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Asbestos Content of Lung Tissue and Carcinoma of the Lung: a Clinicopathologic Correlation and Mineral Fiber Analysis of 234 Cases

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The aim of this study was to investigate the asbestos content of lung tissue in a series of patients with lung cancer and some history of asbestos exposure. This information was then correlated with demographic information, occupational and smoking history, presence or absence of pathologic asbestosis or pleural plaques, and pathologic features of the cancer. The pulmonary concentration of asbestos fibers in 234 cases of primary carcinoma of the lung was determined by means of a tissue digestion technique. Asbestos body counts were performed in 229 cases and fiber analysis by scanning electron microscopy in 221 cases. Asbestos content was recorded as total asbestos fibers, commercial amphibole fibers, noncommercial amphibole fibers, and chrysotile fibers 5 μm or greater in length per gram of wet lung tissue. The study group included 70 patients with asbestosis (Group I), 44 patients with parietal pleural plaques but without asbestosis (Group II), and 120 patients with neither (Group III). The median asbestos body content of Group I was more than 35 times greater than Group II and more than 300 times greater than Group III. The total asbestos fiber count for Group I was nearly 20 times greater than Group II and more than 50 times greater than Group III. The difference was due almost entirely to commercial amphiboles.

In a series of primary lung cancer cases with some history of asbestos exposure, a markedly elevated asbestos content was identified among those with pathologic asbestosis as compared with patients with pleural plaques alone or with neither plaques nor asbestosis. © 2000 British Occupational Hygiene Society. Published by Elsevier Science Ltd. All rights reserved.

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INTRODUCTION

Asbestos is generally recognized to be a cause of carcinoma of the lung, especially among individuals who also smoke cigarettes (Greenberg and Roggli, 1992). However, there is considerable controversy regarding the circumstances under which asbestos exposure can be considered to be a substantial contributing factor to carcinoma of the lung in an individual case (Churg, 1993; Cullen, 1987; Henderson *et al.* 1995; Henderson *et al.*, 1997a; Henderson *et al.*, 1997b; Roggli *et al.*, 1994). Specifically, some investigators believe that asbestosis must be present before lung cancer can be related to asbestos exposure, whereas others believe that it is the dose or tissue burden of asbestos that is the critical factor rather than the presence or absence of interstitial fibrosis.

Hughes and Weill in a study of asbestos cement workers published in 1991 failed to identify an increased risk for lung cancer in patients lacking radiographic evidence of asbestosis (Hughes and Weill, 1991). However, several subsequent studies with greater statistical power than that of the Hughes–Weill study have shown an increased risk of lung cancer among asbestos workers, even in the absence of clinical asbestosis (Hillerdal, 1994; Karjalainen *et al.*, 1994a; Wilkinson *et al.*, 1995). Hillerdal described a modest increase in lung cancer

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mortality (standard incidence ratio of 1:43) in a group of more than 1500 patients with parietal pleural plaques on chest X-ray but without asbestosis, after adjusting for smoking habits (Hillerdal, 1994). Wilkinson *et al.* (1995) and Karjalainen *et al.* (1994a) similarly reported increased lung cancer risks among asbestos workers even in the absence of asbestosis and after adjustments for smoking.

The study by Karjalainen *et al.* (1994a) is of particular interest, since it is the first to demonstrate an increased lung cancer risk based on the pulmonary asbestos fiber burden, independent of pathologic asbestosis and smoking. In a comparison of 113 consecutive resections for lung cancer and 297 medical examiner cases, a pulmonary fiber burden of one million or more amphibole fibers per gram of dry lung tissue as determined by scanning electron microscopy was found to be associated with an odds ratio for lung cancer of 1:7. The odds ratio increased to 5:3 for fiber burdens of five million or more per gram of dry lung. Furthermore, elevated fiber burdens were most strongly associated with lower lobe carcinomas and with adenocarcinoma histology. In a similar study of patients with mesothelioma, Rodelsperger found that a tissue burden of 2 million amphibole fibers ≥5 μm in length per gram of dry lung tissue as determined by transmission electron microscopy was associated with a cumulative fiber burden of 25 fiber-years (Rodelsperger, 1996). Other studies have indicated that this level of exposure is associated with a two-fold increase in lung cancer risk (Henderson *et al.*, 1997b)

The purpose of the present study is to review our own experience with pulmonary mineral fiber burdens in cases of carcinoma of the lung with some history of asbestos exposure. The results of fiber burden analysis by scanning electron microscopy were then examined in the context of the patients' age, sex, occupational history, smoking history, lobe of origin, presence or absence of pathologic asbestosisorparietalpleuralplaques,andhistological type of cancer. These findings on 234 cases of primary carcinoma of the lung form the basis of the present study.

MATERIALS AND METHODS

Patient selection

The consultation files of one of the authors (VLR) were reviewed for cases of carcinoma of the lung for which tissue asbestos analysis had been performed. Cases were selected as primary carcinoma of the lung based on review of the medical records, radiographic studies, and pathologic findings. Most of these cases were medicolegal referrals in asbestos litigation. The histologic pattern was determined using the revised World Health Organization classification of tumors of the lung (World Health Organization, 1982). Information regarding the individual patient's age, sex, smoking history, and lobe of origin was determined from the medical records. Occupational exposure information was obtained by interview of the patient or next of kin.

Pathologic findings

Sections of lung parenchyma, either from the opposite lung or at some distance from the primary tumor, were reviewed for the presence or absence of histologic asbestosis using our previously published criteria (Roggli and Pratt, 1992). In brief, this consisted of peribronchiolar fibrosis with or without alveolar septal fibrosis in association with asbestos bodies in histologic sections. Pleural plaques were identified as present or absent at autopsy or at thoracotomy, and consisted histologically of layers of acellular hyalinized collagen arranged in a 'basket-weave' pattern (Greenberg, 1992). Cases were then classified as asbestosis (Group I), pleural plaques without asbestosis (PPP) (Group II), or as lung cancer with neither plaques nor asbestosis (Group III). Cases which were surgically resected and no information was available regarding the presence or absence of plaques were classified as Group III.

Tissueasbestosanalysis

Formalin fixed or paraffin embedded peripheral lung parenchyma was available in 234 cases of primary carcinoma of the lung. The samples were obtained from autopsies (64%) or from surgically resected specimens (36%). Lung tissue was processed for digestion using the sodium hypochlorite technique as previously described (Roggli *et al.*, 1992). The residue was collected on 0.4 μm pore-size Nuclepore filters. For light microscopic analysis, the filter was mounted on a glass slide for asbestos body quantification. Filters were counted at a magnification of 400 ×, and only bodies with typical morphology and thin, translucent cores were counted as asbestos bodies (Roggli, 1992). Results were reported as asbestos bodies per gram of wet lung tissue (AB/g). Values for the cases were compared with 19 controls for our laboratory with macroscopically normal lungs, no evidence of lung cancer, and no history of asbestos exposure. The normal range for our laboratory is 0–20 AB/g, and the detection limit for a 0.3 g sample size is approximately 3 AB/g. For cases in which no asbestos bodies were detected in the sample, the value was recorded as less than the detection limit for that sample.

For scanning electron microscopic (SEM) analysis, the filter was mounted on a carbon disc with colloidal graphite, sputter-coated with gold, and examined in a JEOL JSM-6400 scanning electron microscope at a screen magnification of 1000× and

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with a screen size of 22.7 × 17.3 cm. Fibers 5 μm or greater in length were counted using a protocol in which 100 consecutive fields or 200 fibers were counted, whichever came first. Fibers were defined as particles with an aspect ratio (length:width) of at least 3:1 and roughly parallel sides. The concentration of fibers for each case was calculated based on the fiber density (i.e., per mm^2) on the filter surface times the effective area of the filter, divided by the weight of the lung sample which was analyzed. The results were reported as total asbestos fibers (coated and uncoated) 5 μm or greater in length per gram of wet lung. The normal range for our laboratory is < 440–2540 asbestos fibers/g (median: < 600 asbestos fibers/g), and the detection limit for a 0.3 g sample size is approximately 440 fibers/g. For cases in which no asbestos fibers were detected in the sample, the value was recorded as less than the detection limit for that sample.

Fiber types were determined using a combination of fiber morphology assessed by SEM and elemental composition assessed by energy dispersive X-ray analysis (EDXA). Fibers were classified as amosite, crocidolite, tremolite, anthophyllite, actinolite or chrysotile as previously described (Roggli *et al.*, 1992). For purposes of analysis, amosite and crocidolite were grouped together as commercial amphiboles (AC), and tremolite, anthophyllite and actinolite were grouped together as non-commercial amphiboles (TAA). In more than 90% of cases, between 10–20 fibers were analyzed per case (mean, 17 fibers per case). The proportion of each fiber type and the total asbestos fiber concentration were used to determine the tissue concentration of AC, TAA, and chrysotile for each case. For cases where no fibers of a particular fiber type were detected, the value was recorded as less than the detection limit for that fiber type for that case.

Statistical Analysis

The lobe of origin and the distribution of histologic types for Groups I–III were compared by a chi-square test. Ages were compared by Student's *t*-test. Duration of exposure was compared using a general linear regression model. For all analyses involving fiber types, the log transformation of the asbestos body or fiber concentration was used, since these values are approximately log-normally distributed. The degree of random variation expected from multiple analyses of a single case have been reported elsewhere (Roggli *et al.*, 1992). For values that were below the detection limit, half of the detection limit was used for purposes of analysis. Asbestos body counts, total asbestos fiber, commercial amphibole, and non-commercial amphibole concentrations were compared among asbestosis (Group I), pleural plaques without asbestosis (Group II), and lung cancer cases with neither plaques nor asbestosis (Group III) using a general linear regression model on the log transformed values and the Wilcoxon two-way nonparametric rank sums test on the original untransformed data. (The *P* values were almost identical using these two methods of analysis, so only the Wilcoxon values are reported in the text). For all statistical analyses, a *P* value of less than 0.05 was considered statistically significant.

RESULTS

Demographic features

Data concerning the number of cases in each category, the age distribution, gender, and smoking history for Groups I–III are summarized in Table 1. The mean age for all 234 cases was 62, and the patients with asbestosis (64 years) and pleural plaques (64.5 years) were slightly older than the patients with neither (60 years) ($P < 0.05$). There were 227 men and seven women; five of the latter were in Group III. Smoking histories were available in 157 of the 234 cases (67%). Of those with known histories, all but eleven cases were smokers or ex-smokers. These eleven cases gave a history of being lifelong nonsmokers.

Table 1. Demographic data on 234 lung cancer patients with asbestos exposure[a]

	Group I[b] ($n = 70$)	Group II[c] ($n = 44$)	Group III[d] ($n = 120$)
Age (yrs)	64 ± 9	64.5 ± 8	60 ± 11
Range:	44–84	44–84	31–85
Gender			
Male	69	43	115
Female	1	1	5
Smoking history			
Smokers or ex-smokers	54	31	61
Non-smokers	1	1	9

[a]Information was unavailable regarding smoking history in 15 cases from Group I, 12 cases from Group II, and 50 cases from Group III. Similarly, ages were unavailable in 24 cases.
[b]Group I — asbestosis.
[c]Group II — parietal pleural plaques without asbestosis.
[d]Group III — neither plaques nor asbestosis.

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Table 2. Occupational information on 163 lung cancer patients with asbestos exposure[a]

Occupational category	Group I	Group II	Group III
Shipyard worker[b]	20 (37)	14 (45)	16 (21)
Insulator/pipe coverer	18 (33)	2 (6)	6 (8)
Welder/pipefitter	3 (6)	4 (13)	6 (8)
Boiler/power plant worker	3 (6)	1 (3)	8 (10)
Sheetmetal worker/mach.	0 (0)	0 (0)	6 (8)
US Navy/merchant marine	0 (0)	1 (3)	8 (10)
Oil/chemical refinery	0 (0)	2 (6)	2 (3)
Other asbestos[c]	8 (15)	6 (19)	23 (29)
Household contact	1 (2)	1 (3)	2 (3)
Environmental exposure	1 (2)	0 (0)	1 (1)
Total	54	31	78

[a]Data presented as number of cases for each category (percentage in parentheses). No data were available in 16 cases from Group I, 13 cases from Group II, and 42 cases from Group III.
[b]Other than insulator (See footnotes to Table 1 for definition of Groups I–III).
[c]Includesmillwright(3),railroadworker(6),refractoryceramicfiberworker(3),brakerepairman(5),asbestosfactory worker,generalserviceoperationengineer,papermillworker,carpenter,custodian,drywallfinisher,constructionworker, roofing plant worker, roofer, military laundry, and asbestos worker NOS (8).

Occupational data

Information concerning the occupational exposure of the patients was available in 163 of the 234 cases (70%), and is summarized in Table 2. The largest single occupational category for all three groups was shipyard worker, accounting for 37% of cases in Group I, 45% in Group II, and 21% in Group III. A higher percentage of lung cancer patients with asbestosis were insulators (33%) as compared to lung cancer patients with plaques alone (6%) or lung cancer patients with neither plaques nor asbestosis (8%) ($P < 0.05$ by chi-square analysis). Household contacts of asbestos workers were found in each of the three groups. One patient in Group I had an environmental exposure to tremolite asbestos as a child while playing on piles of tailings in a vermiculite processing plant (Srebro and Roggli, 1994). One patient in Group III worked in a building with friable asbestos materials in the ceilings for more than 20 years (Roggli and Longo, 1991).

Information regarding duration of asbestos exposure was available for 39 patients in Group I, 22 patients in Group II, and 49 patients in Group III. The duration of exposure to asbestos was 28 ± 10 years (mean and standard deviation) for Group I (range: 2–49 years); 26 ± 11 years for Group II (range: 3.5–43 years); and 24 ± 13 years for Group III (range: 1–49 years). These differences were not statistically significant. No information was available regarding intensity or regularity of exposure forindividualpatients.

Pathologicalfindings

Table 3 presents the data regarding the lobe of origin and laterality of the tumor in this series of cases. The lobe of origin was known in 128 cases and the laterality in 172. Although information is missing in 45% of the cases, it is surprising to note that upper lobe tumors outnumbered lower lobe tumors in all three groups in a ratio of nearly 3:1. Tumors occurred in the right lung slightly more often than in the left in all three groups.

The histological classification was assessed in 97% of the cases, and these data are displayed in Table 4. Adenocarcinomas predominated in all three groups and ranged from 38% to 55% of cases for which information was available regarding histologic type. Three patients had synchronous primary pulmonary malignancies, one each from

Table 3. Tumor location in 172 lung cancer patients with asbestos exposure[a]

	Group I	Group II	Group III
Upper Lobe[b]	30	18	46
Lower Lobe	10	6	18
Right Side[c]	32	18	47
Left Side	20	15	40

[a]See footnotes to Table 1 for definition of Groups I–III.
[b]No information was available regarding upper vs lower lobe localization in 30 cases from Group I, 20 cases from Group II, and 56 cases from Group III.
[c]No information was available regarding tumor laterality in 18 cases from Group I, 11 cases from Group II, and 33 cases from Group III.

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Table 4. Histology in 227 cases of lung cancer with asbestos exposure[a]

	Group I[b]	Group II[b]	Group III[b]
Squamous cell carcinoma	20 (29)	10 (24)	32 (27)
Adenocarcinoma	27 (39)	16 (38)	65 (55)
Small cell carcinoma	13 (19)	9 (21)	12 (10)
Large cell carcinoma	4 (6)	7 (17)	7 (6)
Adenosquamous carcinoma	6 (9)	0 (0)	2 (2)

[a]Values reported as number of cases for each histologic type with percentages indicated in parentheses. No information regarding histologic type was available in 1 case from Group I, 3 cases from Group II, and 3 cases from Group III. Three patients had synchronous primaries, one adenosquamous and one small cell carcinoma (Group I); one small cell and one giant cell anaplastic carcinoma (Group II); and one adenocarcinoma and one squamous cell carcinoma (Group III).
[b]See also footnotes to Table 1 for definition of Groups I–III.

Group I, II and III. The distribution of histologic types was not significantly different among the three groups.

Fiberanalysis

The results of the tissue mineral fiber analysis are presented in Table 5. Asbestos body counts were determined by light microscopy in 229 cases. The median asbestos body count for Group I was 38 times that for Group II and 341 times that for Group III ($P = 0.0001$ for Group I vs II or III, $P = 0.0004$ for Group II vs III using the Wilcoxon rank sums on the untransformed data). Fiber analysis was performed by scanning electron microscopy in 221 cases. The median total asbestos fiber count for Group I was 18 times that for Group II and 51 times that for Group III ($P = 0.0001$ for Group I vs II or III, $P = 0.008$ for Group II vs III). These differences were almost entirely accounted for by the commercial amphiboles, amosite and, to a lesser degree, crocidolite. The non-commercial amphibole content was also greater for Group I as compared to II or III ($P = 0.0001$). The non-commercial amphibole content was not significantly different between groups II and III. Commercial amphiboles were detected in 65 cases from Group I, 37 cases from Group II, and 85 cases from Group III. Non-commercial amphibole fibers were detected in 23 cases from Group I, 24 cases from Group II, and 72 cases from Group III. In contrast, chrysotile fibers were detected in only eight cases from Group I, 5 cases from Group II, and 17 cases from Group III. For comparison purposes, the data for our unexposed background control group are also shown in Table 5.

DISCUSSION

The present study indicates that in a relatively large group of lung cancer patients with some history of asbestos exposure, patients with histologic evidence of asbestosis had a substantially and significantly increased pulmonary asbestos content as compared to those without asbestosis. Furthermore, patients with pleural plaques lacking asbestosis had a higher asbestos content than those with neither plaques nor asbestosis. A higher percentage of patients with lung cancer who also had asbestosis were insulators (33% of Group I as compared with 6% of Group II and 8% of Group III patients). These findings are consistent with our prior observation that insulators have on average the highest pulmonary asbestos burdens of any occupational group we have studied (Roggli *et al.*, 1992). Furthermore, a higher percentage of patients with asbestosis or pleural plaques were shipyard workers as compared to lung cancer patients with neither asbestosis nor plaques (37% of Group I and 45% of Group II as compared with 21% of Group III patients). This observation is consistent with data indicating that for similar exposure durations, shipyard workers have on average higher pulmonary asbestos burdens than non-shipyard workers (Roggli, 1995).

The differences among Groups I–III in our study were almost entirely accounted for by commercial amphiboles, primarily amosite. Indeed, commercial amphiboles were detected in 88% of cases. This is not surprising, considering the widespread use of amosite containing insulation products in the past in the United States and the categories of occupational exposure included in Table 2. There was a significant difference between the non-commercial amphibole and chrysotile levels in Group I as compared to Groups II or III, but this difference was largely an artifact of the higher detection limits for Group I cases. Churg and Vedal found no difference between the non-commercial amphibole and chrysotile levels of disease vs control cases using the more sensitive transmission electron microscopic technique (Churg and Vedal, 1994). Non-commercial amphiboles were identified in 119 of 221 cases (54%), whereas chrysotile fibers were identified in only 30 of 221 cases (14%) in our study. This finding may be attributed to the tendency for chrysotile

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Table 5. Fiber analysis data in 234 cases of lung cancer with asbestos exposure[a]

	AB/g (LM)[c]	SEM[b] Total fibers/g[d]	AC/g[e]	TAA/g[f]	Chrys/g[g]
Group I (n = 70)[h]	27,300 (150–343,000)	253,000 (14,600–8,540,000)	253,000 (< 11,200–8,540,000)	< 22,000 (1460–149,000)	< 22,000 (910–63,900)
Group II (n = 44)	710 (< 3–18,900)	14,000 (< 510–142,000)	8140 (< 490–118,000)	2180 (180–48,900)	< 2000 (180–8600)
Group III (n = 120)	80 (2.6–45,800)	4990 (370–157,000)	3490 (< 370–113,000)	2110 (170–144,000)	< 1800 (< 310– < 14,000)
Controls (n = 19)	2.9 (0.2–22)	< 600 (< 170–2540)	< 600 (< 100– < 2540)	< 600 (< 170–2540)	< 600 (< 100– < 2540)

[a]Data reported as median values and range (in parentheses) for total fibers (coated + uncoated) ≥5 μ in length per gram of wet lung for each fiber type, as determined by scanning electron microscopy; or for asbestos bodies alone (1st column) as determined by light microscopy.
[b]SEM = scanning electron microscopy.
[c]AB/g (LM) = asbestos bodies per gram of wet lung.
[d]Total fibers = total asbestos fibers (coated + uncoated) ≥5 μ long.
[e]AC = amosite + crocidolite.
[f]TAA = tremolite + anthophyllite + actinolite.
[g]Chrys = chrysotile.
[h]See footnotes to Table 1 for definition of Groups I–III.

to be broken down into smaller fibrils and subsequently cleared from the lungs (Roggli and Brody, 1992). Consequently, fiber burden studies do not accurately reflect past exposures to chrysotile. Furthermore, SEM is somewhat insensitive to the detection of chrysotile fibers, many of which are less than 0.1 μm in diameter, particularly at the screening magnification (1000×) used in our study.

Our findings differ from those of Warnock and Isenberg (1986), who studied 75 cases of lung cancer among individuals most of whom were in the shipbuilding trades. The latter authors reported substantial overlap in the fiber burdens for patients with or without asbestosis, and suggested a cut-off level for asbestos-related lung cancer of 100,000 or more commercial amphibole fibers per gram of dry lung tissue (approximately 10,000 fibers per gram of wet lung) as determined by transmission electron microscopy for fibers 0.5 μm or greater in length. Differences between the present study and that of Warnock and Isenberg (1986) may be due to different criteria for a pathologic diagnosis of asbestosis or to the more heterogeneous nature of the occupational exposures to asbestos in our study. Our findings are similar to those of Karjalainen *et al.* (1994b) who found a substantial proportion of patients with pleural plaques alone have fewer than one million fibers per gram of dry lung. Our findings are also similar to those of Thimpont and De Vuyst, who found that an asbestos body concentration of 5000 per gram dry lung (approximately 500 per gram wet lung) was associated with low-grade fibrotic lesions in airways and lung tissue in about 50% of their cases of resections for lung cancer. This concentration of asbestos bodies also correlated with a cumulative exposure of about 10 fiber-years (Thimpont and De Vuyst, 1998).

In our series of cases, pathologic features of the tumor were of little assistance in attributing a lung cancer to prior asbestos exposure. The distribution of histologic types did not differ significantly among Groups I–III, with a predominance of adenocarcinomas in all three groups. Indeed, the highest percentage of adenocarcinomas occurred in the group with the overall lowest pulmonary asbestos burden (Tables 4 and 5). This finding differs from those of Karjalainen *et al.* (1994a) and Johansson *et al.* (1992), and may be due to selection bias for surgical resection (with patients with peripheral adenocarcinomas more likely to be surgical candidates) or to referral bias. However, other investigators have also found no correlation between histologic type and asbestos etiology (Auerbach *et al.*, 1984; Churg, 1985; Ives *et al.*, 1983; Lee *et al.*, 1998; Vena *et al.*, 1985). Furthermore, the lobe of origin was similar for all three groups in our study, with upper lobe tumors outnumbering lower lobe tumors by about 3:1. This finding was somewhat surprising and differs from the lower lobe predominance of asbestos-

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related cancers reported by some investigators (Anttila *et al.*, 1993; Churg, 1983; Karjalainen *et al.*,1993;Karjalainen *et al.*, 1994a; Weiss, 1988) but is similar to the recent results reported by Lee et al. (1998). We cannot explain our findings with regard to lobe of origin on the basis of surgical selection orreferralbias.

Caution must be exercised in extrapolating fiber burden data from one laboratory to another. For example, Karjalainen et al. (1994a) used low temperature ashing, magnification of 5000 × , and reported fibers 1 μm or greater in length per gram of dry lung tissue, whereas our laboratory used wet chemical digestion, magnification of 1000 × , and reported fibers 5 μm or greater in length per gram of wet lung. Nonetheless, some interesting observations may be made by comparing the results of the two laboratories. One million fibers per gram of dry lung is approximately equivalent to 100,000 fibers per gram of wet lung (Roggli *et al.*, 1992). Furthermore, Karjalainen et al. (1994a) reported that approximately 50% of commercial amphibole fibers and 75% of noncommercial amphibole fibers are 5 μm or greater in length using their SEM technique. According to these approximations, one million amphibole fibers ≥1 μm in length per gram of dry lung is roughly equivalent to 50,000 commercial amphibole or 75,000 noncommercial amphibole fibers ≥5 μm in length per gram of wet lung.

Only nine cases from Groups II and III had commercial amphibole fiber counts exceeding 50,000 per gram of wet lung (Table 6). These include four of 41 patients from Group II (10%) and five of 114 patients from Group III (5%). Of these nine cases, only four had adenocarcinomas and one had a lower lobe cancer. Only one patient from Group III (and none from Group II) had more than 75,000 noncommercial amphibole fibers per gram of wet lung (Table 6). This patient had been a roofing plant worker for 34 years and died of squamous cell carcinoma of the right upper lobe. It should be noted that the asbestos body concentrations were of sufficient levels in eight of these ten cases for asbestos bodies to be readily identified in iron-stained histologicsections(Roggli,1992).

In contrast, more than 50,000 AC/g or 75,000 TAA/g were identified in 82% of patients with a pathologic diagnosis of asbestosis. Among the 12 patients with asbestosis with fiber counts less than these values, information was available regarding the histologic grade of asbestosis in ten of these cases. In seven of the ten, the grade of asbestosis was 1 on a scale of 0–4 (i.e., fibrosis confined to the walls of respiratory bronchioles) (Roggli and Pratt, 1992). These findings are consistent with the observations of Churg (1983) that asbestos workers with fibrosis confined to the walls of the respiratory bronchioles (referred to by Churg as asbestos-airways disease) had substantially lower pulmonary asbestos burdens than workers with more diffuse interstitial fibrosis.

It should be noted that asbestosis as described in this study is based on histologic criteria, and that this is different from radiologically diagnosed cases. Indeed, studies have indicated that asbestosis may be identified histologically in lung tissue from patients whose chest radiographs show no evidence of interstitial lung disease (Roggli and Pratt, 1992). Therefore, the findings in this study cannot be extrapolated to studies based on radiographic diagnosis of asbestosis, as for example, the study of Hughes and Weill (1991).

Only seven of the patients in our study were women. One of these also had grade 1 asbestosis (Group I) and one had pleural plaques (Group II). The other five cases belonged to Group III. Four of the seven were household contacts of asbestos workers and were exposed to asbestos brought

Table 6. Demographic, pathologic, occupational, and fiber analysis data on 10 patients without asbestosis but with excessive amphibole burdens

N	Age	Pathology[a]	Occupation	AB/g[c]	AC/g[d]	TAA/g[d]	Chrys/g[d]
1[b]	62	SC	Shipyard sheetmetal worker, 33 yrs	8900	118,000	24,200	< 12,900
2	54	Ad	Marinite worker, 7 yrs	43	113,000	28,000	< 14,000
3[b]	74	ND	Asbestos sawer, 27 yrs	18,900	107,000	7950	< 7950
4[b]	61	LC, Lt.	ND	16,300	71,100	< 8400	8600
5	63	Ad, LLL	Boilermaker, 37 yrs	7650	64,400	< 7990	< 7990
6[b]	60	Sq, RUL	Shipwright, 35 yrs	12,900	73,600	17,400	< 17,400
7	ND	Sq, LUL	Shipyard machinist, 19 yrs	63	59,900	< 3150	< 3150
8	72	Ad	ND	4240	58,000	< 5800	< 5800
9	58	Ad	Shipyard welder, 19 yrs	45,800	55,800	5120	< 5120
10	57	Sq, RUL	Roofing plant worker, 34 yrs	620	13,100	144,000	< 13,100

[a]SC = small cell carcinoma; Ad = adenocarcinoma; LC = large cell carcinoma; Sq = squamous cell carcinoma; RUL = right upper lobe; LLL = left lower lobe; LUL = left upper lobe; Lt. = left, ND = no data.
[b]Indicatespatientswithparietalpleuralplaques.
[c]AB/g = asbestos bodies per gram of wet lung, as determined by light microscopy.
[d]AC = amosite + crocidolite. TAA = tremolite + anthophyllite + actinolite. Chrys = chrysotile, all per gram of wet lung by scanning electron microscopy (fibers ≥5 μ inlength).

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home on the workclothes of their spouse. None of the seven had a pulmonary asbestos burden of combined (commercial plus non-commercial) amphibole fibers exceeding 50,000 fibers/g.

There are a number of limitations of the present study which must be kept in mind. First of all, most of the patients analyzed in this series were medicolegal cases, which may comprise combinations of exposure and disease factors which are nonrepresentative of the overall population of asbestos-exposed individuals. Secondly, fiber burden studies of this type afford limited information regarding the role of chrysotile in asbestos-related lung cancers, since as noted above, chrysotile is broken down in and removed from the lungs and long (≥5μm) thin, chrysotile fibers are not readily detectable by our technique. Furthermore, tremolite levels are a somewhat crude measure of prior chrysotile exposure.

In conclusion, among a selected group of primary lung cancers from the United States with some history of asbestos exposure, a markedly elevated pulmonary asbestos burden was identified among those with a pathologic diagnosis of asbestosis. The finding of pathologic evidence of asbestosis as we have previously defined it (Roggli and Pratt, 1992) is a good marker for more than 50,000 amphibole fibers per gram of wet lung, with 82% of cases exceeding this value. In contrast, only 6.5% of patients without histologic evidence of asbestosis but with some history of asbestos exposure had fiber burdens exceeding 50,000 amphibole fibers/g. Taken together, these findings suggest that an amphibole fiber burden sufficient to induce carcinoma of the lung is most often (but not invariably) accompanied by histologic evidence of asbestosis. Furthermore, the data presented in this study correspond quite well to the recently promulgated Helsinki criteria (Henderson *et al.*, 1997b), in which parietal pleural plaques by themselves are insufficient for attribution of lung cancer to asbestos.

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