Scand J Work Environ Health 1989;15:106—10

Amosite mesothelioma in a cohort of asbestos workers

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RIBAK J, SEIDMAN H, SELIKOFF IJ. Amosite mesothelioma in a cohort of asbestos workers. *Scand J Work Environ Health* 15;1989:106—10. A cohort of 820 asbestos workers with a short duration of exposure to amosite between 1941 and 1945 was followed. These men were alive five years after starting work and were observed until 1988. Seventeen cases of malignant mesothelioma (eight pleural, nine peritoneal) were found. The mean age at the onset of exposure was 33 years for men with pleural mesothelioma and 30 years for those with peritoneal mesothelioma. Chest pain was the main symptom in pleural mesothelioma and abdominal pain in peritoneal mesothelioma. Open lung biopsy was the most useful diagnostic approach for pleural mesothelioma, whereas for peritoneal mesothelioma it was exploratory laparotomy. Pleural patients died of pulmonary insufficiency, and peritoneal patients of wasting and inanition. In both groups the death certificate diagnosis was less accurate than the clinical diagnosis at death. The mean survival was 12.5 months from first symptom to death for the pleural group and 5.4 months for the peritoneal group.

Key terms: age at onset, death certificate, diagnosis, diagnostic procedures, peritoneal, pleural, survival, symptoms.

The question of possible differences in the neoplastic potential of the different kinds of asbestos fibers has attracted much attention. Malignant mesothelioma has been of particular interest in this regard since its occurrence can be well ascribed to asbestos, with little chance of its attribution to other causes. However, whether one or another fiber is more likely to induce mesothelioma has been a question not easily answered.

Mesothelioma can be produced in experimental animals by inhalation or intrapleural inoculation (1, 2). Mesothelioma of the pleura and peritoneum can be caused by all types of asbestos fibers (3—8), including crocidolite, chrysotile, amosite, anthophyllite, and tremolite.

With regard to human mesothelioma, it has been difficult to obtain information about exposure to single fiber types, since most industrial exposures have been "mixed" and generally poorly quantified. However, mining experience has given data about crocidolite (8) and chrysotile (9) mine dust. On the other hand, information regarding mesothelioma in workers exposed predominantly to amosite has been fragmentary (10—12).

Contribution to the knowledge about the carcinogenicity of amosite asbestos in workers has largely come from studies by Selikoff and his co-workers (7, 11, 12). Amosite asbestos workers employed between 1941 and 1945 were followed. Forty-three cases of lung cancer and five cases of mesothelioma (two pleural and three peritoneal) were described in an early report (7). Mortality studies of this group were later extended, and dose-response relationships 5 to 40 years after the onset of exposure were described in detail. Attack rates per million years were also reported for mesothelioma (table 1) (12).

Only very small amounts of amosite asbestos were imported into the United States before 1940 (table 2). At that time, with the needs of the United States (US) Navy, an asbestos products factory was established in Paterson, New Jersey; it started production in June 1941 and made insulation materials, primarily for the Navy.

Present study

We have had the opportunity of studying the occurrence of mesothelioma in workers employed in this plant and, in the present report, describe 17 cases of malignant mesothelioma that have occurred among 820 men employed for some period between 1941 and 1945 and followed to 1988.

Table 1. Rates of pleural and peritoneal mesothelioma among amosite asbestos factory workers (12).

Elapsed years from onset of exposure	Person-years of observation	Pleural mesothelioma (rate per million years)	Peritoneal mesothelioma (rate per million years)
5—9	—	—	—
10—14	—	—	—
15—19	—	—	—
20—24	2 656	372	372
25—29	2 094	1 574	1 049
30—34	1 567	2 539	2 539
35—39	1 086	—	1 842

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Table 2. Estimated asbestos fiber consumption (tons) in the United States.[a]

Year	Crocidolite	Amosite	Canadian chrysotile	Other	Total
1920	No data	No data	152 000	4 000	156 000
1925	No data	No data	200 700	4 100	204 800
1930	1 907[b]		198 200	8 500	208 407
1935	501[b]		154 200	20 500	175 201
1940	8 068[b]		225 900	36 300	270 268
1945	8 700	4 500	355 800	9 000	378 000
1950	8 500	5 400	687 400	27 400	728 700
1955	11 700	18 000	699 100	11 600	740 400
1960	19 600	19 500	605 800	24 600	669 580
1965	17 100	21 400	661 100	20 100	719 700

[a] Source: United States Department of Commerce.
[b] Amosite and crocidolite combined; not separately recorded.

Subjects and methods

The plant had been awarded a patent for amosite insulation in 1936. We have ascertained that amosite asbestos was used almost exclusively (7). [There were also very small amounts of chrysotile utilized (7).]

Not only did the Navy specifications call for this fiber type, but the machinery was designed for such material (R Gaze, Cape Asbestos Company, London), the fiber sold to the company by the Cape Asbestos Company was amosite (R Gaze), materials retrieved from the storerooms of the plant after work ceased was amosite, filters of respirators worn by the employees were amosite, and amosite was also the fiber predominantly found in the lung specimens of workers of the plant, together with limited numbers of chrysotile fibers.

From June 1941, when the factory began operation, through December 1945, 933 men were recruited to work in the plant, which continued to operate until 1954. The initial group was almost entirely made up of white males. Wartime conditions influenced the composition of the work force. Young employees were often recruited to the Armed Forces. Therefore, the men who worked at the plant tended to be older than usual.

In contrast to asbestos insulation workers, a large proportion of this group worked for a short time only, going to other, better paying employment, to the armed forces, or, with the older men, to retirement. Therefore a unique cohort was formed, men often with a very limited duration of heavy work exposure to amosite asbestos, followed by long observation.

Though there were no direct fiber counts in the factory, it is known that exposure was high. Using data from several sources, Dr WJ Nicholson has calculated that average exposures may have been 50 fibers/cm^2 of air (12).

Of the 933 men recruited to work in the factory, 113 men were omitted from further analysis: 21 had prior asbestos work, 14 left for another asbestos job, 40 had died, and 30 were lost to follow-up before five years from initial employment. Eight hundred and twenty were known to be alive five years from the onset of work, they had no prior or subsequent asbestos employment. They constitute the cohort being studied (7).

Table 3. Age and information on exposure to asbestos in 17 consecutive cases of mesothelioma.

	Pleural mesothelioma (N = 8)		Peritoneal mesothelioma (N = 9)	
	Mean	SD	Mean	SD
Age at onset of exposure (years)	32.8	12.9	29.8	4.1
Duration since onset of exposure (years)	30.9	3.6	31.1	2.1
Age at death (years)	63.6	14.2	60.9	3.5
Time worked at factory (months)	25.6	19.9	43.8	15.1

We have traced every death that occurred in the cohort. Pertinent information (clinical records, X-ray films, necropsy reports, histopathological specimens, death certificates) has been sought for every death. All information gathered was evaluated, and a diagnosis of mesothelioma was accepted only after a detailed pathological examination of surgical or postmortem material (by M Kannerstein, J Churg, Y Suzuki). The criteria used for the pathological diagnosis of mesothelioma have been published earlier (13). As of August 1988, 740 men of the cohort were known to be dead. Seventeen ascertained cases of malignant mesothelioma, eight pleural and nine peritoneal, were identified. We describe the clinical characteristics of the disease in those cases, as well as the accuracy of death certificate categorization and survival data.

Results

In all, 17 cases of malignant mesothelioma (eight pleural and nine peritoneal) were identified. Table 3 compares the age at the onset of exposure, the duration since the onset of exposure, age at death, and time worked in the factory for the men with pleural and peritoneal mesothelioma. The numbers are similar, and no significant difference was found between the two

Table 4. Main symptoms and signs in 17 consecutive cases of mesothelioma among amosite asbestos workers.

Symptoms	Pleural mesothelioma (N = 8)
Chest pain	4
Recent onset of shortness of breath	1
Recent increase of shortness of breath	1
Pleural effusion	1
Chest tightness	1

Symptoms	Peritoneal mesothelioma (N = 9)
Abdominal pain	5
Weight loss	2
Abdominal distention	1
Hernia	1

Table 5. Accuracy of diagnosis for the eight cases of amosite pleural mesothelioma.

	Initial clinical diagnosis (N)	Clinical diagnosis at death (N)	Death certificate diagnosis (N)
Pleural mesothelioma	4	5	2
Mesothelioma site not specified	1	—	2
Lung cancer	2	3	4
Pneumonia	1	—	—
Total	8	8	8

Table 6. Accuracy of the diagnosis for the nine cases of amosite peritoneal mesothelioma.

	Initial clinical diagnosis (N)	Clinical diagnosis at death (N)	Death certificate diagnosis (N)
Peritoneal mesothelioma	4	6	5
Carcinomatosis	4	2	3
Other	1[a]	1	1
Total	9	9	9

[a] This case was diagnosed all along as a tumor of the spermatic cord.

groups, with the exception that, for the men with peritoneal mesothelioma, the mean time worked in the plant was almost twice that of the men with pleural mesothelioma (43.8 months versus 25.6 months).

The men's smoking history showed that two-thirds of both groups had smoked. It is known that cigarette smoking has little or no effect on death rates from mesothelioma among amosite workers, as contrasted to lung cancer (14—16).

Clinical information

Table 4 displays the principle symptoms of both the pleural and peritoneal mesothelioma cases. Chest pain was the main symptom in the pleural group, and abdominal pain was predominant in the peritoneal group. During the course of the disease, pleural effusion and shortness of breath accompanied the chest pain in most of the pleural patients, while marked weight loss was noted for the peritoneal patients.

The initial pathological evaluation was reviewed. In seven cases of pleural mesothelioma open biopsy was performed. In four of them the correct diagnosis had been made. In one case diagnosis was equivocal, and in two there was a persumptive diagnosis of lung cancer. Needle biopsy alone was done in one case, and it led to a correct diagnosis of the disease. In the peritoneal group explorative laparotomy was the most frequent approach. It was done for six patients, but yielded a positive diagnosis of mesothelioma for only two.

The immediate cause of death in the cases of pleural mesothelioma was pulmonary insufficiency (seven out of eight), and in the cases of peritoneal mesothelioma the main cause of death was wasting and inanition (seven out of nine).

Accuracy of diagnosis

Table 5 presents the accuracy of diagnosis for the cases of pleural mesothelioma. Comparison is made between the accuracy of the three types of diagnoses mentioned (initial clinical diagnosis, clinical diagnosis at death, and death certificate diagnosis). The denominator for the comparison is the total number of pleural mesothelioma cases (N = 8) established in the review of all data, including, in each case, a pathological examination.

Categorization of pleural mesothelioma and mesothelioma as "not otherwise specified" was, as expected, the least well-designated in the initial clinical diagnosis. It improved with clinical diagnosis at death. The death certificate diagnosis was less accurate than the clinical diagnosis at death, if we include mesothelioma, site not specified. In the peritoneal mesothelioma group (table 6), only four of the cases had been correctly categorized in the initial clinical diagnosis, six were correctly categorized at death, but only five were listed as malignant mesothelioma on the death certificate.

Awareness of previous asbestos exposure

The relationship between the awareness of a history of asbestos exposure and a correct diagnosis of mesothelioma by the treating physician was similar for pleural mesothelioma (exposure known in six out of

the eight cases) and for peritoneal mesothelioma (exposure known in six out of the nine cases).

Survival

The mean survival time from the onset of first symptom to death and from the time of diagnosis to death is presented in table 7. Peritoneal mesothelioma had shorter survival compared with pleural mesothelioma.

Table 7. Survival of the 17 patients with amosite mesothelioma from first symptom to death and from diagnosis to death.

	Pleural mesothelioma (N = 8)		Peritoneal mesothelioma (N = 9)	
	Mean	SD	Mean	SD
Survival from first symptom to death (months)	12.5	7.8	5.4	4.2
Survival from diagnosis to death (months)	8.0	8.1	1.8	3.1

Discussion

We have had the opportunity to study a well-defined cohort of amosite asbestos workers who were followed from 1941 to 1988. This cohort is unique in that exposure was predominantly to one type of fiber (amosite) with extensive postexposure observation (18 190 person-years). The cohort is also unique in the sense that many older workers were recruited to work during World War II. The age at onset of exposure was higher in this cohort than the corresponding age for other insulation workers (14). Most were employed for a relatively short period of time (ranging from less than one month to a few years) with subsequent long observation (7, 11, 12).

Information about mesothelioma caused by exposure to amosite has been scarce. Only five cases (four pleural and one peritoneal) were reported by Acheson et al (10) in a factory using mainly amosite and some chrysotile asbestos. Cochrane & Webster (4) attributed two of 70 cases of mesothelioma to amosite only. Thus the 17 cases described by us represent a relatively large group of patients, and their study includes the advantage of a well-defined population base and uniform, long-term postexposure observation.

As expected, the time from the onset of exposure to the development of malignant mesothelioma was long, ranging from 20 to 41 years. These results are similar to those found earlier for asbestos insulation workers (14). It perhaps is of interest that the men with peritoneal mesothelioma worked longer in the factory than those who died of pleural mesothelioma (table 3). Smoking habits were the same in both groups.

Nine of the 17 cases were peritoneal mesothelioma. It is of interest to note that we also found more peritoneal than pleural mesotheliomas in a previous study of asbestos insulation workers exposed to other types of asbestos fibers (14), whereas in other reported series the ratio between pleural and peritoneal mesothelioma has been reversed (6, 10). This ratio might result, in part, from an underdiagnosis of peritoneal mesothelioma.

The clinical symptoms were similar to those described by us before (14), as were the immediate causes of death. It was once more clearly found that the most productive diagnostic procedure for pleural mesothelioma was open lung biopsy. Exploratory laparotomy and biopsy was the optimum approach for peritoneal mesothelioma.

Many projections and evaluations of the magnitude of the mesothelioma problem are based on reported death certificate designation, often without histological confirmation. Our data indicate that relying on death certificate diagnosis only may result in a serious underdiagnosis of mesothelioma. The accuracy of death certificates has been discussed by Elmes et al (17), Newhouse & Wagner (18), Ducic (19), and McEwen et al (20). All these authors agreed that diagnosis based on the death certificate only without histopathological confirmation is not sufficient to provide a secure diagnosis of malignant mesothelioma.

A comprehensive occupational history taken by the attending physician was important in raising the suspicion of mesothelioma (14). Such awareness was associated with a more accurate diagnostic categorization, somewhat better for pleural than for peritoneal mesothelioma.

Mesothelioma is a lethal disease, usually discovered late, with therapy mostly ineffective. Most of the patients with malignant mesothelioma die within a year of the onset of symptoms. Patients with peritoneal mesothelioma die sooner, probably because the disease is diagnosed relatively late. Patients with pleural mesothelioma tend to come to the physician earlier, usually because the symptoms are easily detected. The mean survival time for the pleural mesothelioma patients in our group was 12.5 months versus 5.4 months for the peritoneal mesothelioma patients.

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Received for publication: 19 September 1988