Asbestos Fiber Analysis in the Lung and Mesothelial Tissues from 168 Cases of Human Malignant Mesothelioma

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Abstract

To identify and characterize asbestos fibers associated with the induction of human malignant mesothelioma, we have investigated type(s), number and size of asbestos fibers detected in the lung and mesothelial tissues taken from 168 cases of human malignant mesothelioma (including 164 males and 4 females; 156 pleural and 12 peritoneal; definite or probable; autopsy or biopsy samples). Their occupational history was diverse including asbestos insulators, pipe fitters, electricians, shipyard workers, sheet metal workers, Navy service men, power plant workers, boiler men, brake lining mechanics, fire fighters, family members of asbestos workers, etc. For the tissue sampling, a bulk tissue digestion, or ashing technique of tissue sections, or both were used. A high-resolution analytical election microscopy was used for the identification of asbestos fibers. Results were as follows: (1) asbestos fibers were present in almost all of the lung and mesothelial tissues in these cases. The average number of the fibers in these tissues was much greater than that found in the general population. (2) The most common types of asbestos fibers in lung were either an admixture of chrysotile with amphiboles, amphibole alone, and occasionally chrysotile alone. In the mesothelial tissues most asbestos fibers were chrysotile. It was suggested that such a disproportion of asbestos types between the lung and mesothelial tissues was caused by chrysotile fibers' strong capacity to translocate from the lung to the mesothelial tissues. (3) In some cases, the only asbestos fibers detected in both lung and mesothelial tissues were chrysotile fibers. (4) The majority of the fibers in these tissues were short (< 5μm in length) and thin (< 0.25μm in width). It was concluded that to determine the types of asbestos fibers associated with the induction of human malignant mesothelioma, both lung and mesothelial tissues must be investigated and that short, thin asbestos fibers should be included in the list of fiber types contributing to the induction of the tumor.

Introduction

It is well known that human malignant mesothelioma is caused almost exclusively by exposure to asbestos. It was reported that a part of inhaled asbestos fibers are cleared from the lung and translocated into other tissues including mesothelial tissues. Asbestos fibers in these tissues can be identified by a high resolution analytical electron microscope, even if they are short (0.1 μm in length) and thin (0.03 μm in width).

Objective

Our objective is to characterize asbestos fibers contributing to the induction of human malignant mesothelioma. To achieve this, the type, number and dimensions of asbestos fibers detected in both the lung and mesothelial tissues taken from human malignant mesothelioma cases were investigated.

Materials

Both the lung and mesothelial tissues (the mesotheliomatous and/or fibroplastic serosal tissues) from 168 cases of human malignant mesothelioma (164 males and 4 females; 156 pleural and 12 peritoneal; definite or probable in the diagnostic certainty) were used. The mesotheliomatous tissue was selected from the primary serosal tumor where the tumor was intimately associated with fibrosis and/or hyaline plaque. Occupational history was diverse and included asbestos insulators, pipe fitters, electricians, shipyard workers, U.S. Navy service men, sheet metal workers, power plant workers, boiler men, brake lining mechanics, fire fighters and family members of asbestos workers.

Methods

To prepare electron microscopic specimens, a digestion technique of bulk tissue using KOH, or a low temperature ashing technique of 25 μm thick sections, or both were used. A high resolution analytical electron microscope (JEOL 100CX equipped with EDX spectrometer) was used for identification and characterization of asbestos fibers. Asbestos fibers were measured in printed electron micrographs, and those with an aspect ration of 3:1 and greater were counted even if they were shorter than 1 μm in length.

Results

Findings for Table 1 were as follows:

a) Asbestos fibers were present in almost all of the lung tissue (117/119; 98.3%) as well as in the mesothelial tissue (114/123; 92.7%).

b) A disproportion in the types of asbestos fibers between lung and mesothelial tissue was common and was present in 49 of 74 cases (66.2%).

c) The most common asbestos types in lung tissue were an admixture of chrysotile with amphiboles (43/119; 36.1%) or amphiboles alone (43/119: 36.1%). Chrysotile alone was seen occasionally (31/119; 26.1%). Rarely, no asbestos fibers were seen (2/119; 1.7%).

d) In mesothelial tissues, the major asbestos type was chrysotile alone (90/123; 73.2%) followed by chrysotile plus amphibole (22/123; 17.9%), no asbestos fibers detected (9/123; 7.3%), and amphibole alone (2/123; 1.6%).

Findings for Tables 2 and 3 were as follows:

a) Except for four cases, the number of asbestos fibers in lung tissue of 49 mesothelioma cases (22 from Table 2 and 27 from Table 3) was greater than the average number in lung tissue in the general population (0.44×10^6 fibers/dry gram).

b) The number of asbestos fibers in mesothelial tissues from 22 mesothelioma cases (Table 2) was also greater in the majority of cases (18/22) than the average of the general population (0.41×10^6 fibers/dry gram).

c) The average number of each type of asbestos fibers in lung (49 cases) was greatest for amosite (36.9×10^6 fibers/dry gram), followed by chrysotile (19.4×10^6 fibers/dry gram), crocidolite (3.13×10^6 fibers/dry gram), tremolite/actinolite (0.69×10^6 fibers/dry gram) and anthophyllite (0.27×10^6 fibers/dry gram). In contrast, in mesothelial tissues (22 cases) the average number of asbestos fibers was greatest for chrysotile (45.2×10^6 fibers/dry gram), followed by amosite (1.3×10^6 fibers/dry gram), anthophyllite (1.03×10^6 fibers/dry gram), crocidolite (0.01×10^6 fibers/dry gram) and tremolite/actinolite (0.69×10^6 fibers/dry gram). A disproportion of the average number of asbestos types was present between lung and mesothelial tissues.

Findings for Tables 4 and 5 were as follows:

a) Dimensions of the 10,575 asbestos fibers:

(1) length: max 82.4 μm (amosite), min 0.07 μm (chrysotile), G.M. 0.62 μm;

(2) width: max 6.50 μm (amosite), min: 0.01 μm (chrysotile), G.M. 0.06 μm.

b) Chrysotile fibers were generally short in length (G.M.: 0.42 μm in lung, 0.39μm in hyaline plaque, 0.35 μm in tumor) and thin in width (G.M.: 0.04 μm in lung, 0.04 μm in both plaque and tumor).

c) Amosite fibers were greater in length (G.M.: 5.08 μm in lung, 2.38 μm in plaque, 4.55 μm in tumor) and thicker in width (G.M.: 0.19 μm in lung, 0.14 μm in plaque, 0.21 μm in tumor).

d) Crocidolite, tremolite and anthophyllite were smaller in number in these tissues, but also longer and thicker, compared with the dimensions of chrysotile fibers.

Findings for Tables 6 and 7 were as follows:

a) Only 10.6% (1,121/10,575) of asbestos fibers detected in lung and mesothelial tissues were longer and/or equal to 5 μm in length.

b) The numerical proportion of long fibers was greatest for amosite (51.6%: 873/1,691) followed by anthophyllite (50.0%: 23/46), crocidolite (48.3%:112/232), tremolite (46.2%: 30/65) and chrysotile (1.0%: 83/8,541).

c) The numerical proportion of short fibers (shorter than or equal to 5 μm in length) detected in the tissues was greater in the ashed section samples (95.2%: 6,811/7,153), compared with the digested bulk samples (77.2%: 2,643/3,422).

Findings for Tables 8 and 9 were as follows:

a) 92.7% (9,808/10,575) of asbestos fibers detected in the issues were smaller than or equal to 0.25 μm in width.

b) The numerical proportion of thin fibers (smaller than or equal to 0.25 μm in width) was greatest for chrysotile (99.8%: 8,521/8,541) followed by crocidolite (87.5%: 203/232), amosite (61.6%: 1,041/1,691), tremolite (47.7%: 31/65) and anthophyllite (26.1%:12/46).

c) 96.4% (6,895/7,153) of asbestos fibers detected in the ashed section samples were smaller than and/or equal to 0.25 μm in width, while 85.1% (2,913/3,422) of fibers were smaller than and/or equal to 0.25 μm in width in the digested bulk tissue samples.

Findings for Table 10 and 11 were as follows:

a) Only 2.3% (247/10,575) of asbestos fibers detected in the tissues fit Stanton's hypothetical dimensions.

b) The numerical proportion of asbestos fibers that fit the hypothetical dimensions was greatest for crocidolite (20.7%: 48/232), followed by amosite (10.5% 178/1,691), tremolite (6.2%: 4/65), chrysotile (0.2%: 15/8,541) and anthophyllite (0%: 0/46).

c) The number of asbestos fibers that fit the hypothesis was proportionally greater for the digested bulk tissues samples (4.9%: 166/3,422), compared with the ashed tissue section samples (1.1%: 79/7,153).

Summary

1) Asbestos fibers were present in almost all of the lung tissue as well as the mesothelial tissues from mesothelioma patients.
2) The most common asbestos fibers in the patients' lung were a mixture of chrysotile with amphiboles or amphiboles alone followed by chrysotile alone. By contrast, in the patients' mesothelial tissues, the majority of asbestos fibers seen were chrysotile followed by chrysotile with amphiboles. It was strongly suggested that such a disproportion of asbestos type between the two tissues was caused by chrysotile fibers' strong capacity to translocate from the lung to the mesothelial tissues.
3) In the mesothelioma cases, the average number of asbestos fibers seen in the lung (56.4×10^6 fibers/dry gram) as well as in the mesothelial tissues (46.5×10^6 fibers/dry gram) was greater than those seen in the general population (0.44×10^6 fibers/dry gram in the lung and 0.41×10^6 fibers/dry gram in the mesothelial tissue).
4) The majority (89.4%: 9,454/10,575) of asbestos fibers detected in the lung and mesothelial tissues were shorter than and/or equal to 5 μm in length, and the majority (92.7%: 9,854/10,575) of these fibers were smaller than or equal to 0.25 μm in width.
5) Only a small proportion (2.3%: 247/10,575) of the asbestos fibers fit Stanton's hypothetical dimension (longer than 8 μm in length and thinner than 0.25 μm in width).
6) It was strongly suggested that the ashing technique of tissue sections was more effective in detecting short, thin fibers compared with digestion technique of bulk tissue samples.

Conclusions

1) To grasp a total picture of asbestos exposure and also to identify asbestos fibers associated with the induction of human malignant mesothelioma, asbestos fiber analysis should be done in both the lung and mesothelial tissues, since a disproportion of both type and number of asbestos fibers is frequently present between the two tissues and also the primary site of the tumor is not the lung but pleural or peritoneal tissue.
2) Short, thin asbestos fibers should be included in those contributing to the induction of human malignant mesothelioma, since such fibers were the majority detected in the lung and mesothelial tissues. High resolution analytical electron microscopy is essential to identify and characterize such short, thin asbestos fibers.
3) The present study supports that chrysotile fibers can induce human malignant mesothelioma, since in some mesothelioma cases, asbestos fibers detected in the lung or mesothelial tissue or both were exclusively chrysotile fibers.

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