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Mesothelioma among Workers in Asbestiform Fiber-bearing Talc Mines in New York State

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Asbestos-related disease among talc miners and millers in a group of mines in two counties of northern New York State has been noted and disputed since the 1930s. One of the two counties was identified as among the 10 in the USA with the highest mesothelioma mortality up to 1981 for both men and women. Eight talc miners had been identified in previous studies as having mesothelioma. In the current study we: (i) report five new cases of mesothelioma among talc workers; (ii) present the results of and demonstrate the similarity between lung fiber burden analyses for selected cases and controls; and (iii) update mesothelioma mortality in this district using demographic and cause of death cancer information from 1950 to 1997. Our results indicate that New York talc exposure is associated with mesothelioma, and deserves further public health attention.

Keywords: mesothelioma; talc; pathology; epidemiology; mortality; scanning electron microscopy; asbestos

BACKGROUND

In 1878 talc mining introduced an economic boon to the rural agricultural counties of St Lawrence and Jefferson in northern New York State. The hub of this industry was Gouverneur, home of several talc mines, at least one of which is still operational. We believe that occupational exposure to dust from the talc mines and mills caused the mesothelioma excess in these counties. We support this by examining the similarity between the lung fiber burden of talc miners with and without mesothelioma, and determining the presence or absence of retained fibers indicative of commercial amphibole asbestos exposure. There are at least eight histologically confirmed cases of mesothelioma among New York State talc miners and millers reported as of 1986, and increased pleural mesothelioma mortality in Jefferson County. Here we report five new mesothelioma cases and epidemiological data to determine if this trend continues.

In the 1930s Merewether (1930) and others begin to describe asbestos exposure and its role in fibrotic lung disease. Pathology related to talc exposure also was being investigated, with a reported range of lung findings from nodular, silicosis-like to diffuse, asbestos-like patterns (Porro *et al.*, 1942). By 1943, Siegal and co-workers were studying New York State talc miners and millers (Siegal *et al.*, 1943). They described the mined talc 'of a fibrous variety…with it is found tremolite…a similar appearing mineral occurring in a fibrous or asbestiform state which… changes over to talc'. Midget impinger concentrations of particles ranged from 6 to 5000 million particles per cubic foot (mpcf) in mining and from 20 to 215 mpcf in milling. They found evidence of marked pulmonary fibrosis on chest roentgenograms in 32, all of whom had a >10 yr exposure history, out of a total of 221 talc workers. This established a clear relationship between lung fibrosis and duration of talc exposure. Fourteen of these workers also had pleural plaques, providing the first documentation of 'talc plaques'. In 1967 Kleinfeld *et al.* documented 9/220 talc workers with lung cancer; this represented a >4-fold excess. In addition, the first pleural 'fibrosarcoma' and peritoneal mesothelioma in talc miners were described in this cohort. Vianna *et al.* (1981) conducted an incidence study of all histologically confirmed mesos in New York State between 1973 and 1978. They found that Jefferson County had a mesothelioma rate twice that of the rest of the state. A total of six cases of mesothelioma (four male, two female) occurred in talc miners. Enterline and Henderson (1987) also concluded a mesothelioma excess in Jefferson County after looking at national mesothelioma incidence by county from 1968 to 1981. They observed four cases in

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Table 1. Diagnosis and immunohistochemical results (where applicable) of three mesothelioma cases

	Description of pleural mesothelioma	Immunohistochemistry
Case 1	Biphasic, diffuse	Pan-cytokeratin (+++), calretinin (+++)
Case 2	Sarcomatous	Cytokeratin (+++), calretinin (–)
Case 3	Epithelial, with rare biphasic areas	CEA (–), alcian blue (+ cellular), mucicarmine (+ rare focal)
Case 4	Diagnosis of mesothelioma made by New York State Worker's Compensation Board. No tissue available	
Case 5	Diagnosis of mesothelioma made by death certificate. No tissue available	

(+++) strongly positive; (+) weakly positive; (–) negative.

Table 2. Pertinent data from New York talc miners diagnosed with malignant mesothelioma

Case	Birth	Death	Smoking history[a]	Relevant occupation(s) in the talc industry[b]	First year on job	Job duration (yr)
1	1931	1989	10	Mucker, driller, Hardinge operator	1952	22
2	1937	1990	0	Packed talc into trucks	1955	4
3	1912	1984	0	Mechanical engineer—helped construct two talc mines	Unknown	2
4	1923	1981	Unknown	Unspecified employment at a single talc company	1953	22
5	1925	1994	Unknown	Roustabout, foreman, packhouse worker	1949	25

[a]In pack-yr (no. of packs per day × no. of yr smoking).
[b]Includes all known dusty jobs (talc or otherwise).

females (0.6 expected), and seven cases in males (1.4 expected). This gave Jefferson County the second and sixth highest mortality rates from mesothelioma for females and males, respectively, in the USA.

METHODS AND RESULTS

Subjects

The SUNY Upstate Medical University serves the catchment area of Jefferson and St Lawrence counties. From 1984 to 1987, 36 biopsy and/or autopsy samples were recovered from talc workers with lung disease. Hospitalization, employment and (when applicable) death information were collected. From the 36 miners, five mesothelioma cases were documented. For three of these, the diagnosis of mesothelioma was histologically and immunohistochemically confirmed using hematoxylin & eosin, alcian blue, mucicarmine, calretinin, carcinoembryonic antigen (CEA) and cytokeratin staining (see Table 1). Case 1 is described in detail as a representative clinical course of mesothelioma. Table 2 contains demographic data for the five mesothelioma cases.

Observed and expected pleural mesothelioma mortality in mining counties

Calculations of mortality were performed at the University of Pittsburgh using the same protocol as that described by Enterline and Henderson (1987). Observed and expected values were updated to include the most recent years available (overall, from 1968 to 1997). Figure 1a,b presents the mesothelioma mortality for males and females, respectively.

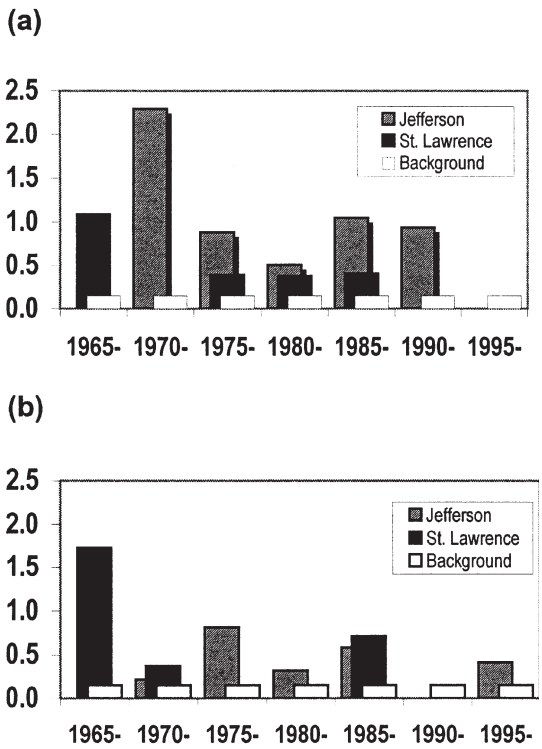

Fig. 1. Yearly mesothelioma mortality rate per 100000 (a) males and (b) females.

Lung-retained particulate and fiber analysis

Lung parenchyma from two mesothelioma cases and eight non-mesothelioma cases was available for analysis. The non-fibrous inorganic particulate lung

burden was measured using morphometric *in situ* analysis of tissue sections (Abraham and Burnett, 1983). For fiber analysis, lung tissue was digested with sodium hypochlorite and the residue collected on polycarbonate filters for analysis of asbestos bodies by light microscopy or fibers by scanning electron microscopy/energy dispersive X-ray spectroscopy (Abraham *et al.*, 1991). The analytical results are displayed in Table 3. For fibers >1 μm, length, width and chemistry were recorded. Log normalized lengths and widths of the fibers found in the mesothelioma cases and the non-mesothelioma cases were compared using Student's *t*-test (Analyze-It Software, Ltd). Significance was defined as $P < 0.05$. Finding no difference between dimensions of each fiber type would support similar dust exposure between miners with and without mesothelioma.

Case 1 illustrates a representative medical history. This was a 43-yr-old, 5′8″, 190 lb, white, hypertensive male, with a 10 pack-yr smoking history who presented in 1974 with 'hardness of breathing' for 4–5 yr. He reported nocturnal wheezing, persistent anterior chest pressure, chronic cough (1 oz daily sputum), occasional hemoptysis, and difficulty walking ~200 m. He had a 22 yr talc dust exposure history, working at times as a mucker, driller and Hardinge™ operator at two New York talc mines. He had optional access to a respirator that proved too cumbersome to work with. Both his father (now deceased) and brother had been diagnosed with talc pneumoconiosis. His physical examination showed a symmetrical chest wall with an increased anteroposterior dimension and diminished inspiratory expansion. Auscultation revealed harsh inspiratory and expiratory bilateral diffuse rhonchi and fine scattered expiratory wheezing. A chest X-ray showed bilateral prominence of mediastinal/cardiac shadows and increased reticular pulmonary markings, particularly over the lower lung zones. He had markedly restricted ventilatory function on spirometry, with FVC = 3.3 l (75% predicted), FEV_1 = 2.5 l (74% predicted) and V_{max} = 60 l/min (39% predicted). Like his brother and father, he was diagnosed with talc pneumoconiosis. His disease progressed, and in <2 yr he was placed on permanent total disability. He died at age 58, 15 yr after presentation. The post-mortem revealed a biphasic diffuse pleural mesothelioma encasing the left lung, which had not been suspected during life. It is noteworthy that 'congestive heart failure' was the only listed cause of death—there was no mention of mesothelioma on the death certificate.

DISCUSSION AND CONCLUSIONS

We have found a continued trend of increased mesothelioma mortality at 5–10 times the background rate in Jefferson County from 1982 to 1997, with five new male cases (two expected) and three new female cases (0.5 expected). We also show that increasing talc exposure duration is associated with an increase in lung burden of both fibrous and non-fibrous talc. Asbestos bodies were also seen in elevated concentration in most men with >10 yr exposure who had not been diagnosed with mesothelioma. The concentrations of each fiber type from mesothelioma and non-mesothelioma cases were similar, except for a high tremolite concentration in case 2. There was no significant difference found between non-mesothelioma and mesothelioma miners with regard to length and width of the tremolite and talc fibers (Tables 4 and 5), supporting our hypothesis that they were exposed to dust with similar

Table 3. Lung-retained particulate analyses of mesothelioma and non-mesothelioma cases

	Mesotheliomas		Non-mesotheliomas							
	1	2	A	B	C	D	E	F	G	H
Age at death	58	52	49	58	60	63	66	71	71	76
Years of talc mining	22	4	21	21	18	30	23	25	2	10
Diagnosis[a]	ATM	ATM	ATSC	ATS	ATP	ATSP	ATPC	ATP	Nl	Pn
Asbestos bodies[b]	350	93	200	10	980	890	417	4850	1	10
Asbestos fibers[c]										
Anthophyllite	5	n/d	12	85	64	4	14	n/d	0.04	0.4
Tremolite/actinolite	2	1110	1	105	7	17	31	43	0.07	0.9
Chrysotile	5	21	7	188	10	21	9	19	0.18	2.6
Talc (fibrous)[c]	46	96	24	716	4 7	157	195	233	0.1	3.1
Talc (non-fibrous)[d]	37	146	511	60	n/a	139	n/a	51	1	1
Silica[d]	7	n/d	15	10	n/a	68	n/a	n/d	1	1

n/a, not available; n/d, not detected.
[a]Nl, normal; Pn, pneumonia; A, asbestosis; T, talcosis; S, silicosis; P, pleural plaques; M, mesothelioma; C, lung cancer.
[b] Thousands of bodies/gram dry lung.
[c] Millions of fibers/gram dry lung.
[d] Millions of non-fibrous particles/ml lung.

Table 4. Dimensional analysis for lung fibers in two New York State talc miners with immunohistochemically diagnosed malignant mesothelioma

Fiber type	n[a]	Width (μm)			Length (μm)			AR[b]
		X[c]	Min	Max	X	Min	Max	
Actinolite	1	0.20	–	–	4.6	–	–	23
Anthophyllite	6	0.15	0.06	0.30	10.6	3.9	30.2	90
Chrysotile	5	0.05	0.03	0.06	4.1	1.9	6.1	93
Tremolite	38	0.22	0.10	0.40	4.5	1.7	10.6	26
Talc	54	0.20	0.05	1.00	5.3	1.4	53.0	43

[a]Number of fibers measured.
[b]Mean aspect ratio = length × width^{-1}.
[c]Geometric mean.

Table 5. Dimensional analysis for lung fibers in eight New York State talc miners with pulmonary disease other than mesothelioma

Fiber type	n[a]	Width (μm)			Length (μm)			AR[b]
		X	Min	Max	X	Min	Max	
Actinolite	7	0.18	0.12	0.25	3.4	2.5	5.4	20
Anthophyllite	85	0.24	0.05	1.60	7.7	1.6	146.0	56
Chrysotile	33	0.08	0.04	0.40	7.4	2.1	36.1	133
Tremolite	51	0.34	0.04	1.00	5.3	1.5	17.0	24
Talc	284	0.33	0.06	2.80	6.4	1.3	219.0	30

[a]Number of fibers measured.
[b]Mean aspect ratio = length × width^{-1}.
[c]Geometric mean.

fiber dimensions. Finally, in all of the 10 cases analyzed, only a single commercial amphibole fiber was found.

New York talc miners are exposed to a mixture of platy talc, silica and fibrous minerals, resulting in a disease process much more complex than pure talcosis. The asbestiform fibers in the New York talc miners' lungs are a mixture of talc, tremolite and related mineral series. Our results indicate that mesos continue to occur at high rates in counties where New York talc mining occurs. Furthermore, New York talc miners without evidence of commercial amphibole asbestos exposure develop mesos. Talc miners with mesos have lung fiber burdens similar to those without, indicating comparable exposures. Increased public health attention to the risks of exposure to New York talc is indicated.

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