Further Evidence for Fiber Width as a Determinant of Mesothelioma Induction and Threshold—Anthophyllite, Bolivian Crocidolite, and Cape Crocidolite

E Ilgren[1], D Van Orden[2], R Lee[2], Y Kamiya[3] and J Hoskins[4]

Affiliations: [1]Consultant Scientist and Physician, Bryn Mawr, Pennsylvania, USA; [2]RJ Lee Group, Pittsburgh, Pennsylvania, USA; [3]Research Analyst, Santa Cruz, Bolivia and [4]Consultant Toxicologist, Haslemere, Surrey, United Kingdom

(Submission Date: 1 March 2012; Accepted Date: 23 April 2012; Publication Date: 19 July 2012)

ABSTRACT

Crocidolite is a well-known causative agent for mesothelioma. However, studies have shown that the pathogenicity of the fiber from different mines varies considerably and it has been postulated the parameter that appears most likely to account for this variation is fiber width although this has never been formally confirmed. To date, crocidolite appears to be the only asbestos mineral for which an epidemiological study comparing the risk of mesothelioma in a population exposed to 'thin' fibers with another exposed to 'thick' fibers of the same species may be carried out. Finnish anthophyllite, South African amosite, and African Transvaal crocidolite can also be classified as thick fibers, and there is a paucity of mesotheliomas in populations exposed to them compared to those exposed to thin Cape crocidolite. No thin occurrences of these minerals are known. Our previous study looked at crocidolite from several sources. The present study considers the amphibole anthophyllite found in many places in the world. This mineral, regardless of source, does not show the same variation in fiber width found with crocidolite from different areas. All anthophyllite fibers that have been mined may be classified as thick and populations exposed show very low levels of mesothelioma. We suggest the most likely explanation is related to the fiber width distribution and a concomitant reduction in the 'Stanton fiber size' fraction.

Keywords: Crocidolite, anthophyllite, mesothelioma, pleural plaques, fiber width

Correspondence: Dr. E B Ilgren, MD, Suite No 503, 830 Montgomery Avenue, Bryn Mawr, Pennsylvania, 19010 USA. Tel: 001 610 624 1510; e-mail: dredilgren@aol.com

INTRODUCTION

Fiber width has been claimed to be an important determinant of carcinogenicity.[1] However, this has never been formally confirmed despite the abundance of evidence. Thus, the risk of mesothelioma consequential upon exposure to long 'thin' amphibole asbestos fibers should be compared epidemiologically with that found in individuals exposed to long 'thick' fibers of the same amphibole species. This has not hitherto been done. As described in our recent report,[2] an opportunity arose several years ago to do so. Shedd[3] examined the fiber dimensions of crocidolites from the world's four crocidolite mining regions namely Cape South Africa, Wittenoom Western Australia, the South African Transvaal, and Bolivia. She found the crocidolite fibers from the Cape and Wittenoon were much thinner than those from the Transvaal and Bolivia, which resulted in a concomitant reduction in the corresponding percentages of 'Stanton-sized' fibers (those with length >8 μm and diameter <0.25 μm) (81%, Cape; 67% to 83%, Wittenoom; 45% to 53%, Transvaal; 18%, Bolivian fibers) that correlated with the incidence of mesothelioma being high in the Cape and Wittenooon and very low and apparently absent in the Transvaal and Bolivia, respectively. Shedd[3] concluded this was due to the fact that the 'crocidolites from Western Australia and the Cape Province had more thin (Stanton sized) fibers than crocidolites from Bolivia and the Transvaal Province'.

The very high incidence of mesothelioma found in the Cape and Wittenoom is well known. Tracing problems preclude detailed studies in the Transvaal. Our recent demographic studies[2] confirmed the apparent lack of an attendant mesothelioma risk in Bolivia. Here, we provide further evidence for the low potential of thick amphibole asbestos fiber to produce mesothelioma from studies of populations exposed to anthophyllite from Finland and Japan. The findings compared to Cape and Bolivian crocidolite shown to have high[3] and low[2] potential for mesothelioma induction.

ANTHOPHYLLITE AND MESOTHELIOMA INDUCTION

Finnish Anthophyllite

Anthophyllite was first mined from a remote rural area in Eastern Finland 4000 years ago and historically used widely throughout Scandinavia. Numerous studies of the modern (1918 to 1975) Finnish anthophyllite mining and milling workforce have been published.[4] The mining and milling of Finnish anthophyllite was exceedingly dusty and resulted in numerous cases of asbestosis.[5] Exposures from the extensive anthophyllite deposits in the region of the mine and mill were also sufficient to produce a very high percentage of endemic pleural plaques in residents without any occupational history.[6,7] Noro[7] said the pleural calcifications in rural Finns living near the anthophyllite districts probably came from contamination of soil or air. The people with endemic pleural plaques residing in the region of the mine failed to demonstrate an attributable mesothelioma excess.[8–10] Similarly, despite more than adequate latency, long-term, high dose exposure,[1] and detailed follow-up, fewer than four mesotheliomas have been identified in the occupational cohort, one of which may be diagnostically suspect.[11] Others claim Finnish anthophyllite alone may cause mesothelioma, if only because it was the predominant amphibole fiber found in patients lungs,[12,13] but a role for crocidolite/amosite[14] or amosite[15] cannot be completely excluded.

Japanese Anthophyllite

A high prevalence of pleural plaques was found in the region of Matsubase on the island of Kyushu. Forty-one percent of Matsubase inhabitants over the age of 40 years showed typical plaques.[16] A large-scale open cast asbestos mine and mill had been in operation in Matsubase between 1883 and 1970, releasing asbestos dust into the environment for a period of approximately 80 years. Most patients had lived in the same residential areas for a long time (i.e. typical of Japanese rural areas). Many were farmers, and only one patient had been exposed to asbestos occupationally. He was a resident of Matsubase, and he showed accompanying pleural plaques. Since no occupational asbestos exposure could be determined in many cases, the pleural plaques were attributed largely to environmental exposure to asbestos originating from the contamination caused by the mining and milling as well as from exposure from non-commercial naturally occurring deposits. A special follow-up system was instituted for 5 years, from 1989 to 1993, to investigate the health of the inhabitants with pleural plaques. The center for respiratory diseases servicing the Matsubase area at the National Kumamoto Minami Hospital failed to find any evidence of a malignant mesothelioma excess. Mass screening programs for lung cancer in inhabitants over 40 years of age were also conducted in almost all towns in Kumamoto since 1986 and the incidence of lung cancer was not found to be higher than in other regions of the Kumamoto prefecture.[16] Hiraoka et al.[16] concluded that the 'high prevalence of pleural plaques but low mortality rate from lung cancer and no evidence of mesothelioma was in accordance with the characteristics of anthophyllite asbestos exposure' and said 'These findings agree with those from an earlier study from Finland[17]'. This noted: 'anthophyllite [is] an interesting mineral, causing a high prevalence of pleural plaques but only rarely mesotheliomas'.[16]

American Anthophyllite

There is limited evidence of anthophyllite-induced disease in the U.S. non-commercial anthophyllite asbestos deposits that occur in at least 12 different states.[18,19] Some of these are in heavily populated areas. As a consequence, anthophyllite is commonly found in the lungs of non-occupationally exposed populations. The sources are not only the anthophyllite deposits but also anthophyllite contaminated chrysotile, talc, cordierite, and phlogopite.[20] Geological similarities also exist between parts of Finland and the United States, thus accounting for the existence of large amounts of anthophyllite in association with cordierite[2].[21] Despite such common sources of exposure to anthophyllite, no areas of endemic anthophyllite pleural plaques similar to those found in Finland and Japan have been identified in the United States thus far.

Commercially, anthophyllite asbestos was mined historically on a small scale in at least three states.[18,19] To our knowledge, the health experience of those operations has never been described nor do we have information about the distribution and use of the products made by any of these mining concerns[3]. Anthophyllite asbestos does not appear to have been used widely in the manufacturing sector in the United States possibly due to its very limited commercial application on a worldwide basis.[22] Anthophyllite was apparently used in one plant in the Northeast as a component in the manufacture of plastic tanks.[23] Dodson and Levin[24] said 'To our knowledge, the use of anthophyllite in the United States consists largely of two manufacturing facilities in Delaware and a small facility in Minnesota. The anthophyllite was brought to the facilities from Finland.' Rom et al.[13] referred to an American factory that imported 4.5 million pounds of Finnish anthophyllite asbestos for tank and pipe production between 1964 and 1972. Dodson and Levin[24] also found anthophyllite in the lungs of an iron foundry worker but were not sure where this was used in the plant.

A few reports alleging the occurrence of mesothelioma due to anthophyllite alone have been reported in the United States. Finnish anthophyllite was said to have been used in each case (see above). Dodson et al.[15] reported one such case (number 28) from alleged environmental exposures incurred from nearby building renovation. The lung burden, however, was well into the occupational range (3 159 000 f/g lung dry weight), suggesting other routes of exposure while the 4-year interval between diagnosis and death cast doubt on the diagnosis. Rom et al.[13] also claimed that mesothelioma arose solely from early 'neighborhood' exposures from a factory that used only anthophyllite. However, the wording of their report made it unclear if any other fiber was found on lung burden analysis.

South African Anthophyllite

Phillips and Murray[25] reported a mesothelioma case allegedly due solely to anthophyllite. However, the exposure history given by the authors strongly suggests that crocidolite was also probably present but not detected due to the use of scanning electron microscopy (SEM). Certain aspects of the case also bring the diagnosis into question. The source of the anthophyllite was also not clear[4].

Australian Anthophyllite

Kottek and Kilpatrick[26] said anthophyllite was mined outside of Perth during WWII and then brought to a suburb of the city to be milled. They commented that 'as the milling of anthophyllite ceased 52 years ago, it is most likely that no environmental cases of mesothelioma have been caused by this source of environmental anthophyllite exposure'.

THE ROLE OF FIBER WIDTH AND MESOTHELIOMA INDUCTION: ANTHOPHYLLITE COMPARED WITH CAPE AND BOLIVIAN CROCIDOLITE

The low mesothelioma potential of Finnish anthophyllite has been recognized by various workers[4,9,17,26–30] and attributed to increased fiber width.[11,26,29] This is consistent with the relatively low percentage of Stanton size fibers found in Finnish anthophyllite (5%–26%) (see **Table 2**).[5] The same is true for Japanese anthophyllite since increased fiber width was cited as being responsible for the rarity of mesotheliomas observed in rural Kyushu. Similarly, lung burden studies of Japanese residents with pleural plaques showed significantly increased mean fiber diameters (0.84 μm) (**Table 1**).[31] The Cape Crocidolite used in Finland and Japan in some commercial processes was found to be comparatively very thin[11,26] (**Table 1**) with a far greater percentage of Stanton size fibers (**Table 2**).

These observations also support the role of increased fiber width as an explanation for the low mesothelioma potential of Bolivian crocidolite.[2] The mean width of Bolivian crocidolite (**Table 1**) and the percentage of Stanton size fibers (**Table 2**) are thus very similar to Finnish and Japanese anthophyllite. The exceptional width of Bolivian crocidolite[6] is further supported by the fact that it could be mounted as

Table 1. Comparison of the Mean Diameters of Anthophyllite and Crocidolite

Finland	Finnish Anthophyllite	Cape Crocidolite	Bolivian Crocidolite[a]
Occupational asbestos disease	0.35 μm[b]	0.13 μm[b]	ND
	0.42 μm[c]	0.09 μm[c]	ND
Occupational (no disease stated)	0.61–0.73 μm[d]	ND[d]	0.3–0.48[e]; 0.40[f]
Mesothelioma	0.35 μm (13% < 0.1 μm)[g]	ND[g]	
	0.35 μm[h]	0.06 μm[h]	
	0.2 μm[i]	ND[i]	
Non-occupational	0.4 μm[i]	ND[i]	
	0.6 μm[j]	ND	
United States	**Finnish Anthophyllite**	**Cape Crocidolite**	
Non-occupational	0.25 μm[k]	0.17 μm[k]	
Meso (women)	0.33 μm[l]	0.12 μm[l]	
Mesothelioma	0.35 μm[m]	0.11 μm[m]	
Asbestosis (foundry worker)	0.22 μm[n]	ND[n]	
Japan	**Japanese Anthophyllite**	**'Cape' Crocidolite**	
Endemic plaque	0.84 μm (0.6% < 0.2 μm)[o]	(27% < 0.2 μm)[o]	
South Africa	**'Finnish' Anthophyllite**	**Cape Crocidolite**	
Mesothelioma	0.94 μm[p]	ND[p]	
No disease	ND	0.11–0.14[f]	

[a]Not found in Finland; sent from Bolivia to the USBUM.
[b]SEM.[29]
[c]TEM.[54]
[d]TEM.[55]
[e]van Orden et al. (paper in preparation)/TEM.
[f]TEM.[3]
[g]STEM.[11]
[h]TEM.[14]
[i]SEM.[36]
[j]TEM.[55]
[k]Reference.[23]
[l]Reference.[20]
[m]Reference.[15]
[n]Reference.[24]
[o]Reference.[31]
[p]Reference.[25]

Table 2. Comparison of the Percentage of Stanton Size Fibers for Anthophyllite and Crocidolite

United States	Finnish Anthophyllite	Cape Crocidolite	Bolivian Crocidolite
Non-occupational	5%[a]	0%[a]	ND
Mesothelioma (women)	26%[b]	68%[b]	ND
Mesothelioma (US)	8%[c]	32%[c]	ND
Occupational	ND	81%[d]	18.5%[d]
	ND	ND[e]	17%–25%[e]

[a]Reference.[23]
[b]Reference.[20]
[c]Reference.[15]
[d]Reference.[3]
[e]Van Orden et al. (paper in preparation).

single crystals under the microscope for fine scale x-ray diffraction (XRD) analysis (Whittaker, personal communication, 1991) and used to determine for the first time the detailed structure of an amphibole asbestos fiber.[32] Similarly, the large width of Finnish anthophyllite also enabled it to be resolved under the optical microscope with phase contrast microscopy (PCM)[33,34] for special biological studies.[35]

Some[36] suggest that anthophyllite fibers from non-occupational settings tend to be thicker than those seen occupationally. While that is not borne out by the data shown in **Table 1**, it would not be surprising to find commercial anthophyllite exposures to be composed of a finer fiber population if they had been highly processed. To the extent that was so, it might resemble the situation seen with amosite where fiber dimensional studies of the fiber as mined suggested it was relatively coarse and wide[37] and very few mesotheliomas were consequently reported from the South African amosite mining fields.[38–41] The intense fiberization required to use amosite commercially[7] created significant thin fiber populations that appeared to be sufficient to cause a mesothelioma risk.[41] However, it is difficult to strictly apply the analogy. Thus, it has been difficult to trace and follow-up the amosite miners and also to be sure that they, as well as those exposed to the commercially processed amosite, did not incur crocidolite exposures, a known potential confounder in those that worked at the UK Uxbridge plant.[42,43] and a probable confounder at the Paterson New Jersey amosite plant[44][8] as well.

CONCLUSION

The findings of this report and the preceding contribution provide further support for the importance of fiber width in mesothelioma induction. In any sample of long amphibole asbestos fibers, there is a very sizable fraction that can penetrate the deep lung (width <0.6 μm). However, a significant proportion of such fibers particularly those wider than 0.2 μm appear to have a much reduced mesothelioma potential. This has important biological and regulatory implications. Biologically, those thinner than 0.2 μm are more likely to translocate to the pleura, thus explaining in part the reduced potency for mesothelioma of fibers greater than this width. A greater number of such 'thin' (<0.2 μm) fibers may accumulate intracellularly than those greater than this diameter. The appearance of a reduced mesothelioma potential for these thinner fibers may therefore also be another manifestation of 'threshold' at the cellular level. The regulatory implications are clear since most regulated PCM fibers are wider than 0.25 μm wide. Fiber counts restricted to those visible by PCM may fail to adequately assess the true attendant risks particularly when the mean diameter of the long fiber population is increased. Similarly, counts of fibers composed primarily of cleavage fragments and many types of 'elongated particles' will also overestimate the risks since their mean diameters will also be increased.

Notes

1. As evidenced by the fact that all four of them incurred very high [probably in excess of 50 f.ml (Ref. 29)], long term (13 to 31 years) sufficient to produce very high lung burdens (275–1100 f/g lung dry wt.) and concomitant asbestosis.
2. From an area that produced a few million pounds of copper.
3. There are anecdotal reports that anthophyllite was used at the Powhattan Point Baltimore operation making some friction products sent from the Powhattan anthophyllite mine in North Carolina [van Orden pers com]. Anthophyllite deposits in the Greater Region of the City of Atlanta have also been described from Soapstone Ridge and said to be a potential source of significant dust exposure.[45]
4. Anthophyllite from Russia or Bulgaria or other major commercial sources, may also have been used.[45]
5. The high end figure of 26% noted by Dodson et al.[20] was seen in women with mesothelioma largely due to household exposure. Domestic exposures of this kind are thought by some to release a higher percentage of fine fibers, thus accounting for an enhanced mesothelioma inducing potential (Browne, personal communication).
6. To be distinguished from the small percentage of long 'non-durable', non-asbestiform Bolivian crocidolite cleavage fragments also found in the deposit.[46–51] These are probably broken down and removed when the ore is fiberized.[52]
7. Commercial use required special fiberizers (Browne, personal communication, 1997).
8. Earlier unrecognized exposures to asbestos in other facilities may also confound the Paterson studies.[53]

REFERENCES

1. Wylie A, Bailey K, Kelse J, Lee R. The importance of width in asbestos fiber carcinogenicity and its implications for public policy. *Am Ind Hyg Assoc J*. 1993;54:239–252.
2. Ilgren E, Ramirez R, Claros E, Fernandez P, Guardia R, Dalenz J, et al. Fiber width as a determinant of mesothelioma induction and threshold—bolivian crocidolite: epidemiological evidence from bolivia—mesothelioma demography and exposure pathways. *Ann Resp. Med*. 2012; On line first.
3. Shedd K. U.S. Department of the Interior: Fiber Dimensions of Crocidolite from Western Australia. Bolivia, and the Cape and Transvaal Provinces of South Africa, by K. B. Shedd (U.S. Bureau of Mines Report of Investigations *8998). Washington, DC: United States Department of the Interior, Bureau of Mines; 1985.
4. Meurman LO, Pukkala E, Hakama M. Four cases of mesothelioma among Finnish anthophyllite asbestos miners in Finland. *Occup Environ Med*. 1994;51:421–425.
5. Ahlman K, Partanen T, Rintala E, Wiikeri M. Anthophyllite mining and milling as a cause of asbestosis. In: *Biological Effects of Asbestos*. IARC Sci Pub. No. 8. Lyon, France: IARC; 1973. pp. 165–168.
6. Kiviluoto R. Pleural calcification as a roentgenologic sign of non-occupational endemic anthophyllite asbestosis. *Acta Radiol Suppl*. 1960;194:1–67.
7. Noro L. Occupational and non-occupational asbestosis in Finland. *Am Ind Hyg Assoc J*. 1968;29:195–201.
8. Neuberger M. Pleural Plaques from Low Levels of Asbestos. In: Peters GA, Peters BJ, eds. *Sourcebook on Asbestos Diseases*. Vol. 4 (Medical Research). New York: Garland Publications/Salem: Butterworth Publications; 1980. pp. 231–275.
9. Hillerdal G, Zitting A, Assendelft A, Kuusela T. Rarity of mineral fiber pleurisy among person exposed to Finnish anthophyllite and with low risk of mesothelioma. *Thorax*. 1984;39:608–611.
10. Karjalainen A, Vanhala E, Karhunen PJ, Lalu K, Penttila A, Tossavainen A. Asbestos exposure and pulmonary fiber concentrations of 300 Finnish urban men. *Scand J Work Environ Health*. 1994;20:34–41.
11. Karjalainen A, Meurman L, Eukkala E. Four cases of mesothelioma among Finnish anthophyllite miners. *Occup Environ Med*. 1994;51:212–5.
12. Vilkman S, Lahdensuo A, Mattila J, Tossavainen A, Tuomi T. Asbestos exposure according to different exposure indices among Finnish lung cancer patients. *Int Arch Occup Environ Health*. 1993;65:269–274.
13. Rom W, Hammar S, Rusch V, Dodson R, Hoffman S. Malignant mesothelioma from neighborhood exposure to anthophyllite asbestos. *Am J Ind Med*. 2001;40:211–214.
14. Tuomi T. Fibrous minerals in the lungs of mesothelioma patients: comparison between data on SEM, TEM, and personal interview information. *Am J Ind Med*. 1992;21:155–162.
15. Dodson R, Graef R, Shepherd S, O'Sullivan M, Levin J. Asbestos burden in cases of mesothelioma from individuals from various regions of the United States. *Ultrastruct Pathol*. 2005;29:415–433.
16. Hiraoka T, Ohkura M, Morinaga K, Kohyama N, Shimazu K, Ando M. Anthophyllite exposure and endemic pleural plaques in Kumamoto, Japan. *Scand J Work Environ Health*. 1998;24:392–397.
17. Meurman LO, Kiviluoto R, Hakama M. Mortality and morbidity among the working population of anthophyllite asbestos miners in Finland. *Br J Ind Med*. 1974;31:105–112.
18. Chidester A, Shride A. Asbestos in the United States (Exclusive of Alaska and Hawaii). US Geological Survey; 1955.
19. Van Gosen B. The geology of asbestos in the United States and its practical applications. *Environ Eng Geosci*. 2008;13:55–68.
20. Dodson RF, O'Sullivan M, Brooks DR, Hammar SP. Quantitative analysis of asbestos burden in women with mesothelioma. *Am J Ind Med*. 2003;43:88–195.
21. Lindgren W. The cordierite anthophyllite mineralization at Blue Hill, Maine, and its relation to similar occurrences. *Proc Natl Acad Sci U S A*. 1925;11:1–5.
22. Selikoff IJ, Lee DHK. *Asbestos and Disease*. New York: Academic Press; 1978. pp. 51–69.
23. Dodson R, Williams M, Huang J, Bruce J. Tissue burden of asbestos in non-occupationally exposed individuals from East Texas. *Am J Ind Med*. 1999;35:281–286.
24. Dodson R, Levin J. An unusual case of mixed-dust exposure involving a 'non-commercial' asbestos. *Environ Health Perspect*. 2001;109:199–203.
25. Phillips J, Murray J. Malignant mesothelioma in a patient with anthophyllite asbestos fibres in the lungs. *Ann Occup Hyg*. 2010;54:412–416.
26. Gibbs AR. Role of asbestos and other fibers in the development of diffuse malignant mesothelioma. *Thorax*. 1990;45:649–654.
27. Kottek M, Kilpatrick D. Re: malignant mesothelioma from neighborhood exposure to anthophyllite asbestos. *Am J Ind Med*. 2002;41:514.
28. Meurman LO, Kiviluoto R, Hakama M. Combined effect of asbestos exposure and tobacco smoking on Finnish anthophyllite miners and millers. *Ann N Y Acad Sci*. 1979;330:491–495.
29. Tossavainen A, Karjalainen A, Karhunen PJ. Retention of asbestos fibers in the human body. *Environ Health Perspect*. 1994;102(suppl 5):253–255.
30. Anttila S, Karjalainen A, Taikina-aho O, Kyyrönen P, Vainio H. Lung cancer in the lower lobe is associated with pulmonary asbestos fiber count and fiber size. *Environ Health Perspect*. 1993;101:166–170.
31. Murai Y, Kitigawa M, Hiraoka T. Fiber analysis in lungs of residents of a Japanese town with endemic pleural plaques. *Arch Environ Health*. 1997;52:263–269.
32. Whittaker E. The structure of Bolivian crocidolite. *Acta Cryst*. 1949;2:312–322.
33. Timbrell V, Gilson JC, Webster I. UICC standard reference samples of asbestos. *Int J Cancer*. 1968;3:406–408.
34. Timbrell V, Pooley F, Wagner JC. Characteristics of respirable asbestos fibers. In: Shapiro HA, ed. *Proceedings of an International Conference on Pneumoconiosis*, Johannesburg, 1969. London: Oxford University Press; 1970. pp. 120–125.
35. Morgan A, Talbot R, Holmes A. Significance of fiber length in the clearance of asbestos fibers from the lung. *Br J Ind Med*. 1978;35:146–153.
36. Tuomi T, Segerberg-Konttinen M, Tammilehto L, Tossavainen A, Vanhala E. Mineral fiber concentration in lung tissue of mesothelioma patients in Finland. *Am J Ind Med*. 1989;16:247–254.
37. Gibbs GW, Hwang CY. Dimensions of airborne asbestos fibers. In: Wagner JC, ed. *Biological Effects of Mineral Fibers*. Intl Agency Res Cancer, Vol. 1. IARC Scientific Publication No. 30. Lyon, France: IARC; 1980. pp. 30, 69–78.
38. Timbrell V, Griffiths DM, Pooley FD. Possible biological importance of fibre diameter of South African amphiboles. *Nature*. 1971;232:55–56.
39. Selikoff IJ, Hammond EC, Churg J. Carcinogenicity of amosite asbestos. *Arch Environ Health*. 1972;25:183–186.
40. Webster I. Asbestos and malignancy. *South African Med J*. 1973;47:165–171.
41. Ribak J, Ribak G. Human health effects associated with the commercial use of grunerite asbestos (amosite): Paterson, NJ; Tyler, TX; Uxbridge, UK. *Regul Toxicol Pharmacol*. 2008;52:S82–S90.
42. Acheson ED, Gardiner MJ, Winter PD, Bennett C. Cancer in a factory using amosite asbestos. *Int J Epidemiol*. 1984;13:3–10.
43. Gibbs AR, Gardner MJ, Pooley FD, Griffiths DM, Blight B, Wagner JC. Fibre levels and disease in workers from a factory predominantly using amosite. *Environ Health Perspect*. 1994;102:261–263.
44. McCullagh SF. Amosite as a cause of lung cancer and mesothelioma in humans. *J Soc Occup Med*. 1980;30:153–156.
45. Hodgson A. Scientific Advances in Asbestos: 1967–1985. UK: Anjalena Press; 1986. ISBN 0-95104811.
46. King D. The occurrence and comparative mineralogy of South Australian Magnesian crocidolites. *Trans R Soc S Aust*. 1961;84:120–130.
47. Ahfeld F. Los yacimientos de crocidolita en los Yungas de Cochabamba (Bolivia). Instituto del Museo de la Universidad Nacional de La Plata. Notas del Museo de La Plata. Tomo VIII Geologia; 1943: No. 27. pp. 1–23.
48. Rameriz R. Estudio de Ingeniera Global Esinglo. Los Minerales de Asbesto en El Chapare. Consideraciones Geologicas y Mineralogicas. Doctoral thesis, School of Engineering; 1989.**
49. Redwood S. Crocidolite and magnesite associated with Lake Superior type banded iron formation in Chapare Group of eastern Andes, Bolivia. *Trans Inst Min Metal (Sec B: Appl Earth Sci)*. 1993;102:114–23.

50. Zuazo F. Crocidolita de Chapare. Servicio Geologico de Bolivia. Pereara G, Director; 1963. pp. 1–90.**
51. Salinas W. La crocidolita magnesiana del Chapare. *Revista Minera Bamin*. 1977;92:25–46.**
52. Ilgren E. The biology of cleavage fragments: a brief synthesis and analysis of current knowledge. *Indoor Built Environ*. 2004;13:343–56.
53. Seidman H, Selikoff IJ, Gelb SK. Mortality experience of amosite asbestos factory workers: dose–response relationships 5 to 40 years after onset of short term work exposure. *Am J Ind Med*. 1986;10(5/6):479–514.
54. Uibu T, Vanhala E, Sajantila A, Lunetta P, Mäkelä-Bengs P, Goebeler S, et al. Asbestos fibers in para-aortic and mesenteric lymph nodes. *Am J Ind Med*. 2009;52:464–70.
55. Timbrell V. Deposition and retention of fibers in the human lung. *Ann Occup Hyg*. 1982;26:347–68.

**Available on request from the authors.