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Asbestos Fiber-type and Mesothelioma Risk in the Republic of South Africa

R. P. NOLAN [a], M. ROSS [a], G. L. NORD [a], M. RASKINA [a], J. I. PHILLIPS [b], J. MURRAY [b] and G. W. GIBBS [c]

[a] *Center for Applied Studies of the Environment & Earth and Environmental Sciences of the Graduate School and University Center of the City University of New York, 365 Fifth Avenue, New York, NY 10016, USA*
[b] *National Institute for Occupational Health and School of Public Heath University of Witwatersrand, Johannesburg, Republic of South Africa*
[c] *Safety and Health International, 38 Athabasca Avenue, Devon, Alberta T9G, 1G2C Canada*

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ABSTRACT

This report focuses on identifying the important asbestos fiber- type(s) in the etiology of the asbestos-related cancer mesothelioma. In the last century all three of the commercial fiber types – grunerite (amosite) asbestos, chrysotile asbestos and riebeckite (crocidolite) asbestos- were mined, milled and used to fabricate asbestos-containing products in South Africa. The cases are a consecutive series of occupational and environmental mesotheliomas referred to South Africa's National Institute for Occupational Health.

The authors recovered the inorganic particles from the lung parenchyma in 43 human mesothelioma cases and used analytical transmission electron microscopy to determine the types and concentrations of fibrous minerals present. The predominant, often the only asbestos fiber-type, found in the pulmonary tissues was riebeckite (crocidolite) asbestos. The highest concentration of riebeckite (crocidolite) asbestos found was 10,500,000 fibers per gram of dried lung tissue. The mean concentration was 0.27 million fibers per gram of dried lung tissue which is between 4 to 59-fold below the concentration of chrysotile asbestos in general population where asbestos is found without asbestos-related disease. The results are consistent with the epidemiological reports indicating mesothelioma can develop in individuals with exposures to riebeckite (crocidolite) asbestos described as brief and/or slight.

Key words: Asbestos, Amphiboles, Asbestos-related disease, Mesothelioma, Electron microscopy

INTRODUCTION

Mesothelioma is a rare disease that was first convincingly identified by a cluster of cases occurring in a regional hospital in the Republic of South Africa[1]. It was not immediately apparent that the etiological agent was asbestos. More than half of the 33 mesothelioma cases Wagner et al reported in 1960 were not among workers but rather individuals whose exposures were environmental. None of the early cases admitted to mining asbestos or were referred from the asbestos mines[2]. The cluster occurred in a regional hospital at Kimberly about 200 miles west of the nearest asbestos field. There was some evidence to support the hypothesis that the mesothelioma cases were related to asbestos exposure, for example asbestos bodies were found in the first case. Careful questioning of the patients and their relatives over time indicated that 32 of the 33 cases could be traced to exposure to riebeckite (crocidolite) asbestos (commonly called blue asbestos) in the many Cape Province mines or industrial work with asbestos. Commonly, the exposures were environmental with a latency period of 40 years or more, although the youngest case occurred in a 21 year old male. As 15 year latency is commonly regarded as a minimum for this type of cancer to develop exposure early in life is an important risk factor. Annual production of riebeckite (crocidolite) asbestos was about 10,000 tons per annum when most of initial 33 mesothelioma cases had their exposures. Few, if any, cases were identified which could be associated with exposure to chrysotile and grunerite (amosite) asbestos within the Transvaal region of South Africa although mining methods and production were similar to those in the northwest Cape Province where the mesothelioma cluster was identified.

Lung content analysis to determine the types and concentrations of asbestos-fibers retained in human lung

parenchyma was used to determine the etiology in a series of human mesothelioma cases. Mesothelioma cases in South Africa can be referred to the National Institute for Occupational Health in Johannesburg from all parts of the country to determine if they are asbestos-related and therefore entitled to compensation. Mesothelioma cases claiming environmental asbestos exposure, although not compensable, are from time to time referred for review. The evaluation is based on occupational history, the appearance of the tumor at autopsy, histological evaluation of the tumor and analysis of asbestos fiber-types and concentrations recovered from lung parenchyma measured using analytical electron microscopy.

In South Africa there are large populations with occupational exposure to the three principal commercial asbestos fiber types: [grunerite (amosite) asbestos, chrysotile and riebeckite (crocidolite) asbestos], all formerly mined in the country. In addition small amounts of tremolite and anthophyllite were produce between 1939 and 1976. The objective of this study is to use asbestos lung content analysis of these referral cases to determine and characterize which of the asbestos fiber type(s) are etiologically linked to mesothelioma in South Africa.

EXPERIMENTAL

The forty-three mesothelioma cases in this study were consecutive cases referred requesting compensation for an occupational disease or identification of environmental disease. In each case lung parenchymal (uninvolved with the mesothelioma) and tumor tissue were collected at autopsy and used for the lung content analysis and histological diagnosis respectively. This series of mesothelioma cases were born between 1925 and 1963 with deaths occurring between 1999 and 2001. Males accounted for 79% of all the cases while three of the four environmental cases occurred in females with an average age of all at time of death of about 60. The group selected for comparison was an autopsy series in the general population of New York City from 1966 to1968, the years of very high asbestos consumption in the United States. Of the 107 cases in the general population series, not thought to be occupationally exposed to any form of asbestos, lung content analysis found chrysotile in 50% of the cases at concentration of 1.8-15.8 million fibers per gram dried lung[3, 4]. Only 0.34% of the fibers in the New York City cases were ≥5μm and the amphibole asbestos, if present, was at trace concentrations. The comparison series from the general population of New York City is not known to be at increased risk of mesothelioma due to their asbestos exposure.

All the lung tissues were obtained as formalin fixed tissues; representative samples were weighed and dried to obtain a factor for converting from wet to dried tissue weight. The results of the lung content analysis are reported in millions of fiber per gram of dried lung tissue. After weighing each tissue was added to 30mL of 5% potassium hydroxide and heated for several hours at 95C to digest the tissue. The average weight of wet parenchymal lung tissue used for each lung content analysis was 2,370 mg (range 920-6,300 mg) and the dry weight on average was 4-fold lower. The insoluble particles were then pelleted by centrifugation at 10,000g and the pellet was re-dispersed in a known volume of distilled water with a 10 second burst of ultrasound. The procedure was repeated 5-7 times to until the supernatant was clear. The final pellet was re-suspended again using sonication in a known volume of distilled water. A 10μL aliquot of the dispersed suspension was placed on a carbon-coated formvar 200-mesh copper locator grid, three or four grid were prepared for each case. All the reagents were filtered to remove potential contaminants and no asbestos fibers of any type were found on the blank grids.

Each grid preparation was examined for the presence of fibers at 20,000x magnification using a JEOL-2010 analytical transmission electron microscope equipped with a Princeton Gamma Tech IMIX ultra thin window detector. Any object, of any length, having a length to width ratio (or aspect ratio) of 3 to 1 or greater was analyzed. Fiber concentration values are expressed as the number of fibers/gram of dried lung tissue.

RESULTS AND DISCUSSION

The concentration of asbestos ranged from none detected in six cases to 10,500,000 fibers per gram of dried lung (Table 1). Of the 33 occupational mesothelioma cases where asbestos was detected the mean concentration was less than 270,000 fibers per gram of dried lung tissue. A total of 614 fibers were analyzed in the 37 mesothelioma cases where asbestos was present. Almost 96% of the fibers were found to have elemental compositions consistent with one of the asbestos minerals and all six fiber-types were identified. Selected area electron diffraction was used on selected fibers to complete the identification of the fiber-types present. Ninety-four percent were the two commercial amphibole asbestos minerals- 72% riebeckite (crocidolite) asbestos and 22% grunerite (amosite) asbestos- the remaining 6% were chrysotile, tremolite and anthophyllite accounting for 4%, 1% and 1% respectively. Besides being the most common fiber found riebeckite (crocidolite) asbestos was present in 81% of *all* the cases and in 35 of the 37 cases in which asbestos was detected, occurring as the only fiber in 32% of the cases (Figure 1, Table 1). Of the four environmental mesothelioma cases riebeckite (crocidolite) asbestos was found in every case. In three of the cases it was the only fiber detected and in the fourth 96% of the fibers were riebeckite (crocidolite) asbestos (Table 1).

The second most common asbestos fiber found was grunerite (amosite) asbestos occurring in 30% of the cases. Eighty percent of these fibers were found in just two cases so when present grunerite (amosite) asbestos was commonly at a low concentration. Tremolite fibers were found in 21% of the cases occurring as the only fiber in just one case. Grunerite (amosite) asbestos also occurred alone in just one case, in both cases the concentration of tremolite and grunerite (amosite) asbestos was low. In 66% of the cases chrysotile was not detected when tremolite fibers were present.

Table 1 The exposure history of the forty-three mesothelioma cases for the Republic of South Africa with the results of the lung content analysis for fiber type and concentration.

Case N°/ExpHistory/Race/Sex/Age	Fiber Type from History	Fiber Type from ATEM %Crocidolite	Other(1)	Concentration (millions per gm of dried lung) Total
9/Unknown/White/F/67	Unknown	85	15%Trem	**10.5**
34/Mining/Colored/F/68	Crocidolite	92	8%Am	**10.2**
41/Asbestos Mining/Colored/M/61	Crocidolite	93	7%Am	**5.6**
1/Manufacturing/Black/F/57	Unknown	88	8%Am	**3.7**
10/MiningWhite/M/66	Amosite	15	85%Am	**3**
35/Mining/Manufacturing/White/M/58	Unknown	7	93%Am	**2.4**
8/Mining/Black/M/61	Crocidolite	85	9%Trem	**2.3**
23/Mining/Manufacturing/Black/M/49	Mixed	100		**1.8**
7/Iron Mining/Black/M/57	Unknown	95	5%Trem	**1.1**
26/Mining/ManufacturingBlack/M/46	Unknown	100		**0.96**
6/ Manufacturing/White/M/55	Unknown	43	43%Anth	**0.78**
5/Gold Mining/Black/M/37	Unknown	55	36%Trem	**0.55**
33/Unknown/White/M/77	Unknown	25	75%Am	**0.54**
27Mining/Manufacturing/White/M/62	Unknown	100		**0.29**
32/Manufacturing/White/M/66	Unknown	50	50%Am	**0.28**
19/Mining/White/M/61	Unknown	100		**0.27**
4/Non-Miner/White/M/51	Unknown	67	17%Trem	**0.27**
3/Mining/Colored/M/47	Crocidolite	75	25%Trem	**0.24**
12/Mining/White/M/52	Unknown	100		**0.25**
42/Asbestos Mining/Black/F/57	Unknown	78	22%Am	**0.24**
28/Gold Mining/White/M/71	Unknown	83	17%Am	**0.2**
18/End User/White/M/61	Unknown	92	8%Trem	**0.11**
11/Manufacturing/White/M/63	Unknown	100		**0.11**
29/End User/White/M/64	Unknown	33	67%Am	**0.11**
39/Miner/Colored/M/75	Unknown	0	100%Trem	**0.087**
36/Unknown/Black/M/48	Unknown	100		**0.058**
43/Unknown/White/M/69	Unknown	0	100% Am	**0.05**
40/Mining/Manufacturing/White/M/82	Unknown	100		**0.05**
25/End User/White/M/61	Unknown	100		**0.021**
14/End User/White/Male/59	Unknown	67	33%Chry	**0.072**
16/Manufacturing/White/M/59	Unknown	100		**0.033**
24/Mining/Manufacturing/White/M/55	Unknown	100		**0.022**
38/Mining/White/F/58	Amosite	100		**0.02**
21/Environmental/White/F/67	Crocidolite	100		**2.6**
37/Environmental /Black/M/57	Crocidolite	96	4%Am	**0.95**
22/Environmental/Black/F/65	Crocidolite	100		**0.084**
2/Environmental/White/F/53	Crocidolite	100		**0.06**
31/UnknownWhite/M/62	Unknown	0		**<0.037**
13/Unknown/White/M/70	Unknown	0		**<0.033**
30/End User/White/M56	Unknown	0		**<0.030**
15/Mining/White/M/52	Crocidolite	0		**<0.019**
17/End User/White/M/63	Unknown	0		**<0.014**
20/Unknown/White/M/71	Unknown	0		**<0.013**

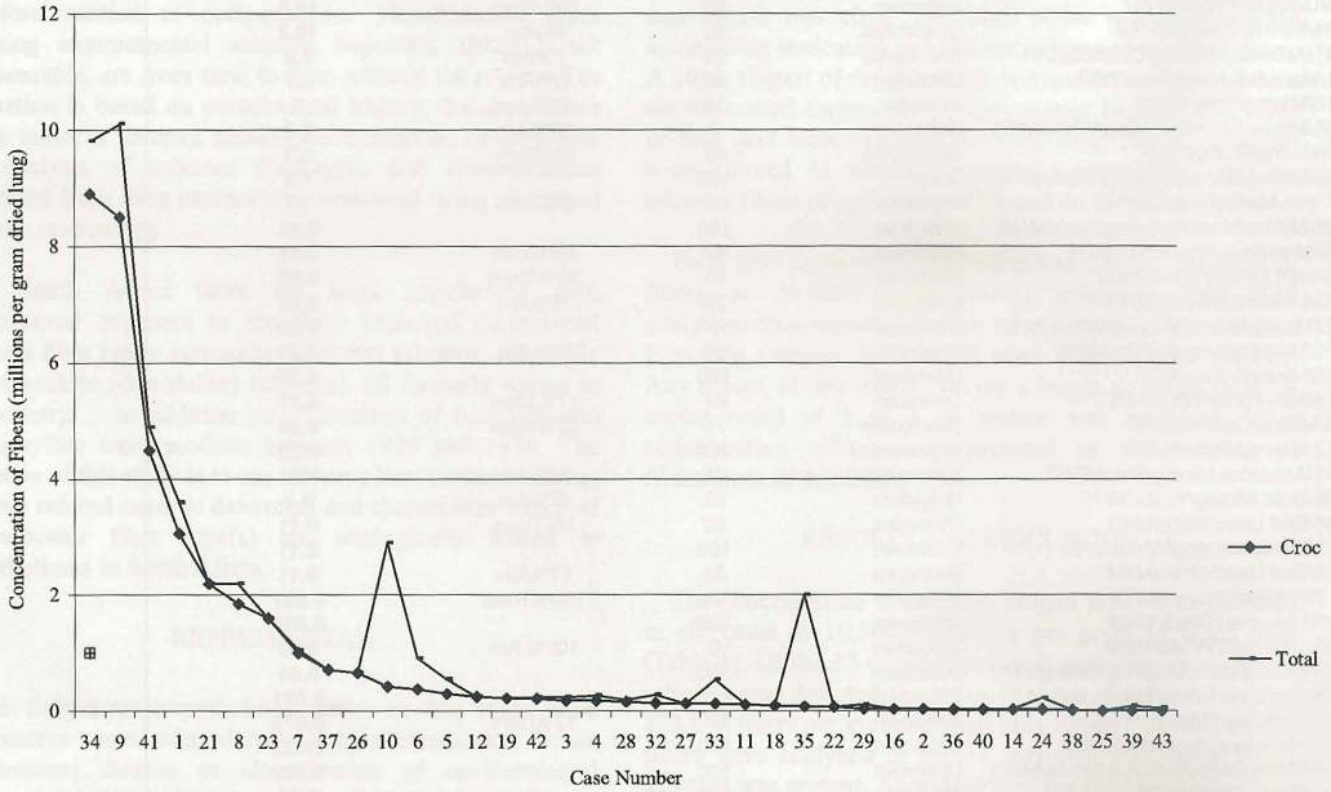
(1) The other fiber is the second most common fiber found in the lung parenchymal Trem, Am and Anth denote tremolite, amosite and anthophyllite.

Although present in 9.3% of the cases chrysotile was never found alone (riebeckite (crocidolite) asbestos was always present) and in the cases where chrysotile was detected tremolite was found 75% of the time. Anthophyllite occurred in about half the number of cases as chrysotile although, it never occurred alone. In the cases where chrysotile and anthophyllite were detected riebeckite (crocidolite) asbestos was always present and at a higher concentration in all the chrysotile cases and all but one of the anthophyllite cases.

Mesothelioma is a very rare cancer which was pathologically defined as a disease at the same time the first etiological agent, Cape blue crocidolite asbestos was identified[1]. With only about four mesotheliomas cases occurring among 1,000,000 females in the United States each year, predominately in two sites (pleural and peritoneal) and having a myriad of histological presentation in the absence of a cluster around some etiological agent the tumor occurs too rarely to have been convincingly demonstrated to be a unique tumor type[5]. Although a few cases had earlier been reported mainly in large autopsy series, indicating such a malignancy might exist[6]. The opportunity for such an observation was due to a cluster of 33 mesothelioma cases occurring in the northwest Cape Province in South Africa.

South Africa provides a unique opportunity to study the various asbestos fiber-types as it is the only country in the world where all of the regulated asbestos fiber-types were mined and milled with total historical asbestos production in excess of 9.9 million tons prior to the end of asbestos mining in 2001 (Robert Virta, personal communication). Riebeckite (crocidolite) asbestos, grunerite (amosite) asbestos, chrysotile and tremolite asbestos included with anthophyllite asbestos represent 39.40%, 32.22%, 28.18% and 0.06% respectively of total historical production. The raw fiber was also fabricated into various asbestos-containing products. Assuming the important asbestos exposures in this

Figure 1. Results of lung content analysis for fiber type and concentration of fibers (greater than or equal to 5 microns) in the 37 mesothelioma cases where fibers were detected.



group occurred at least 15 years earlier the total riebeckite (crocidolite) asbestos production from the start to the time mesothelioma was first identified in 1960 was less than 160,000 tons.

In this series of cases, deaths occurred between 1999 and 2001. Allowing for the latency the important exposures occurred 15 years earlier before 1986. Asbestos production for grunerite (amosite) asbestos and chrysotile in South Africa, from the start of mining until the important exposures in our mesothelioma cases ended in 1985 production exceeded 2 million tons for each fiber-type. Asbestos production and use in South Africa provided a myriad of exposure opportunities and we assume that large populations were exposed to all of three principal asbestos fiber-types with sufficient latency for mesothelioma to develop. Any of these asbestos exposed individual would be included in our series if they develop a mesothelioma and applied for compensation. The importance of riebeckite (crocidolite) asbestos exposure in increasing the risk of human mesothelioma has been well established in South Africa[7]. Also, there is convincing evidence that certain types of environmental exposure to this asbestos mineral, even in non-mining environments, increases the risk of developing human mesothelioma[8,9].

CONCLUSIONS

The results of the lung content analysis demonstrate the importance of riebeckite (crocidolite) asbestos as the etiological agent in these cases. It is the most frequently occurring asbestos fiber type. In the 7 of the 9 cases with 1,000,000 or more fibers per gram of dried lung tissue 85% or more of the fibers are riebeckite (crocidolite) asbestos. It occurs alone in 12 of 33 occupational cases and 3 of 4 environmental cases (Table 1). In the fourth environmental case 96% of the asbestos fibers are riebeckite (crocidolite) asbestos. Grunerite (amosite) asbestos and tremolite occur alone only once while chrysotile did not occur alone in any case. Riebeckite (crocidolite) asbestos occurs more commonly in the lower exposure cases. When the total asbestos concentration is 250,000 fibers per gram of dried lung or less, in 8 of 16 cases riebeckite (crocidolite) asbestos was the only fiber-type identified (Table 1). The results of lung content analysis indicate a slight, if any role; for the other two major commercial asbestos fiber-types –grunerite (amosite) asbestos and chrysotile– in the etiology of these mesothelioma cases (Table 1, Figure 1). The evidence for developing a mesothelioma after environmental asbestos exposure is consistent with a role only for riebeckite (crocidolite) asbestos (Table 1).

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