (years)	Age range
Partial	Male	35	27·5 ± 14·4	57·6 ± 10·2	35–76
	Female	34	23·4 ± 13·2	54·9 ± 11·6	26–76
	Total	69 (71%)	24·9 ± 13·8	56·3 ± 10·9	26–76
Continuous	Male	15	57·2 ± 11·7	57·2 ± 11·7	32–81
	Female	13	51·6 ± 13·0	51·6 ± 13·0	33–80
	Total	28 (29%)	54·6 ± 12·4	54·6 ± 12·4	32–81

TABLE 3. Details of asbestos exposure periods and ages at time of disease appearance in relation to cell types of 81 patients whose cell types had been classified

Cell type	Epithelial	Mixed	Sarcomatous
Total number of patients	47	19	15
Men	26	7	9
Women	21	12	6
Asbestos exposure	39 (83%)	18 (95%)	14 (93%)
Continuous	14 (36%)	5 (12%)	2 (13%)
Partial	25 (64%)	13 (88%)	12 (87%)
Mean age (years)	55·9 ± 11·4	51·2 ± 11·8	59·9 ± 11·9
Range	26–81	38–63	38–78
Mean exposure period	36·6 ± 18·2	29·9 ± 19·2	34·5 ± 22·6
Range	7–81	12–63	10–78

As a consequence of asbestos contamination in white soil and the high number of people exposed to it, asbestos-related diseases are endemic to our region. It would be no great exaggeration to say that, after smoking, asbestos exposure is one of the most serious health hazards to our rural population.

In our 97 patients with environmental exposure to asbestos, there was a 1:1 ratio of men to women (50/47), which is different from the usual occupational exposure ratio, which usually ranges from 3 to 12:1 (14–17). This ratio reflects the environmental exposure to asbestos in rural areas, as women and men live in the same rural environment and conditions. Mean lengths of exposure were the same for both sexes.

The mean age of disease appearance was 56 years (range 26–81). As the patients had been exposed to asbestos from birth, the 'latency period' was equivalent to the age of the patient at diagnosis. The latency period in occupational exposure series is generally given as 30–40 years (4,18–21). In the environmental asbestos exposure series for Selçuk, the average age was 50 years, with one-quarter of the patients below 40 years (13). The reasons for the difference in latency time between occupational exposure and environmental exposure are not clear. One possibility is that, on average, occupational exposure levels are much higher. A high level of exposure might thus shorten the latency time. However, accumulation of low grade exposure does not seem to affect the latency.

The average duration of asbestos exposure for the 69 periodic exposure patients was 25 years, and 54 years for the 28 continuous exposure patients, but the difference in latency time was not significant. This result was also found when separate evaluations were made for men and women. These results suggest that the duration of asbestos exposure is less important as the development of mesothelioma depends rather on attaining a threshold level of asbestos. Any further increase in exposure above this threshold will not affect development significantly.

Childhood mesothelioma and, in particular, aetiological characteristics, are still under discussion (4,14). In our hospital, only one patient with childhood mesothelioma was diagnosed in the period 1989–1997. This was a boy, aged 14 years, with pleural epithelial mesothelioma and white-soil exposure, but since the patient was seen in another clinic he was not included in the present study. Therefore, no detailed information was recorded. The fact that we have encountered only a single childhood mesothelioma patient strengthens the argument that disease is not expected to appear within 10 years of the initial exposure. The chest and pediatric surgery departments of our hospital are sources of reference for our entire region. If environmental asbestos exposure were an important

aetiological factor in childhood mesothelioma, more patients would have been recorded.

Our investigation of patients' smoking habits revealed a high rate of smokers among the men (78%) and a very low rate among women (6%). This was not surprising, as in rural areas of Turkey very few women smoke. These findings support the view that cigarette smoking has no role in the aetiopathogenesis of DMPM (22). On the other hand, the high rate of smoking seen among men gives rise to another consideration, namely the risk of bronchial carcinoma. The importance of environmental asbestos exposure in the occurrence of this disease needs to be studied in the future.

Acknowledgements

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