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# Asbestos in Extrapulmonary Sites*

## Omentum and Mesentery

*Ronald F. Dodson, PhD, FCCP; Michael F. O'Sullivan, BS; Ju Huang, MS; David B. Holiday, PhD; and Samuel P. Hammar, MD, FCCP*

***Study objectives:*** **Asbestos fibers have not been reported in tissues from the peritoneal cavity. Therefore, omentum, mesentery, and lung tissues from 20 individuals in whom mesothelioma was diagnosed were analyzed for asbestos bodies and asbestos fibers.**
***Design:*** **Tissue was digested and prepared filters were analyzed by light microscopy and analytical transmission electron microscopy.**
***Results:*** **Asbestos bodies were found in the lungs of 18 individuals, mesentery samples from 5, and omentum samples from 2. Uncoated asbestos fibers were found in lungs of 19 patients, 17 of whom had fibers in at least one extrapulmonary site. The most common asbestos in the omentum and mesentery was amosite. Several features of asbestos found in lung influenced the likelihood of amphibole fibers being found in the omentum or mesentery. Lung features included total amphibole fiber burden, length, aspect ratio, and ferruginous body burden. An increased total ferruginous body burden was strongly associated with increased likelihood of detecting amphiboles in the omentum ($p < 0.05$).**
***Conclusion:*** **Asbestos fibers reach areas in the peritoneal cavity where some mesotheliomas develop. This study suggests their presence can be predicted based on concentrations and characteristics of fiber burdens in lung tissue.** ***(CHEST 2000; 117:486–493)***

**Key words:** asbestos; extrapulmonary; mesothelioma

**Abbreviations:** AB = asbestos body; ATEM = analytical transmission electron microscopy; FB = ferruginous body

Inhaled articles are removed by several mechanisms, including the mucociliary escalator of larger airways and additional mechanisms at the alveolar level.[1–3]

The lymphatics relocate particles from the lung to pleura and to hilar and more distant lymph nodes.[1] Becklake[4] and Hillerdal[5] suggested the lymphatic route for asbestos relocation from the lung (the original site of deposition) to other parts of the body. A limited number of studies have reported asbestos bodies in the hilar and mediastinal lymph nodes.[6–8]

Our laboratory has compared the burden of uncoated fibers and asbestos bodies from thoracic nodes to the concentration of asbestos fibers in pleural plaques and lung tissue.[8]

Although we have shown asbestos fibers in thoracic loci where mesotheliomas develop, few or no data exist concerning the presence or absence of asbestos fibers in the linings of the peritoneal cavity, where 10 to 15% of mesotheliomas occur. It is reasonable to assume that asbestos fibers relocate to these sites and, through their physical and chemical properties, stimulate tissue reactions that favor the development of mesothelioma. Based on our previous findings, it is assumed that fibers reaching the peritoneal cavity will require transmission electron microscopy to be detected.

In this study, tissue from 20 individuals with mesotheliomas, most with a history of asbestos exposure, were evaluated. The questions to be answered included whether asbestos fibers would be found in the omentum and mesentery, and, if so, would their presence be predicted by various qualitative and quantitative features of asbestos bodies (ABs) and asbestos fibers in the lung from the same individuals.

## Materials and Methods

### *Description of Cohort*

In 20 individuals, malignant mesothelioma was diagnosed at autopsy examination by one author (S.P.H.). The diagnosis was based on macroscopic, histologic, immunohistochemical, and

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occasionally ultrastructural features. All individuals were male, and the majority had worked in professions where contact with asbestos in the workplace would be expected (Table 1). The mean age was 69.8 ± 8.3 years. Seventeen cases were pleural mesotheliomas (85%), and three (cases 6, 7, and 9) were peritoneal mesotheliomas (15%).

*Tissue Analysis*

Tissue analyzed at the Tyler, TX, laboratory included right and left lung, omentum, and mesentery from each patient. Multiple sites of tumor-free, formalin-fixed lung parenchyma were dissected from each lung. An area adjacent to each site was taken to determine the

**Table 1—*Historical Data for Mesothelioma Cases****

| Assay No. | ID No. | Age/Sex | CS | Occupational History Years of Exposure | Mesothelioma Location Histologic Type | Pleural Plaque | Pathologic Asbestosis | DOD |
|---|---|---|---|---|---|---|---|---|
| 1 | L-68-90 | 74/M | NS | Shipyard insulator > 1941–44<br>Brakeworker > 1945–70 | Right pleura<br>Sarcomatoid | Yes<br>Parietal pleura | Yes<br>Grade 1–3 | Mar-90 |
| 2 | L-132-93 | 72/M | nd | Boilermaker > 1939–72 | Parietal pleura<br>Epithelial with focal variable differentiation | Yes<br>Pericardium | Yes<br>Grade 1 | Jul-93 |
| 3 | L-235-92 | 64/M | nd | Shipfitter and insulator > 1956–75 | Left pleura<br>Epithelial | Yes<br>Parietal pleura | Yes<br>Grade 1 | Nov-92 |
| 4 | L-67-93 | 60/M | 50+ | US Coast Guard and contractor > 1938–88 | Right pleura<br>Sarcomatoid with osseous differentiation | No | No | Apr-93 |
| 5 | L-228-93 | 73/M | 15 | Brickmason > 1946–77 | Left pleura<br>Sarcomatoid/desmoplastic | Yes<br>Parietal pleura | Yes<br>Grade 1–2 | Oct-93 |
| 6 | L-450-97 | 75/M | 25 | Shipyard insulator and machinist > nd | Peritoneal<br>Biphasic | Yes<br>Parietal pleura | Yes<br>Grade 1–2 | Oct-97 |
| 7 | L-241-92 | 58/M | 50+ | Shipyard insulator > 1954–62 | Peritoneal<br>Epithelial | Yes<br>Parietal pleura | Yes<br>Grade 1–2 | Nov-92 |
| 8 | L-93-93 | 52/M | 34 | Shipyard rigger > nd | Right pleura<br>Sarcomatoid/desmoplastic | Yes<br>Parietal pleura | Yes<br>Grade 1 | May-93 |
| 9 | L-37-93 | 67/M | 43 | Pipefitter and marine insulator > 1951–53 | Peritoneal<br>Epithelial | Yes<br>Parietal pleura | Yes<br>Grade 1 | Mar-93 |
| 10 | L-1-93 | 73/M | 40+ | Laborer > 1940–44<br>Shipyard electrician > 1947–70 | Right pleura<br>Sarcomatoid/desmoplastic | Yes<br>Parietal pleura | Yes<br>Grade 1 | Jan-93 |
| 11 | nd | 75/M | 38 | Shipyard painter > 1941–46<br>Painter > 1946–76 | Left pleura<br>Variable differentiation | Yes<br>Parietal pleura | Yes<br>Grade 1 | Apr-91 |
| 12 | L-101-92 | 82/M | 49 | Shipyard electrical engineer and technician > 1942–73 | Left pleura<br>Biphasic | No | Yes<br>Grade 1 | May-92 |
| 13 | L-140-93 | 80/M | 10 | Shipyard sheet metal worker > 1942–47 | Right pleura<br>Predominantly sarcomatoid with focal variable differentiation | Yes<br>Parietal pleura | Yes<br>Grade 1 | May-93 |
| 14 | L-278-91 | 85/M | 13 | Railroad worker > 1921–46<br>Construction > 1947–64<br>Shipyard painter > 1965–71 | Right pleura<br>Epithelial | Yes<br>Parietal pleura | Yes<br>Grade 1 | Nov-91 |
| 15 | L-259-92 | 69/M | nd | Merchant Marine > 1945–75 | Right pleura<br>Biphasic predominantly sarcomatoid | Yes<br>Parietal pleura | No | Dec-92 |
| 16 | L-448-97 | 73/M | 38 | Plant machinist and foreman > 20–25 yrs ago | Right pleura<br>Sarcomatoid | Yes<br>Parietal pleura | Yes<br>Grade 1 | Oct-97 |
| 17 | L-227-93 | 64/M | 20 | US Naval machinist > 1947–67 | Right pleura<br>Variable differentiation | Yes<br>Parietal pleura | Yes<br>Grade 1 | After May-93 |
| 18 | L-239-93 | 62/M | 38 | Heavy equipment operator > 1957–88 | Right pleura<br>Biphasic predominantly epithelial | Yes<br>Parietal pleura | No | ? |
| 19 | L-233-94 | 66/M | NS | Truck driver and terrazzo helper and mechanic > 1959–72 | Left pleura<br>Epithelial | No | No evaluation | After May-94 |
| 20 | L-296-93 | 73/M | nd | Retired | Right pleura<br>Predominantly sarcomatoid but showing variable differentiation | Yes<br>Parietal pleura | nd | nd |

*CS = cigarette smoking in pack years; DOD = date of death; nd = no data; NS = nonsmoker.



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wet/dry ratio. Omentum and mesentery tissue was processed through the modified bleach digestion procedure of Williams et al.[9]

Tissue from lungs was pooled into right and left samples. The right digest pool contained an average of 0.3588 g dry weight of lung tissue (range, 0.1295 to 0.9745 g), and the left digest pool contained an average of 0.3700 g of dry weight (range, 0.1544 to 0.7738 g). The number of asbestos fibers and ferruginous bodies (FBs) consistent with ABs was averaged from the left and right lung digests.

The average omentum sample contained 1.7308 g dry tissue (range, 1.008 to 2.9382 g), and the average mesentery sample had 1.7787 g dry tissue (range, 0.3928 to 2.8621 g). All solutions used in the procedures were prefiltered through a 0.2-μm Nuclepore filter (Nucleopor Corp; Pleasanton, CA). Dry weights were calculated based on a wet/dry ratio obtained for each digest pool.

Aliquots of the pools were collected on 0.2-μm pore polycarbonate filters for analytical transmission electron microscopy (ATEM) and on 0.22-μm pore mixed cellulose ester filters for quantitation of ABs by light microscopy.

The mixed cellulose ester filters contained an average tissue weight of 0.0331 g dry weight (range, 0.0211 to 0.0671 g) for lung samples. The method for screening the filters by light microscopy has been previously described by Dodson et al.[10]

The polycarbonate filters contained an average of 0.0066 g dry weight of lung (range, 0.0027 to 0.0134 g), 1.3429 g dry weight of mesentery (range, 0.3928 to 1.6910 g), and 1.3174 g dry weight of omentum (range, 0.8093 to 1.6913 g).

The quality assurance issues, as well as the analytical counting scheme used for the ATEM facet of the study, have previously been reported.[10]

Data for lung samples were reported as a weighted average obtained from the two sides. The quantity and quality of asbestos fibers from the lung, omentum, and mesentery are described in Table 2

### *Statistical Analysis*

Computations were done on a Digital Alpha 8200 mainframe computer (DEC; Compaq; Houston, TX) running a Digital Unix (Release 4.0) operating system. The Statistical Analysis System (SAS, Version 6.12; Cary, NC) was used (PROC MEANS, PROC CORR, PROC LOGISTIC).

Logistic regression was used to model the probability of the occurrence (presence) of certain fiber types in the omentum and mesentery, as a function of the burden and other aspects of these fibers, as described in Table 2. These values should be interpreted in terms of the given sampling procedure used in the present study. Independent variables were simple transformations of lung indexes, including total asbestos (fibers/g dry weight), total asbestos amphibole (fibers/g dry weight), median fiber length (μm), median fiber width (μm), median fiber aspect ratio (length/width), and total ABs (ABs/g dry weight) from light microscopy. Width was not used in some analyses because it is essentially redundant once the length and aspect ratio are known.

Up to four response indicator variables were used in PROC LOGISTIC: $Y_1$ indicated presence of any asbestos in the omentum; $Y_2$ indicated any amphiboles in the omentum; $Y_3$ indicated any asbestos in the mesentery; and $Y_4$ indicated any amphiboles in the mesentery. Separate models were used for each of four independent variables, as previously described.

The zero logit solutions were back-transformed to the original scales. These are interpreted as the value of the predictor for which the probability of detecting asbestos at an extrapulmonary site is "more likely than not" as a function of the magnitude of the lung predictor. The exact p values were reported to enable readers to make a judgment for significance of the curvature in the logistic model.

## Results

### *AB Burden*

Eighteen individuals (90%) had ABs in their lung tissue (Table 2). No ABs were found in lung samples from two cases (10%). The average AB concentration in the 18 positive samples was 183,638 ABs/g dry weight (range, 229 to 1,337,948 AB/g dry weight). The subject (case 1) with the highest number of ABs had pleural mesothelioma. The second highest number was found in a case of peritoneal mesothelioma (case 7).

In the ATEM scan, ABs were found in lung digests from 12 cases (60%). The cores of 172 ABs were analyzed, and all were found to contain amosite cores with one exception, a tremolite asbestos core.

ABs were found in the mesentery in five patients (25%; Table 2). Two of the five cases positive for ABs in the mesentery (cases 6 and 7) were peritoneal mesotheliomas. The concentration of ABs in the positive samples ranged from 1 to 38/g dry tissue. The highest number occurred for the case with highest number of ABs in lung tissue (case 1). Only two cases (10%) were found to have ABs in their digest from the omentum (cases 1 and 10; Table 2). The range was from 1 AB/g dry weight of tissue (case 10) to 37/g dry weight (case 1). As in the mesentery, the highest number of ABs in the omentum was found in the individual with the highest number of ABs in lung tissue (case 1). Core analysis by ATEM of ABs from the omentum and mesentery of case 1 confirmed that all were formed on amosite cores. All FBs counted by light microscopy of samples from lung, omentum, and mesentery were considered to be ABs if they had features consistent with such structures.

### *Uncoated Asbestos Fibers*

Uncoated asbestos fibers were found in the lungs of 19 of 20 individuals (95%). Only in case 19 were asbestos fibers not found, as based on the detectable limits within the study. The range of uncoated asbestos fibers in lung tissue was from 13,601,236/g dry weight in an individual with a peritoneal mesothelioma (case 7) to nondetectable (Table 2, Fig 1). The second highest lung burden of uncoated fibers (12,908,314 fibers/g dry weight) occurred in an individual with pleural mesothelioma (case 1). Ten cases (50%) had an uncoated asbestos burden of $>$ 1.4 million asbestos fibers/g dry weight, with all peritoneal mesothelioma cases (cases 6, 7, and 9) having $>$ 1 million asbestos fibers/g dry weight. Two cases of peritoneal mesothelioma (cases 7 and 9) were in the top five for total uncoated asbestos burden.

Seventeen cases (85%) were found to have un-



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**Table 2—*Ferruginous Body and Uncoated Fiber Burden of Lung, Omentum, Mesentery per Case (FBs/g dry or fibers/g dry)***

| Assay No. | Tissue | FB/g dry | Total Asbestos Fibers | Total Asbestos Fibers/FB's Ratio | Chrysotile | Amosite | Tremolite | Crocidolite | Anthophyllite | Actinolite | Non-Asbestos Fibers |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Lung | 1,337,948 | 12,908,314 | 10 | 105,806 | 12,802,509 | 0 | | | | 687,738 |
| | Omentum | 37 | 6,553 | 177 | 0 | 6,208 | 345 | | | | 517 |
| | Mesentery | 38 | 4,311 | 113 | 172 | 3,966 | 172 | | | | 1,380 |
| 2 | Lung | 102,688 | 4,008,137 | 39 | 124,476 | 3,659,603 | | 224,058 | | | 597,487 |
| | Omentum | 0 | 6,077 | | 868 | 4,630 | | 289 | 289 | | 2,604 |
| | Mesentery | 1 | 5,445 | 5,445 | 0 | 5,445 | | | | | 573 |
| 3 | Lung | 106,906 | 696,395 | 7 | 81,929 | 491,573 | 61,447 | 20,482 | 20,482 | | 245,787 |
| | Omentum | 0 | 1,544 | | 1,029 | 258 | | | | 258 | 2,573 |
| | Mesentery | 0 | 4,178 | | 0 | 3,969 | | 209 | | | 6,058 |
| 4 | Lung | 0 | 223,119 | | 99,164 | 49,582 | | | 74,373 | | 570,194 |
| | Omentum | 0 | 799 | | 799 | 0 | | | | | 16,782 |
| | Mesentery | 0 | 3,713 | | 743 | 743 | | 2,228 | | | 5,198 |
| 5 | Lung | 357,551 | 3,836,779 | 11 | 47,662 | 3,669,962 | 47,662 | 47,662 | | 23,831 | 1,263,039 |
| | Omentum | 0 | 2,889 | | 0 | 2,889 | | | | | 667 |
| | Mesentery | 2 | 1,303 | 652 | 0 | 1,303 | | | | | 217 |
| 6 | Lung | 218,578 | 1,744,106 | 8 | 0 | 1,724,059 | | | 20,047 | | 140,330 |
| | Omentum | 0 | 2,555 | | 0 | 2,555 | | | | | 547 |
| | Mesentery | 2 | 3,009 | 1,505 | 0 | 3,009 | | | | | 401 |
| 7 | Lung | 1,008,797 | 13,601,236 | 13 | 212,519 | 13,388,717 | | | | | 566,718 |
| | Omentum | 0 | 852 | | 0 | 852 | | | | | 3,410 |
| | Mesentery | 1 | 1,937 | 1,937 | 0 | 1,660 | | 277 | | | 2,213 |
| 8 | Lung | 14,434 | 1,468,028 | 102 | 110,795 | 1,357,233 | | | | | 249,288 |
| | Omentum | 0 | 1,644 | | 0 | 1,644 | | | | | 411 |
| | Mesentery | 0 | 761 | | 381 | 0 | | | 381 | | 9,135 |
| 9 | Lung | 32,091 | 3,988,091 | 124 | 33,514 | 3,451,875 | 134,054 | 134,054 | | 234,594 | 804,320 |
| | Omentum | 0 | 1,180 | | 0 | 1,180 | | | | | 295 |
| | Mesentery | 0 | 447 | | 0 | 447 | | | | | 15,427 |
| 10 | Lung | 80,714 | 1,893,778 | 23 | 49,836 | 1,345,579 | 348,854 | | 49,836 | 99,673 | 697,708 |
| | Omentum | 1 | 443 | 443 | 0 | 443 | | | | | 664 |
| | Mesentery | 0 | 525 | | 0 | 175 | 175 | | 175 | | 2,625 |
| 11 | Lung | 14,448 | 292,643 | 20 | | 73,161 | 97,547 | | 121,935 | | 146,321 |
| | Omentum | 0 | 0 | | | | | | | | 4,625 |
| | Mesentery | 0 | 707 | | | 707 | | | | | 2,121 |
| 12 | Lung | 3,661 | 239,055 | 65 | | 19,921 | 19,921 | | | 19,921 | 737,085 |
| | Omentum | 0 | 0 | | | | | | | | 1,820 |
| | Mesentery | 0 | 581 | | 581 | | | | | | 5,812 |
| 13 | Lung | 1,132 | 898,183 | 794 | | 752,532 | 24,275 | 97,101 | | | 388,403 |
| | Omentum | 0 | 193 | | | 193 | | | | | 579 |
| | Mesentery | 0 | 447 | | 224 | 224 | | | | | 2,014 |
| 14 | Lung | 14,088 | 1,435,107 | 102 | 18,883 | 1,057,447 | 321,011 | | 37,766 | | 1,208,511 |
| | Omentum | 0 | 184 | | | 184 | | | | | 1,286 |
| | Mesentery | 0 | 189 | | | 189 | | | | | 567 |
| 15 | Lung | 8,292 | 62,118 | 7 | | 62,118 | | | | | 393,417 |
| | Omentum | 0 | 215 | | | 215 | | | | | 2,149 |
| | Mesentery | 0 | 0 | | | | | | | | 827 |
| 16 | Lung | 1,934 | 15,141 | 8 | | | 15,141 | | | | 969,019 |
| | Omentum | 0 | 174 | | | 174 | | | | | 2,085 |
| | Mesentery | 0 | 173 | | | | 173 | | | | 2,428 |
| 17 | Lung | 229 | 277,857 | 1,215 | | 250,071 | | | 27,786 | | 138,929 |
| | Omentum | 0 | 224 | | | 224 | | | | | 4,927 |
| | Mesentery | 0 | 185 | | | 185 | | | | | 739 |
| 18 | Lung | 277 | 20,208 | 73 | | | 20,208 | | | | 303,125 |
| | Omentum | 0 | 0 | | | | | | | | 5,045 |
| | Mesentery | 0 | 0 | | | | | | | | 747 |
| 19 | Lung | 0 | 0 | | | | | | | | 968,473 |
| | Omentum | 0 | 0 | | | | | | | | 2,645 |
| | Mesentery | 0 | 0 | | | | | | | | 593 |
| 20 | Lung | 1,721 | 1,520,103 | 883 | | 1,447,717 | 24,129 | | 48,257 | | 120,643 |
| | Omentum | 0 | 0 | | | | | | | | 189 |
| | Mesentery | 0 | 0 | | | | | | | | 7,033 |



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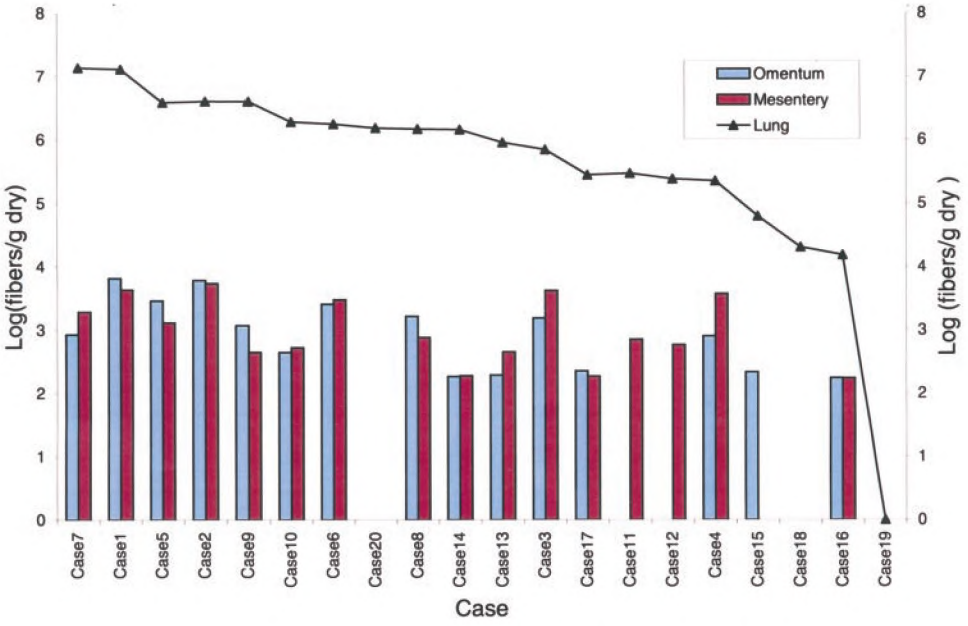


FIGURE 1. Logarithm of uncoated asbestos fiber burden in lung, omentum, and mesentery, by case.

coated asbestos fibers in at least one extrapulmonary site. Fourteen individuals (70%) had uncoated asbestos fibers in the mesentery and omentum (Table 2, Fig 2).

The most prevalent type of asbestos in the mesentery and omentum was amosite (Fig 2). Thirteen mesentery samples (65%) and 14 omentum samples (70%) contained amosite.

The range of amosite fibers among 13 positive mesentery samples was 175 to 5,445 fibers/g dry weight, while in the 14 positive omentum samples, amosite concentrations ranged from 174 to 6,208 fibers/g dry weight. Amosite was found in all three sites (lung, mesentery, and omentum) in 11 cases (55%; Table 2). The longest uncoated amosite fiber found in the lung was 100 μm (case 2) and the

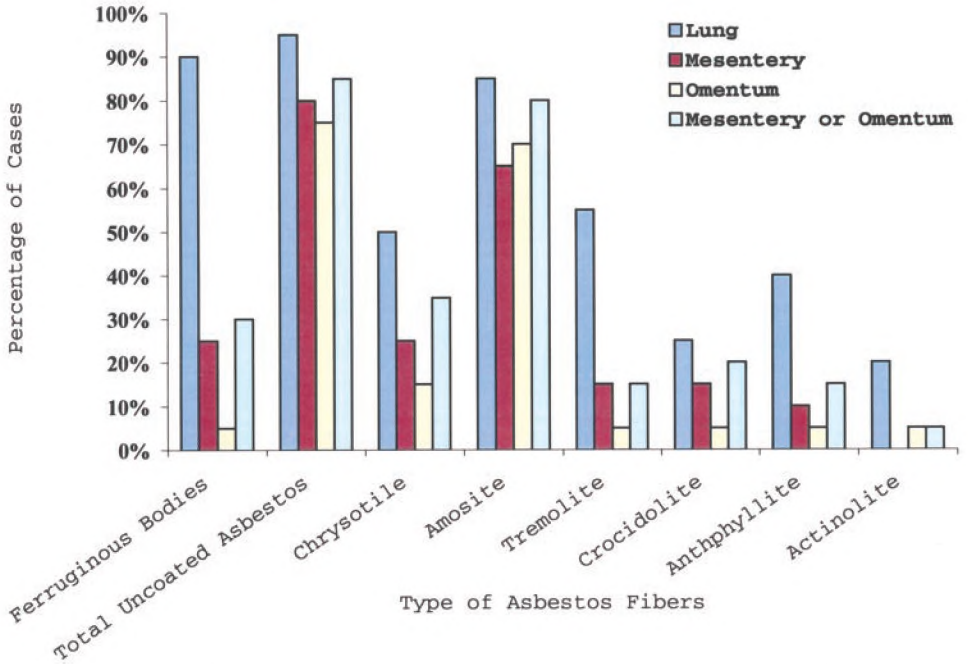


FIGURE 2. Percentage of cases with coated and uncoated asbestos fibers by tissue site.



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shortest amosite fiber was 0.5 μm (case 7). The average length of uncoated amosite fibers in lung from all 20 cases was 11.23 μm. The width of uncoated amosite fibers found in lung ranged from 0.03 μm (case 7) to 1.6 μm (case 7).

The longest amosite fiber in the omentum was 70.0 μm (case 2); the longest in the mesentery was 40.0 μm (case 11). The width of amosite in the mesentery ranged from 0.06 to 1.1 μm; and in the omentum, 0.06 to 0.8 μm.

Other results showed that 74.1% of amosite in the lung sampled was ≥ 5.0 μm long. The percentage of those in the omentum that were ≥ 5.0 μm long was 73.3%, and in the mesentery, 72.4%. The evidence that both long chrysotile and amosite fibers reach these extrapulmonary sites is presented in Table 3.

The second most common type of asbestos found in the extrapulmonary samples, chrysotile, was found in 10 lungs (50% of cases). There were five positive mesentery samples (25% of the sites) and three positive omentum samples (15% of the sites; Fig 2).

The amount of chrysotile ranged from 172 to 743 fibers/g dry weight in mesentery samples and from 799 to 1,029 fibers/g dry weight in the omentum. Chrysotile was found in the lung tissue from each of the individuals with positive omentum samples and in three of five individuals with positive mesentery samples (Table 2).

The length of the uncoated chrysotile fibers in lung tissue ranged from 0.50 μm (case 1) to 23.0 μm (case 4). In samples of mesentery, chrysotile fibers ranged from 1.2 to 17.0 μm long. In the omentum, chrysotile length ranged from 1.0 to 14.5 μm. The width of chrysotile fibers ranged from 0.04 to 0.4 μm in lung, from 0.04 to 0.34 μm in the mesentery, and from 0.04 to 0.2 μm in the omentum. The percentage of chrysotile ≥ 5.0 μm long in each site was 57.1% in the lung, 42.9% in mesentery samples, and 10.0% in the omentum (Table 3).

Crocidolite was found in five lung samples (25%; range, 20,482 to 224,058/g dry weight), in three mesentery samples (15%; range, 209 to 2,228/g dry weight), and in one omentum sample (5%; 289/g dry weight), as shown in Table 2 and Figure 2.

The individual with a positive omental sample for crocidolite was positive for crocidolite in the lung sample (Table 2). One of three positive mesentery samples was from a patient (case 3) found to have crocidolite in his lung sample (Table 2). The length of crocidolite fibers in the lung ranged from 2.0 μm (case 2) to 35.0 μm (case 2), and the length of uncoated crocidolite in the mesentery ranged from 1.0 μm (case 4) to 26.0 μm (case 3). In the omentum, the crocidolite fiber was 9.0 μm long; 74.1% of the crocidolite fibers in the lung were ≥ 5.0 μm. In the mesentery, 40% of crocidolite fibers were ≥ 5.0 μm, and in the omentum, 100% were that length.

One omentum sample contained an anthophyllite fiber, and another sample was positive for tremolite (Table 2). Two samples of the mesentery were positive for anthophyllite (Table 2)

Two of three mesentery samples positive for tremolite (cases 10 and 16) were from individuals who had tremolite in their lung tissue, while only one sample of omentum was positive for tremolite (case 1). Although this subject had the second highest level of total uncoated asbestos fibers, no tremolite was detected in his lung tissue.

Tremolite fibers ranged from 1.6 μm (case 14) to 23.5 μm long (case 14) in lung tissue, from 3.0 μm (case 16) to 10.5 μm long (case 10) in the mesentery, and 18.0 μm to 30.0 μm long (case 1) in the omentum. The percentage of tremolite fibers ≥ 5.0 μm was 34.1% in lung, 100% in the omentum, and 66.6% in the mesentery.

In the one subject (case 10) whose lung tissue was negative for ABs and uncoated asbestos fibers, the omentum and mesentery also were negative.

### *Logistic Modeling*

The features used to model the likelihood of amphibole presence in the omentum or mesentery (total asbestos burden in lung, median fiber length, median aspect ratio, and AB burden in lung) are described in Table 4. The logistic model using the median light microscopy AB burden (in the lung) had the most significant curvature within the range

**Table 3—*Fiber Length Characteristics***

| Length ≥ 5.0 Lung | Mesentery | Omentum | | Length ≥ 8.0 Lung | Mesentery | Omentum | |
|---|---|---|---|---|---|---|---|
| Asbestos | | | | Asbestos | | | |
| 72.2% | 70.8% | 67.2% | Within site | 47.1% | 44.2% | 54.3% | Within site |
| Chrysotile | | | | Chrysotile | | | |
| 53.8% | 42.9% | 10.0% | Type | 42.3% | 14.3% | 10.0% | Type |
| Amosite | | | | Amosite | | | |
| 74.2% | 72.4% | 73.3% | Type | 48.7% | 46.9% | 58.4% | Type |



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**Table 4—*Estimated Values of Lung Predictors for Which the Probability of Detecting Any Amphibole Fibers in the Omentum and Mesentery Exceeds a 50% Level in Similar Mesothelioma Populations**

| Univariate Predictor†: Lung Burden/Attribute | Extrapulmonary Site‡ | p Value§ | Antilog‖ |
|---|---|---|---|
| Total amphibole asbestos fibers/g dry weight | Omentum | 0.0866 | >72,515 |
| | Mesentery | 0.0809 | >45,801 |
| Median fiber length, μm | Omentum | 0.1384 | >5.41 |
| | Mesentery | 0.9973 | >2.55¶ |
| Median fiber aspect ratio | Omentum | 0.1163 | >17.3 |
| | Mesentery | 0.8266 | >8.53 |
| Light microscopy FB/g dry weight | Omentum | 0.0473 | >778 |
| | Mesentery | 0.0938 | >48.1 |

*Estimated by a univariate logistic regression model with response 1 = any amphibole detected at the given site (omentum or mesentery), 0 = otherwise; the 50th percentile was selected to reflect a level for which a preponderance of evidence exists.

†These independent variables, calculated from the lung sites, were allowed in the logistic model, while limiting the model to only one predictor at a time. The variable was first log-transformed to eliminate the skewed nature of their distributions.

‡Dependent response variables indicating the presence of any amphiboles at each of these two extrapulmonary sites were separately considered.

§$\chi^2$ test for significance of logistic model within the range of the observed data; a small p value suggests statistically significant curvature in the logistic model, which means the lung attribute predicts the probability (likelihood) of the extrapulmonary event.

‖The 50th percentile of the log-transformed attribute was first estimated from the logistic model. This is the antilog in terms of the original unit of measurement that defines the 50th percentile. The attached signs (> or <) indicate whether the probability increases or decreases (from 0.50), respectively, for larger values of this cutoff point. As the p value approaches 1.0, the estimate of this percentile becomes unstable and less accurate because the probability tends to flatten out within the range of the observed attribute.

¶This estimated cutoff value may be unstable due to the flatness in the model as indicated by the high p value.

of the observed data ($p = 0.0473 < 0.05$, modeling frequency of amphiboles in the omentum; Table 4). The curvature in the models approached significance ($p < 0.10$) for total asbestos ($p = 0.0866$) when used to predict the probability of *any* amphibole in the omentum. The same predictors approached significant curvature for modeling the probability of detecting any amphiboles in the mesentery ($p = 0.0809$, $p = 0.0938$; Table 4). Although the values were not statistically significant, Table 4 suggests that the median length and median aspect ratio of amphiboles are perhaps more significant predictors of the presence of amphiboles in the omentum ($p = 0.1384$, $p = 0.1163$) than the mesentery ($p = 0.9973$, $p = 0.8266$). (Note: A p value of 1.0 would indicate a flat estimate of the probability for all values of the predictor.)

In this study group, allowing marginal significance ($p < 0.10$), an amphibole burden of > 72,515 fibers/g dry lung tissue resulted in a > 50% probability (preponderance) of there being an amphibole asbestos fiber found in the omentum (Table 4). Similarly, whenever the AB burden/g dry lung tissue as assessed by light microscopy was > 778, it is estimated that amphiboles will be seen in the omentum in a majority of mesothelioma cases in similar populations.

The relationships between lung variables and the probability of finding asbestos fibers in the mesentery were also determined. A total amphibole burden in lung of > 45,801 fibers/g dry lung, or an AB burden of > 48.1/g dry lung, resulted in a preponderance for asbestos fibers being found in the mesentery ($p < 0.10$; Table 4). Similar percentiles can be estimated from the model for any chosen level of probability.

## Discussion

We demonstrated that asbestos fibers were found in the omentum and mesentery, and that the likelihood of this occurrence could be predicted by features of the asbestos in the lung tissue. Heavier inhaled exposures, especially as evidenced by increased FB counts, and, to a lesser extent, total amphibole burden tended to favor the migration of amphibole fibers to these extrapulmonary sites. The longer and thinner amphibole fibers seemed to migrate more readily to the omentum than to the mesentery. This raises an interesting question regarding the nature of the lymphatic or other mechanisms involved for relocation to extrapulmonary sites.

In this cohort, there was a considerable amphibole burden in all asbestos-positive sites sampled. These primarily consisted of amosite and crocidolite, both commercial amphiboles. The presence of these types of fibers in the omentum and mesentery was less surprising than their size was.

By comparison, no ABs were found in our earlier studies of pleural plaques, and only a small percentage of uncoated fibers in the plaques were > 5.0 μm long.[8,11] Unlike those extrapulmonary sites, 67.2% of



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the asbestos fibers in the omentum and 70.5% in the mesentery were ≥ 5.0 μm. Asbestos fibers in these sites were predominantly longer amphiboles, particularly amosite. While the shorter chrysotile fibers arguably may clear more readily from the lung, longer chrysotile fibers did reach these extrapulmonary sites: 42.9% of chrysotile fibers in the mesentery and 10% in the omentum were ≥ 5.0 μm. These percentages exclude ABs, which are formed only on fibers that are ≥ 8.0 μm long.[12]

There was a match between at least one type of asbestos found in the extrapulmonary sites in this study with the type(s) of asbestos found in the lung. Animal studies have concluded that chrysotile fibers clear more rapidly from the lung than do amphiboles.[13] Chrysotile has also been suggested as having a relatively rapid turnover in human lungs, whereas amphiboles have a slower rate of turnover.[14] Lippmann[15] has even suggested that those chrysotile fibers that do escape clearance by the mucociliary escalator may be insufficiently biopersistent because of dissolution during translocation to extrapulmonary sites, which influences the transformation or progression to mesothelioma.

While we do not choose to comment on chrysotile clearance from the lung, we note that chrysotile fibers reached the omentum and/or mesentery in 25% of the cases. Furthermore, there was no apparent degradation of these fibers, and a portion of them were long fibers (≥ 5.0 μm).

Long fibers of chrysotile reached the omentum in several cases, which indicates that chrysotile is also translocated and could be potentially important in the pathogenesis of peritoneal mesothelioma.

We conclude that individuals whose exposure and lung burdens conform to the defined population parameters would reasonably be expected to have fiber relocation to the omentum and mesentery. Vulnerable individuals in such groups with sufficient exposures would have fiber burdens available for the stimulation of cells in the omentum and mesentery, which could pose additional risks for the development of peritoneal mesothelioma.

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