Asbestos Fibers and Pleural Plaques in a General Autopsy Population

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It has been claimed that symmetric lower zone pleural or diaphragmatic plaques are markers of asbestos exposure both in asbestos workers and the general population. In this study, total pulmonary asbestos burden was analyzed for 29 patients selected because pleural plaques were found at autopsy, and the results were compared with values obtained for 25 patients who had no occupational asbestos exposure. The average number of asbestos bodies in the plaque groups was 1732/g wet lung, and in the control group, 42/g wet lung. Uncoated asbestos fibers were extracted from lung and counted, measured, and identified by morphologic examination, electron diffraction, and energy-dispersive x-ray spectroscopy. The total number of fibers/per gram wet lung in the plaque group (114×10^3) was similar to that in the control group (99×10^3), as was the number of chrysotile fibers (51×10^3 versus 68×10^3) and noncommercial amphiboles (13×10^3 versus 29×10^3). However, the plaque patients had a marked increase in the number of the commercially used high aspect ratio amphiboles, amosite and crocidolite (50×10^3 versus 1×10^3). A retrospective history of fairly certain asbestos exposure was obtained for 16 of the plaque patients, and such a history correlated strongly with increased numbers of commercial amphiboles in lung. It is concluded that 1) in this general autopsy population, two subgroups of patients are present. About one half of the patients appear to have developed pleural plaques as a result of asbestos exposure, while the etiology of the plaques in the other half is unclear; 2) the presence of pleural plaques correlates with a modest (50-fold) increase in numbers of long high-aspect ratio commercial amphiboles in lung tissue but does not correlate with numbers of chrysotile fibers, noncommercial amphiboles, or the total number of asbestos fibers; 3) asbestos-induced lesions are related to a complex set of mineralogic parameters and not to mere numbers of fibers in lung. (Am J Pathol 1982, 109:88–96)

PLEURAL PLAQUES are hard, white, slightly elevated collagenous structures found on the pleurae and diaphragm. They may be completely flat or knobbed, and, at least when associated with exposure to asbestos, tend to follow the rib outlines over the lower parietal pleurae. Plaques associated with asbestos exposure are almost always bilateral and most commonly are confined to the lower lung zones; the morphologically identical structures that may be seen after trauma to the chest or after infection are generally unilateral and may be found in any lung field. Plaques are frequently found to be calcified on both pathologic and radiographic examination; the radiographic appearance of calcified diaphragmatic plaques has been considered pathognomonic of asbestos exposure.[1,2]

The epidemiologic association of exposure to high levels of asbestos and the development of plaques is firmly established.[2,3] Whether pleural plaques found in a general population also are invariable markers of asbestos exposure or represent a nonspecific process is uncertain. Selikoff and Lee[2] noted that calcified plaques were found in about 2% of chest radiographs of relatives of asbestos workers. Navratil and Trippe[4] showed that relatives of asbestos workers and persons living near an asbestos factory had about 15 times the incidence of calcified plaques, compared

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with controls not living near the factory. Similar results for this type of (presumably) modest exposure to commercial exploitation of asbestos were obtained by Hourihane et al,[5] by Kiviluoto,[6] and by Meurman.[7] Burilkov and Mikhailova[8] demonstrated that in a district in Bulgaria in which plaques were endemic in both men and cattle, the soil contained amphibole asbestos fibers. Of particular interest are recent reports from Turkey[9] showing a high incidence of plaques and mesothelioma in a region in which the soil and local building rocks contain not asbestos but the fibrous mineral erionite. These findings suggest that plaques may appear with rather minimal exposure to asbestos or any other long, thin fibrous material.

In contrast, some case-control studies on the general population have failed to show an association of plaques and asbestos exposure. In a recent British report,[10] about the same number of plaque and control patients gave a history of asbestos exposure, but the plaque patients had a significantly higher incidence of old inflammatory or traumatic events. Rous and Studeny[11] also could not find an association of plaques and asbestos exposure in a Czechoslovakian population, but did find a familial trend, which they attributed to tuberculosis.

"Asbestos" is a generic name for a variety of naturally fibrous silicates. More than 90% of the asbestos used commercially is the serpentine mineral, chrysotile. The remaining forms of asbestos are members of the amphibole group of minerals; of this large group, only amosite (fibrous grunerite) and crocidolite (fibrous riebeckite) have extensive commercial application, while actinolite, anthophyllite, and tremolite are common contaminants of other minerals but have little industrial value.

Plaques have been found in persons with high-level occupational exposure to every type of asbestos fiber, but even in such populations there is little detailed information about the types and amounts of dust needed to produce disease and about the actual dust content of the lungs. With the use of the insensitive techniques of counting asbestos bodies or uncoated fibers by light microscopy, it has been shown that persons with plaques and a history of occupational exposure have more bodies or fibers than control subjects.[1,7,12] Le Bouffant analyzed the plaques themselves in 2 cases and found that only chrysotile was present; the chrysotile fibers were considerably more numerous in the plaques than in the lungs.[13] Gibbs[14] suggested that differences in the mineral species found in local asbestos deposits accounted for the dramatic differences in the incidence of calcified plaques in Thetford Mines, as opposed to Asbestos, both asbestos mining regions of Quebec.

For this report, I selected a series of general autopsy subjects who had typical "asbestos-related" plaques and examined both a detailed occupational history and the actual asbestos content of the lungs in an attempt to determine whether history or analysis supported an etiologic role for asbestos in these lesions, and, if so, whether the presence of plaques could be related to total numbers of fibers, sizes of fibers, or some other mineralogic parameter.

Materials and Methods

Patient Selection

The test group for this study consisted of 29 general autopsy subjects selected only because they were found to have had lower lobe parietal or diaphragmatic plaques. The control group consisted of 25 patients. Of these, 11 men were previously included in a report on asbestos fibers in a general autopsy population[15] and were selected on the basis of a lack of history of asbestos exposure and an asbestos body count of fewer than 100 bodies/g wet lung, as determined by light-microscopic examination with the use of our previously published methods.[16] This number of asbestos bodies appears to indicate a lack of occupational asbestos exposure. An additional 14 subjects were selected so as to form a close match for age, sex, and smoking values with the test group, but without regard to asbestos exposure history or asbestos body count. This latter group included 1 woman and 13 men. The patients had had a variety of occupations, largely blue collar; there were a number of nonasbestos miners and quarriers. To obtain better sex matching (since 28 of the 29 subjects in the plaque group were male), I did not include in the present control group the 10 women who were included in the original report on asbestos fibers in the general population.[15]

A detailed smoking, residential, and occupational history was obtained for each subject by interview with relatives with a standardized questionnaire, as previously described.[16] Clinical data was obtained by review of the patient's chart. Interviews, chart reviews, and fiber analysis were performed independently.

Preparation of Tissue for Light- and Electron-Microscopic Examination

For each case, four samples (peripheral lower and peripheral upper lobes, central lower and central up-

per lobes) of approximately 2–3 g wet weight of formalin-fixed lung were used. Tissues were prepared by bleach digestion and collection of the sediment on a Millipore filter. This filter was cleared and mounted for light-microscopic quantitation of asbestos bodies or pieces of the filter transferred to electron microscope grids for evaluation of uncoated fibers. Details of the methods have been previously published.[15,16] Fibers were identified by a combination of electron optical morphologic study, electron diffraction, and energy-dispersive x-ray spectroscopy. Numbers of fibers and asbestos bodies were calculated as described.[15,16]

In 4 cases, pieces of pleural plaque were dissolved in bleach and treated with HCl to remove calcium. Electron-microscopic samples were then prepared as described for lung tissue.

A blank was run with each sample. I prepared this by running the entire procedure without any tissue, preparing an electron microscope grid from a Millipore filter as above, and counting 25–50 squares to detect the presence of asbestos fibers. Only short fibers of chrysotile were seen in these preparations, and then in only occasional samples. When chrysotile fibers were found, the equivalent value of fibers per gram was subtracted from the sample value. The maximum value (minimum limit of detectability) for chrysotile determined in this fashion was 10,000 fibers/g wet lung. All samples were examined at a screen magnification of 18,000×.

To determine the reproducibility of the method, I prepared a series of standards from UICC asbestos samples, and replicate preparations were made. These showed that the maximum difference between the highest and the lowest count for the given sample was a factor of 2. Details of these results will be published separately.

Histologic Examination

Histologic sections of lung and, where possible, gross specimens were reviewed for each case. Sections were also prepared from each plaque to ensure that the typical collagenous appearance was present.

Standards

The UICC Standard Reference Asbestos Samples, University of Chicago Tremolite Sample 1611, and a sample of actinolite from San Bernadino County, California, were used as standards. I ran the standards through the bleach and peroxide solutions to determine whether compositional changes were produced by these procedures. No significant differences were found. For the purposes of this paper, identification of chrysotile was based on the presence of tubular forms, a chemical composition of primarily magnesium and silicon, and, when present (which was rare), the typical diffraction pattern of chrysotile. Amphiboles were identified on the basis of a diffraction pattern consistent with an amphibole (particularly the 5.3-Å spacing seen in a number of silicate minerals) and a typical chemical composition. This level of identification corresponds to the "best estimate" category of Chatfield.[17] Magnesium, silicon, calcium, and iron containing amphiboles with approximately 10% calcium and equal or greater iron were called actinolite; those with less iron were called tremolite. I have somewhat arbitrarily classified as crocidolite a high-aspect-ratio mineral that produces an amphibole diffraction pattern but has a composition closely resembling that of glaucophane, since fibrous high-aspect-ratio glaucophane apparently does not exist (see Results).

Statistical Methods

Because, in my experience, the distribution of fiber counts is not normal, nonparametric tests for paired data (Wilcoxan signed rank test) and for correlation (Spearman rank correlation) were employed.

Results

Demographic Data

Detailed histories were obtained for 28 of 29 subjects with pleural plaques. The mean age was 65, with a range of 47 to 82. Twenty eight subjects were men (Table 1). Twenty five of the men and the 1 woman smoked cigarettes; the mean number of pack-years smoked was 54 ± 35 (mean ± standard deviation). In the control group there were 24 men and 1 woman. The mean age was also 65 years, and the range was 47 to 83. The 1 woman and 22 of the men smoked cigarettes; the mean number of pack-years smoked was 59 ± 36.

Table 1—Comparison of Plaque and Control Patients

	Control group ($n = 25$)	Plaque group ($n = 29$)
Age (mean)	65	65
Sex (males : females)	24 : 1	28 : 1
Smoking (mean pack-years)	59	54
Asbestos bodies (mean)	42	1732
Total asbestos fibers (mean)	99×10^3	114×10^3

Table 2—Numbers and Sizes of Asbestos Fibers in Plaque and Control Patients

Fiber type	Total fibers (% of all fibers)	Fibers in various size categories		
		1-4.9 (%)	5-9.9 (%)	10+ (%)
Plaque patients				
Chrysotile	51 × 10^3 (45%)	44 × 10^3 (86%)	5.9 × 10^3 (11%)	1.5 × 10^3 (3%)
Noncommercial amphibole	13 × 10^3 (10%)	8.6 × 10^3 (67%)	2.9 × 10^3 (22%)	1.4 × 10^3 (11%)
Crocidolite	24 × 10^3 (22%)	14 × 10^3 (56%)	7.4 × 10^3 (30%)	3.1 × 10^3 (14%)
Amosite	26 × 10^3 (23%)	11 × 10^3 (42%)	8.2 × 10^3 (31%)	7.1 × 10^3 (27%)
Control patients				
Chrysotile	68 × 10^3 (69%)	60 × 10^3 (88%)	7.3 × 10^3 (11%)	0.7 × 10^3 (1%)
Noncommercial amphibole	30 × 10^3 (30%)	25 × 10^3 (84%)	3.9 × 10^3 (13%)	0.9 × 10^3 (3%)
Amosite	1.0 × 10^3 (1%)	0.3 × 10^3 (30%)	0.6 × 10^3 (60%)	0.1 × 10^3 (10%)

All values are fibers per gram of wet lung.

Asbestos Bodies

The mean asbestos body count for the 29 plaque patients was 1732 ± 4149 bodies/g wet lung (mean ± standard deviation), with a range of 0 to 19,400 bodies/g. Seventeen of the patients had greater than 100 asbestos bodies/g of lung. For the control patients, the mean number of bodies was 42 ± 39/g; 2 of the patients had greater than 100 asbestos bodies/g (120 and 130 bodies/g).

Uncoated Asbestos Fibers: Numbers and Sizes

For the purposes of this report, the term "commercial amphibole" is used to refer to amosite and crocidolite fibers and "noncommercial amphibole" to tremolite, actinolite, and anthophyllite fibers, with recognition that the latter types may all contaminate commercial chrysotile.

Numbers of fibers for the plaque and control group are shown in Tables 1 and 2. The average number of chrysotile fibers for the 29 plaque patients was 51 × 10^3 ± 123 × 10^3, of noncommercial amphiboles 13 × 10^3 ± 16 × 10^3, of crocidolite 24 × 10^3 ± 87 × 10^3, and of amosite 26 × 10^3 ± 64 × 10^3. As shown in Table 2, amosite and crocidolite together accounted for 45% of the total asbestos fibers, amosite for 23% and crocidolite for 22%. The noncommercial amphiboles constituted only 10% of the total, and chrysotile 45%. For the 25 control patients, the mean number of chrysotile fibers was 68 × 10^3 ± 100 × 10^3, of noncommercial amphiboles 30 × 10^3 ± 22 × 10^3, and of amosite 1.0 × 10^3 ± 3.5 × 10^3. No fibers of crocidolite were identified in the control group.

For both groups, distinct differences in fiber size distribution were seen among the different fiber types (Table 2). In the plaque group, 86% of the chrysotile was shorter than 5 μ, whereas almost half of the commercial amphiboles were longer than 5 μ, and approximately 20% were longer than 10 μ. The results for the control group showed that 88% of chrysotile fibers were shorter than 5 μ, whereas 70% of the commercial amphiboles were longer than 5 μ and 10% were longer than 10 μ. These differences probably reflect both the tendency of chrysotile to fragment into very short fibers, and the fact that most of the chrysotile burden in these patients was derived from atmospheric chrysotile, fibers that are commonly quite short, compared with the fibers used commercially.

Aspect Ratios and Widths

Aspect ratios for the plaque case fibers are shown in Table 3, and widths in Table 4. The mean aspect ratio for all chrysotile fibers was 109, for amosite 89, and for crocidolite 88. There was a consistent increase in aspect ratio with increasing length for chrysotile and the commercial fibers. By contrast, the mean aspect ratio for all the noncommercial amphiboles was 22, and no consistent increasing trend was present. The chrysotile fibers were the thinnest overall, with a mean width for all fibers of 0.054 μ. For amosite, the mean width was 0.232 μ and for crocidolite 0.182 μ. The noncommercial amphiboles were considerably wider (mean width for all fibers 0.533 μ), with the longest actinolite fibers reaching a mean width of 1.0 μ. All of the amphibole fibers showed a consistent increase in width with increasing length. The values of aspect ratios and widths for the control group were

Table 3—Plaque Cases: Fiber Aspect Ratios

Fiber type	Aspect ratios for various-sized groups (mean ± standard deviation)			
	1-4.9	5-9.9	10+	Mean
Chrysotile	56.9 ± 63.6	147 ± 153	358 ± 498	109
Amosite	32.4 ± 38.8	66.3 ± 82.6	123 ± 161	89
Crocidolite	43.7 ± 48.0	93.7 ± 99.1	156 ± 178	88
Tremolite	10.9 ± 12.4	18.6 ± 29.7	28.1 ± 35.3	18
Anthophyllite	8.9 ± 9.5	37.0 ± 42.5	45.9 ± 73.8	27
Actinolite	16.1 ± 29.4	41.3 ± 62.6	17.8 ± 15.7	22

Table 4—Plaque Cases: Fiber Width

Fiber type	Widths for various fiber size groups (values in microns, mean ± standard deviation) 1-4.9	5-9.9	10+	Mean
Chrysotile	0.043 ± 0.046	0.059 ± 0.071	0.112 ± 0.133	0.054
Amosite	0.152 ± 0.201	0.200 ± 0.274	0.273 ± 0.338	0.232
Crocidolite	0.142 ± 0.197	0.194 ± 0.301	0.234 ± 0.327	0.182
Tremolite	0.368 ± 0.412	0.633 ± 0.686	0.740 ± 0.838	0.563
Anthophyllite	0.385 ± 0.360	0.418 ± 0.518	0.687 ± 0.791	0.463
Actinolite	0.388 ± 0.480	0.610 ± 0.812	1.000 ± 0.812	0.617

quite similar to the values in the plaque group and to the values in our previously published control group and are not reproduced here.

Fiber Composition

Fiber composition is detailed in Table 5. For most of the fiber types, the plaque cases showed good agreement with the standards. As was true of the control cases,[15] and as has been demonstrated in experimental animals, chrysotile was extensively leached of magnesium. The crocidolite that we identified was considerably more aluminum-rich and iron-poor than the UICC crocidolite and, in fact, rather resembled the composition of glaucophane, a mineral closely related to crocidolite.[18] However, I have been unable to find reports of an asbestiform glaucophane with such a high aspect ratio.

Fiber Distribution

The distribution of fibers for the plaque group between peripheral and central samples and between upper and lower lobes was compared for all fiber types and for short (less than 5 μ long) and long (greater than 5 μ long) fibers of all types using the Wilcoxan test. No significant differences were found in the distribution of crocidolite, noncommercial amphibole fibers, or chrysotile. Statistically significant accumulations of amosite fibers were found in the two subpleural samples, compared with the 2 central samples ($Z = 1.96$, $P < 0.05$); the difference was even more significant when only long fibers were compared ($Z = 2.2$, $P < 0.03$). There were no differences in the distribution of any fibers between upper and lower lobes.

Fibers in Pleural Plaques

Only chrysotile fibers were found in the four pleural plaques analyzed; no amphiboles were observed, despite the fact that 1 case, (369), had very large numbers of amphiboles in lung, as shown in Table 6. The numbers of chrysotile fibers in the plaque was less than the lung in 3 of 4 cases, and markedly greater in 1 case.

Table 5—Fiber Composition (Expressed as Elemental Percentages)

Mineral	Plaque cases	Control cases	Reference standard
Chrysotile			
Mg	43 ± 12.7	45 ± 9.3	55 ± 2.4
Si	57 ± 12.2	56 ± 9.3	45 ± 2.4
Amosite			
Na	1 ± 3.3	3 ± 4.1	1 ± 2.3
Mg	5 ± 2.4	5 ± 3.6	7 ± 2.5
Al	1 ± 3.4	0	0
Si	41 ± 4.6	40 ± 3.6	40 ± 3.8
Ca	0 ± 0.8	1 ± 1.0	0
Fe	51 ± 4.6	51 ± 3.9	52 ± 3.1
Crocidolite			
Na	5 ± 5.3	*	8 ± 3.2
Mg	4 ± 5.2		2 ± 2.1
Al	8 ± 6.2		1 ± 0.8
Si	50 ± 6.2		40 ± 2.1
Ca	0 ± 1.3		0
Fe	33 ± 10.2		49 ± 3.3
Tremolite			
Na	1 ± 1.9	1 ± 2.0	1 ± 2.0
Mg	27 ± 3.9	29 ± 3.5	30 ± 1.6
Al	1 ± 1.9	0 ± 1.0	0
Si	57 ± 3.7	57 ± 3.2	54 ± 0.9
Ca	11 ± 3.2	11 ± 2.9	14 ± 1.0
Fe	3 ± 3.1	2 ± 2.5	0 ± 0
Anthophyllite			
Na	0	1 ± 2.2	0 ± 0
Mg	36 ± 5.5	34 ± 4.0	35 ± 2.5
Al	0	0	0
Si	59 ± 3.7	58 ± 4.0	52 ± 2.0
Ca	1 ± 2.5	1 ± 1.0	1 ± 1.7
Fe	3 ± 4.1	5 ± 3.5	12 ± 3.1
Actinolite			
Na	0	0	0
Mg	18 ± 5.4	20 ± 5.4	25 ± 1.5
Al	1 ± 2.2	2 ± 2.2	1 ± 1.5
Si	50 ± 4.2	51 ± 3.2	52 ± 3.0
Ca	11 ± 3.3	9 ± 1.2	10 ± 0.8
Fe	20 ± 5.8	18 ± 6.9	12 ± 1.1

* Not specifically identified in these patients.

Table 6—Number of Asbestos Fibers in Pleural Plaques (Fibers per Gram Wet Tissue)

Case	Chrysotile in plaque	Chrysotile in lung	Total amphibole in lung
441	17×10^3	23×10^3	35×10^3
440	148×10^3	37×10^3	21×10^3
369	3×10^3	20×10^3	820×10^3
359	16×10^3	37×10^3	48×10^3

Correlations of Numbers of Fibers and Numbers of Asbestos Bodies

Correlation of these parameters was performed for the plaque group with the use of the Spearman test. Results are shown in Table 7. A strongly positive correlation was observed between the number of asbestos bodies and the number of amosite fibers, and between the number of bodies and the number of crocidolite fibers. No correlation at all was observed between numbers of bodies and noncommercial amphiboles or chrysotile fibers. The total number of amosite fibers also correlated strongly with the total number of crocidolite fibers ($\varrho = 0.725$, $P < 0.001$).

Correlation of Fibers, Bodies, and Occupational Categories

Occupations are correlated with asbestos body and fiber counts in Table 8. Eleven of the plaque patients had a history of shipyard work, and 4 more had probable exposure to asbestos during employment as pipefitters, electricians, construction workers, and insulators. Nine males had a variety of blue collar occupations that were not noted for asbestos exposure. Three of the patients (Cases 445, 446, and 369) were considered to have been white-collar workers, but examination of the fiber data indicated that patient 369, despite employment as a petroleum chemist, must have had substantial asbestos exposure (see below). Patient 242 made sheetrock for shipyards during World War II for a period of 6 weeks only; she had very large amounts of chrysotile and large amounts of tremolite and actinolite in her lungs (see Churg and Warnock[15]).

Asbestos body and fiber counts for the various occupational subgroups are shown in Table 8. The shipyard and the other exposure groups had large numbers of bodies (mean approximately 1400 and 5000/g) and also considerably higher numbers of uncoated amosite fibers (approximately 25,000/g in each group) than the other groups. The distribution of crocidolite fibers was less clearly correlated with occupational group. Noncommercial amphiboles were roughly the same for all categories.

Because an asbestos body count of 100 bodies/g of lung appears from previous work[16] to separate exposed and nonexposed occupational groups, I examined numbers of uncoated fibers when the cases were separated by this criterion (Table 9). The majority of the chrysotile fibers were found in the groups with fewer than 100 bodies/g. Noncommercial amphiboles were the same in both groups, but the commercial fibers were almost entirely found in the group with greater than 100 bodies/g. The distribution of fiber counts in the groups with fewer than 100 bodies/g is very similar to that in the control population (see Discussion).

Histopathologic and Clinical Data

Patchy fibrosis was seen in a number of cases and appeared to be represent either nonspecific old scars or the results of current therapy, especially radiation. Diffuse interstitial fibrosis of the type that might be expected in asbestosis was found in only 1 case, but no asbestos bodies were seen in tissue section. Whether this case should be counted as asbestosis is unclear: the fiber count values (chrysotile, 62,000, amosite, 12,000, crocidolite, 4300 fibers/g) are below the average for the plaque group as a whole.

Discussion

This report has analyzed the occupational histories and pulmonary asbestos burden in a series of 29 patients selected from a general autopsy population because they were found to have typical "asbestos-associated" pleural plaques. The results are compared with a series of 25 persons selected from a general autopsy population. These patients did not have plaques. Eleven of 25 were originally chosen because of a documented absence of asbestos exposure; the other 14 were selected only to produce a good match for age, sex, and smoking, and general occupational group (largely blue collar), but without regard to asbestos

Table 7—Correlations Between Numbers of Asbestos Bodies and Numbers of Asbestos Fibers for Plaque Cases (Spearman's Rank Correlation Test)

Sample group	ϱ	Significance
Bodies with amosite	0.71	$P < 0.001$
Bodies with crocidolite	0.49	$P < 0.006$
Bodies with noncommercial amphibole	.022	P = NS
Bodies with chrysotile	.10	P = NS

Table 8—Asbestos Bodies and Fibers for Plaque Patients by Occupational Category (Fibers per Gram Wet Lung)

Category (number of patients)	Chrysotile	Noncommercial amphibole	Crocidolite	Amosite	Bodies
Any history of shipyard work (11)	28×10^3	13×10^3	7.8×10^3	25×10^3	1411
Other probable exposure (construction, electrician, etc.) (4)	60×10^3	8.8×10^3	17×10^3	23×10^3	4963
Remaining blue collar men (9)	26×10^3	8.5×10^3	5.2×10^3	5.1×10^3	139
White collar men (Cases 445 and 446 only)	20×10^3	6.5×10^3	11×10^3	0.9×10^3	62
Case 369*	20×10^3	25×10^3	460×10^3	334×10^3	12,100
Case 242†	680×10^3	75×10^3	1.6×10^3	0	36

* See text concerning separation of this case.
† Female blue-collar worker.

exposure. No patient in the latter set was found to have a history of asbestos exposure. Examination of the demographic data shows that the groups were quite well matched by age, sex, and smoking habits. Most of the patients (22 of 25) were blue-collar workers. Since we are examining the significance of pleural plaques in a general population, and few persons in such a population will have had occupational asbestos exposure, the control group appears to be appropriate. This control group could not be used for a determination of differences in the mineral content of lungs between persons with known exposure with plaques and persons with known exposure without plaques, and the results of this study should not be interpreted in such a manner.

The major difference between the two groups is in the number of asbestos bodies and of commercial amphibole fibers. The total number of fibers, and the numbers of noncommercial amphiboles and of chrysotile are roughly comparable, and the distribution of fibers sizes and aspect ratios is also similar between the two groups. The plaque group had an average of 1700 bodies and 50,000 fibers of amosite and crocidolite per gram of wet lung, whereas the control group had an average of 42 asbestos bodies and 1000 fibers of amosite per gram. The values for chrysotile and noncommercial amphiboles in the two groups were quite similar (Table 2). However, the plaque group is not a homogeneous population. When the numbers of fibers in the plaque group are separated according to an asbestos body level of greater or fewer than 100 asbestos bodies per gram (a value previous work has shown to indicate an approximate separation of occupational and nonoccupational exposure to asbestos[16]), the group with the lower body count has 6900 fibers of amosite and crocidolite per gram of wet lung, whereas the group with the higher body count has 80,000 fibers/g (Table 9). The implication of this finding is that the plaque group, like blue-collar male workers in general,[16] is composed of two subpopulations, one with occupational asbestos exposure and one with exposure similar to that found in the general population.

If one attempts to correlate occupation with the number of fibers in the plaque group, the concept that this population is composed of two subgroups is reinforced. The commercial fibers are clearly, in the case of amosite, and less strongly in the case of crocidolite, associated with known occupational exposure (Table 8). In this particular group, the 11 men with histories of shipyard work and the 4 men with other likely exposure had 10 times the amount of amosite and 5 times the amount of crocidolite as the 9 other blue-collar male workers. If one compares the numbers of fibers found in two white-collar male workers (Cases 445 and 446), then the group with exposure by

Table 9—Numbers of Fibers in Plaque Patients With Greater and Fewer Than 100 Asbestos Bodies per Gram of Lung (Fibers × 10^3/g Wet Lung)

Group	Asbestos bodies	Chrysotile	Total amphibole	Noncommercial amphibole	Commercial amphibole	
					Amosite	Crocidolite
Less than 100 bodies/g lung	46 ± 34	82 ± 190	17 ± 21	10 ± 20	3.3 ± 6.4	3.6 ± 6.1
Greater than 100 bodies/g lung	2886 ± 5165	32 ± 29	93 ± 191	14 ± 12	42 ± 81	38 ± 110

occupational history had more than 10 times the amount of amosite, but only 2.5 times the amount of crocidolite. However, we have emphasized in the past[15] the dangers of relying on occupational history to rule in or rule out asbestos exposure, and Case 369 in this report illustrates this problem. This patient was a petroleum engineer who had no history of occupational exposure. He did, however, do home construction work, which may have been the source of the high numbers of fibers in his lungs.

The result shown in Table 8 is actually not surprising in light of the statistical data in Table 7, which show that there is a strongly significant correlation between the number of bodies observed by light microscopy and the number of amosite and crocidolite fibers. This observation reinforces the concept expressed in our study of the control population[15] that numbers of bodies are an indicator of long, and probably of high-aspect-ratio, amphiboles and provide no information about chrysotile content of the lung. Moreover, this correlation is only statistical, and numbers of asbestos bodies are probably a valid screen for total asbestos burden only when large numbers are found. The 1 woman with plaques (Case 242) had extremely large numbers of chrysotile fibers and of noncommercial amphiboles present despite an asbestos body count of 36/g.

It is noteworthy that, with the possible exception of 1 case, none of the patients in our plaque population had pathologic evidence of asbestosis. Comparison with fiber number data from another laboratory,[19] where patients with asbestosis were found to have on the order of 10^7–10^8 fibers/g dry lung (10^6–10^7 fibers/g wet lung), reinforces the conclusions drawn from epidemiologic studies that the pleura is much more sensitive than the parenchyma to the fibrosing effects of asbestos.[2]

In our previous report on the control patients,[15] we observed that short chrysotile fibers tended to accumulate under the pleura, an observation also made by others in man and experimental animals. In the plaque group we were unable to observe any differences between pleura and deep parenchyma for chrysotile, but did find significantly greater numbers of amosite fibers in both subpleural samples; no differences were seen between upper and lower lobes. Whether this implies a direct physical concentration effect in the genesis of pleural plaques is unclear. It is noteworthy that I found no amphibole fibers in the plaques themselves, but only chrysotile fibers. The numbers of chrysotile fibers in the few plaques examined appeared to have no relation to the numbers in the underlying lung.

The results presented in this paper thus suggest that bilateral lower-zone or diaphragmatic plaques in the general population are frequently but not consistently associated with asbestos exposure. It may be argued that those persons in the plaque group who did not have large numbers of commercial amphiboles had all been exposed to chrysotile that had subsequently dissolved. However, my experience in analyzing chrysotile miners and the experience of others[20] has been that chrysotile is usually accompanied by contaminating tremolite and actinolite fibers, which over the long term persist in large numbers, often larger than the remaining chrysotile burden. The 1 patient in this group who appeared to have plaques because of chrysotile exposure in fact showed a large number of noncommercial amphibole fibers (Table 8, Case 242). Additionally, if the argument that plaques are induced by chrysotile that has disappeared is correct, it would be difficult to account for the good correlation between occupational history of exposure and increased numbers of commercial amphiboles, and it would also be difficult to account for the excellent correspondence for numbers of each type of mineral fiber between our control population, who appear to have had only environmental exposure, and the values for the subgroup of plaque patients who had fewer than 100 asbestos bodies per gram, a number that appears to mark environmental exposure.

It is more likely that two subgroups are present in this general population. One group had pleural plaques as a result of exposure, most likely occupational exposure, to commercial high-aspect-ratio amphiboles; the number of commercial fibers averaged about 50 times that of the control population. This argument should not be taken to imply that chrysotile exposure does not produce pleural plaques but points out that in this particular population the exposure, with one exception, was to amphiboles. The other subgroup had pleural plaques of unknown etiology. The cause might have been infection or trauma, as has been suggested, but might also conceivably have been exposure to other types of mineral fibers, since long, thin mineral fibers of many sorts appear to cause pleural disease.[21] We are currently evaluating the nonasbestos mineral fibers in this population.

From the point of view of understanding the pathogenesis of asbestos-related disease, the useful point emerges from this study that asbestos-induced lesions may not be merely reflections of numbers of fibers; they probably depend on complex mineralogic parameters. Thus, in this instance the plaque and control groups had about the same number of total

fibers, but the plaque group had much larger numbers of long high-aspect-ratio amphiboles. Detailed studies of this type will be required for evaluation of the role of asbestos in cases of malignancy and interstitial fibrosis, and may have a role in setting exposure standards.

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