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Carcinoma of the Colon in Asbestos-Exposed Workers: Analysis of Asbestos Content in Colon Tissue

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Epidemiological studies have indicated an increased incidence of carcinoma of the colon in asbestos workers. The present study evaluated the colon tissue asbestos burden, by light and electron microscopic analytic techniques, in patients with a history of occupational asbestos exposure and colon cancer. Asbestos fibers and/or asbestos bodies were present in colon tissue from 14 of 44 (31.8%) asbestos workers with colon carcinoma (range 142,199 to 15,231, 543 fibers/g/wet weight, mean 2,517,823). Chrysotile was identified in 9 patients and amosite in 3 patients. Both amosite and chrysotile were found in the colonic wall in one individual. Other forms of asbestos (e.g., crocidolite, tremolite, or anthophyllite) were not found. Asbestos fibers and asbestos bodies were not found in colon tissue from 20 control patients (colon carcinoma and no asbestos exposure). Asbestos fibers frequently enter and reside in the wall of the colon and are often intimately associated with tumor tissue at the site of colon carcinoma in workers with asbestos exposure and colon carcinoma.

Key words: colon cancer, asbestos exposure, chrysotile, amosite, electron microscopy

INTRODUCTION

There is an increased number of deaths from colon cancer in asbestos workers [Selikoff et al., 1979; Miller, 1978; Puntoni et al., 1979; Newhouse and Berry, 1979; Hilt et al., 1985; Ehrlich et al., 1985; Frumkin and Berlin, 1988]. In a study of 17,800 asbestos insulation workers, where 38.1 deaths due to cancer of the colon and rectum could have been expected, there were 59 [Selikoff et al., 1979]. Asbestos was demonstrated by light and electron microscopy in the colon carcinoma and mesentery of an asbestos worker and asbestos bodies have been found in colon tissue from patients with occupational asbestos exposure [Ehrlich et al., 1985; Kobayashi et al., 1987]. To determine the frequency, amount, and type of asbestos present in colon tumor and non-neoplastic bowel wall from patients with a history of occupational

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TABLE I. Workers With Occupational Asbestos Exposure and Colon Carcinoma: Analysis of Colon Tissue: Positive Asbestos Burden Study*

Case no.	Colon tumor		Normal colon		Occupation	Years exposure
	Bodies[a]	Fibers[a]	Bodies[a]	Fibers[a]		
1	90	ND[b]	ND	ND	Machinist	30
2	40	ND	ND	ND	Insulator	16
3	60	ND	BDL[c]	ND	Construction	24
4	150	1,129,104 amosite	BDL	BDL	Cleaner R.R.	22
5	10	ND	10[d]	185,886[d] amosite	Insulator	32
6	BDL	121,000 chrysotile	BDL	BDL	Pipefitter	29
7	BDL	227,000 chrysotile	BDL	BDL	Machinist	29
8	BDL	5,000,000 chrysotile	BDL	BDL	Boiler maker	30
9	BDL	211,444 chrysotile	BDL	BDL	Engineer	20
10	BDL	3,026,000 chrysotile	BDL	BDL	Carpenter	37
11	BDL	15,231,543 chrysotile	BDL	586,434 amosite	Pipe coverer	40
12	BDL	142,199 chrysotile	ND	ND	Electric shop	37
13	BDL	2,219,913 chrysotile	BDL	BDL	Boiler room	42
14	BDL	201,959 chrysotile	ND	ND	Near pipe fitters	26

*Case 5 previously reported [Ehrlich et al., 1985].
[a]Gram wet weight.
[b]ND = Not done.
[c]BDL = below detection limits.
[d]Mesentery.

asbestos exposure and colon cancer, digested colon tissue was examined by light and electron microscopy for identification of asbestos bodies and asbestos fiber burden. Similar studies were performed on colon tissue from patients with colon cancer and no asbestos exposure.

MATERIALS AND METHODS

Occupational history data, medical records and colon tissue from 44 asbestos workers with colon carcinoma living in various rural and urban environments in the United States were referred to the medical center (Tables I and II). There were no other forms of asbestos-related neoplasia in this group of patients, e.g., lung cancer or mesothelioma. Twenty patients with colon carcinoma from the New York metropolitan area, without, on careful screening, a history of occupational, hobby, or other exposure to asbestos, served as the control population.

The histologic sections were examined in all cases to confirm the diagnosis of colon carcinoma and to exclude other types of malignancy. The histologic sections

TABLE II. Workers With Occupational Asbestos Exposure and Colon Carcinoma: Analysis of Colon Tissue: Negative Asbestos Burden Study

Case no.	Occupation	Years exposure	Colon specimen
15	Boiler maker	20	Tumor
16	Brake worker	24	Tumor
17	R.R.-Mechanic	25	Tumor
18	Electrician-Navy	35	Tumor + nontumor
19	Insul/pipe fitter	13	Tumor
20	R.R. insulator	29	Tumor + nontumor
21	Insulator	30	Tumor
22	Shipyard	43	Tumor
23	Air conditioning	24	Tumor
24	Electrician	21	Tumor
25	Cook-Navy	20	Tumor
26	Electrician	34	Tumor
27	Shipyard	39	Tumor
28	Boiler maker	28	Tumor
29	Insul. locomotive	30	Tumor + nontumor
30	Sheet metal	30	Tumor + nontumor
31	Steam eng. refitter	40	Tumor
32	Fireman-turbine	27	Tumor
33	Plumber	39	Tumor
34	Salvage recovery	29	Tumor + nontumor
35	R.R.-Machinist	44	Tumor + nontumor
36	Railroad	38	Tumor + nontumor
37	Ship fitter	35	Tumor + nontumor
38	Shipyard-boiler	35	Tumor + nontumor
39	Sheet metal	34	Tumor + nontumor
40	Shipyard-welder	30	Tumor
41	Machinist	44	Tumor + nontumor
42	Asbestos removal salvage	29	Tumor
43	Scrapped steam engines	40	Tumor + nontumor
44	R.R.-insulator	11	Tumor

were utilized to select paraffin blocks containing bowel wall infiltrated by colon carcinoma and colon tissue uninvolved by tumor. The paraffin-embedded tissue was cut from the paraffin blocks, the paraffin was melted, and the tissue was washed in xylene and rehydrated. The tissue wet weight ranged from 0.1 to 0.8 g with a mean of 0.4 g. In case 5 and the 20 control cases, 5 g of formalin-fixed surgical tissue from the tumor and non-neoplastic bowel wall were utilized. The deparaffinized and formalin-fixed tissues were diced into small pieces and digested in 5% potassium hydroxide (KOH) for 1–3 hours at 70°C. The digested material was washed in distilled water and centrifuged for 15 minutes 3 times at 14,000 rpm. The digested material was resuspended in 10 ml of distilled water. Ten microliters of the 10 ml suspension was placed on formvar-coated nickel grids. The specimens were given a code number, and a minimum of 40 grid spaces on 3 different grids were counted for fibers by 2 investigators utilizing a JEM 100 CX II STEM electron microscope equipped with TN 2000 Tracor Northern Energy Dispersive Spectroscopy Unit. The detection limits were determined utilizing a modification of published procedures for air samples

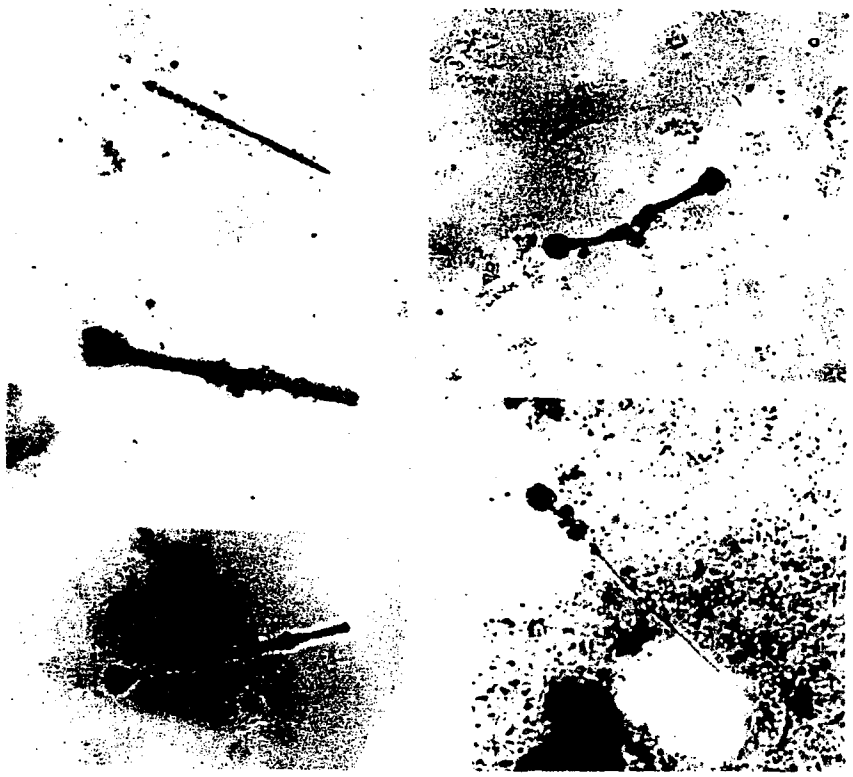

Fig. 1. Asbestos bodies found in digests of colon carcinoma in cases 1–5 (original magnification ×320).

[Yamate et al., 1984]. Cytocentrifuge specimens were prepared from .2 ml samples placed in right-angle cytofunnel plastic containers with a 6 mm diameter round opening and centrifuged (Shandon-Cytospin No2) at 1,200 rpm for 10 minutes onto a slide clamped against the opening [Ehrlich and Suzuki, 1987]. The sediment on the glass slide was examined for asbestos bodies by light microscopy. Cases 1–3 were examined only by light microscopy.

RESULTS

Asbestos bodies (Fig. 1) were found in digested colon tissue in 5 cases (11.3%) and asbestos fibers in 11 (25.0%). The number of asbestos bodies ranged from 10 to 150 bodies per gram wet weight, with a mean of 72 asbestos bodies per gram wet weight. The number of asbestos fibers ranged from 142,199 to 15,231,543 fibers per gram wet weight with a mean of 2,517,823. The detection limits were an average of 7,565 fibers per gram wet weight for the control group and 94,563 fibers per gram wet weight for the asbestos-exposed group. Chrysotile (Fig. 2) was identified in 9 patients (cases 6–14) and amosite (Fig. 3) in 3 patients (cases 4, 5, and 11). Both amosite and chrysotile were found in case 11. Other forms of asbestos were not

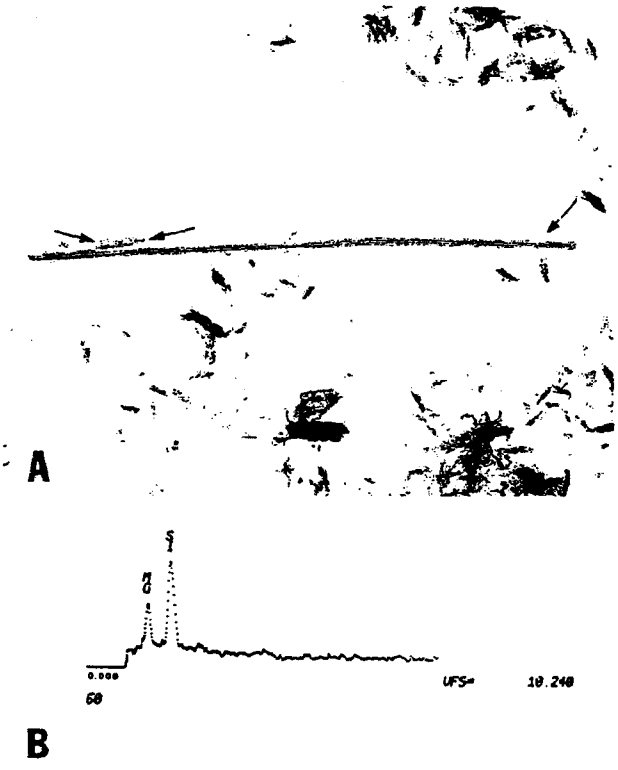

Fig. 2. A: Electron photomicrograph of 2 chrysotile fibers (arrows) in colon carcinoma of case 6 (original magnification × 13,000). B: Fibers were identified as chrysotile by energy dispersive spectroscopy. Fibers with the same morphology and spectrum were seen in cases 7–14.

found, e.g., crocidolite, tremolite, or anthophyllite. Asbestos fibers were seen by electron microscopy in digested colon wall tissue from a site uninvolved by carcinoma in 1 patient (No. 11). Asbestos bodies and fibers were not found by light or electron microscopy in the digested normal bowel tissue from the 20 control patients.

DISCUSSION

The Standard Mortality Ratio (SMR) of asbestos-exposed workers with colorectal carcinoma has been reported as 2.5 to 3.0 times higher than that of the general population [Selikoff et al., 1979; Miller, 1978; Puntoni et al., 1979, Newhouse and Berry, 1979; Hilt et al., 1985; Frumkin and Berlin, 1988]. Some epidemiological studies report the contrary, i.e., no increase in the incidence of gastrointestinal cancers in asbestos-exposed workers [Levine, 1985; Morgan et al., 1985; Doll and Peto, 1985; Edelman, 1988]. However, when cohorts of published epidemiologic studies of asbestos exposure and gastrointestinal malignancy are stratified by dose, there is an elevated SMR for gastrointestinal cancer [Frumkin and Berlin, 1988]. Doll and Peto indicated that, although they concluded that there was no increase in the

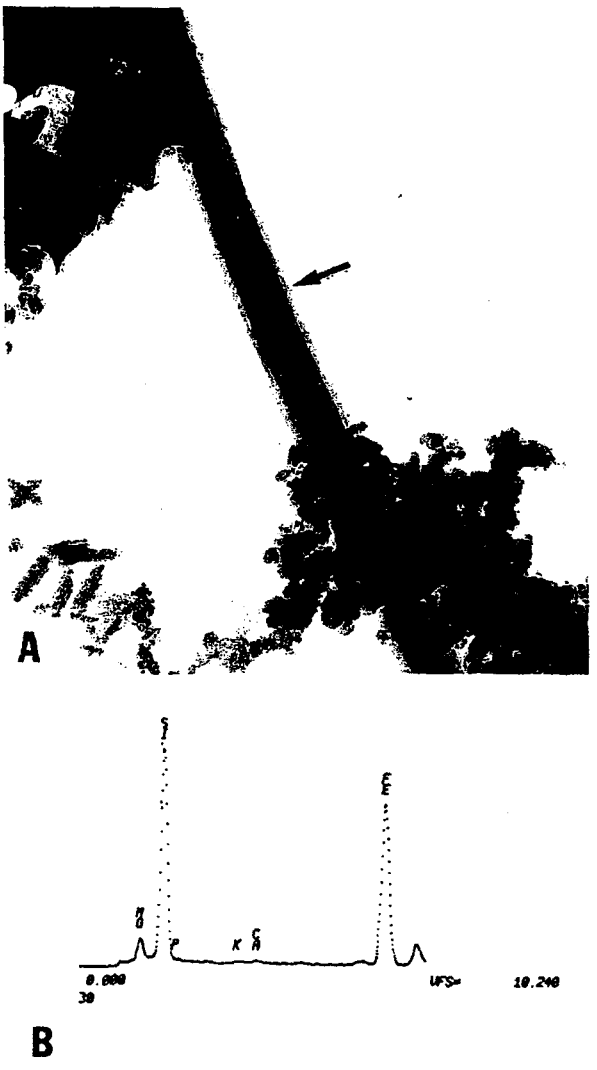

Fig. 3. A: Electron photomicrograph of an amosite fiber (arrow) in colon carcinoma of case 4 (original magnification ×26,000). B: Fiber was identified as amosite by energy dispersive spectroscopy. Fibers with same morphology and spectrum were seen in cases 5 and 11.

SMR of gastrointestinal cancer in asbestos workers, "this conclusion would be weakened if further evidence indicated that substantial numbers of carcinogenic fibers reach certain organs" [Doll and Peto, 1985]. The present study of workers with occupational exposure to asbestos indicates that asbestos fibers reach the colonic wall tissue in substantial amounts and are not found in the general population with colon carcinoma. The fibers remain in the colon wall for extended periods as evidenced by the formation of asbestos bodies.

Asbestos bodies and asbestos fibers were not found in the control group even though the tissue samples were approximately 10 times as large as the samples from the asbestos-exposed subjects, with detection limits of 7,565 fibers per gram wet weight vs. 94,563 fibers per gram wet weight, respectively. In addition, the control group consisted of urban dwellers where the air concentration of asbestos tends to be higher than in the combined urban and rural areas from which the group of asbestos workers was drawn [Langer et al., 1971]. A prior light microscopic study of the digest material from 27 specimens of colon adenocarcinoma from the general public did not find asbestos bodies [Rosen et al., 1974]. Kobayashi found an average of 0.6 asbestos bodies per gram of non-neoplastic colon in 7 of 19 autopsies of asbestos-exposed workers using light microscopy, and no asbestos bodies in similar digested colon tissue from 8 unexposed workers [Kobayashi et al., 1987]. The observed higher frequency of asbestos bodies found in normal colon of asbestos workers by Kabayashi may be due to the much larger samples utilized (5 g).

Asbestos fibers can readily enter the gastrointestinal tract by swallowing bronchial mucus. A considerable proportion of the dust deposited in the respiratory tract after inhalation is transported on the mucociliary blanket lining the airways which moves entrapped material upward to the buccal cavity where it is swallowed. As much as 25–50% of inhaled fibers enter the pharynx [Selikoff et al., 1979]. After swallowing, asbestos penetrates the bowel wall as has been shown in rats [Westlake et al., 1965; Amacher et al., 1974]. Asbestos bodies and fibers were demonstrated in the serosa of an asbestos worker with colon carcinoma which could have reached this site through the bowel wall [Ehrlich et al., 1985]. The incidence of peritoneal mesothelioma exceeds that of pleural mesothelioma suggesting that considerable quantities of asbestos fibers reach the abdomen, possibly through the gastrointestinal tract [Selikoff et al., 1979]. Animal experiments, however, have failed to produce gastrointestinal cancer utilizing asbestos although penetration of the mucosa and increased synthesis of DNA were shown in the colon of rats following gavage administration of chrysotile fibers [Amacher et al., 1974]. It has recently been shown that the introduction of exogenous DNA on the surface of asbestos fibers into eukayrotic cells could cause mutations and contribute to the induction of oncogenesis [Appel et al., 1988].

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