Mesothelioma from Chrysotile Asbestos: Update

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PURPOSE: There are different mineral classes of asbestos, including serpentines and amphiboles. Chrysotile is the main type of serpentine and by far the most frequently used type of asbestos (about 95% of world production and use). There has been continuing controversy over the capability of chrysotile asbestos to cause pleural and peritoneal mesothelioma. This review is to help clarify the issue by detailing cases and epidemiology studies worldwide where chrysotile is the exclusive or overwhelming fiber exposure.

METHODS: A worldwide literature review was conducted of asbestos and associated mesothelioma including case series, case-control and cohort epidemiology studies searching for well documented chrysotile asbestos associated mesothelioma cases.

RESULTS: Chrysotile asbestos exposures have occurred in many countries around the world from mining, manufacturing and community exposures. There have been many documented cases of mesothelioma from those exposures.

CONCLUSIONS: Chrysotile asbestos, along with all other types of asbestos, has caused mesothelioma and a world-wide ban of all asbestos is warranted to stop an epidemic of mesothelioma.

INTRODUCTION

Wagner et al. (1) discovered mesothelioma of the pleura and peritoneum from asbestos exposure in 1960. Fifty years later there is overwhelming evidence that asbestos is responsible for this fatal cancer. Mesothelioma from asbestos involves a quickly fatal disease that has a very long latent period, and causative asbestos exposures may only have had to be low. Although it is a very rare cancer as compared with most, epidemics of mesothelioma have been reported in the United States (2) and worldwide (3) and potentially continuing into the future if asbestos continues to be used.

There is overwhelming documentation by classic studies by Selikoff et al. (4) and others (5) of asbestos as an occupational cause of asbestosis, pleural plaques, lung cancer, pleura and peritoneal mesothelioma, larynx cancer, and other cancers. Environmental cancer’s most famous synergism was shown by Selikoff et al. (6) and Hammond et al. (7) for occupational asbestos exposure and cigarette smoking in the incidence of lung cancer. Although cigarettes are paramount in the lung cancer—asbestos connection, cigarettes have no place in mesothelioma causation.

Asbestos has two main classes, the serpentines (of which chrysotile is the most common type) and the amphiboles (of which crocidolite, amosite, tremolite, anthophyllite, and actinolite are the main types). A total of 95% of world asbestos production has been chrysotile, largely in the past from Canada, but also from mines in several other countries around the world. Some toxicologists and other scientists have sought to delay policy (8) implementation of preventive medicine to ban all asbestos, stating that chrysotile is not causative for mesothelioma, whereas all other types are. For approximately 30 years there has been the “amphibole hypothesis,” the assertion that chrysotile asbestos was incapable of causing mesothelioma (9).

By 2011, there are numerous occupational epidemiology and registry and case studies clearly linking all types of asbestos, including chrysotile, to pleural and peritoneal mesothelioma. The global 15-year (1994–2008) magnitude of mesothelioma is estimated to be 174,300 in a group of 56 countries that report the disease, and 38,900 for the same 15-year period by extrapolation to a group of 33 countries that do not systematically report the disease. The actual cases are probably much greater, as one mesothelioma is missed in every four or five reported cases, because of the difficulty in pathologic diagnosis (3).

There have been many risk assessments and reviews of asbestos and mesothelioma with differing conclusions, especially as to fiber type and causality (10–16). This review and commentary will lay out the studies and cases from all over the world, where the overwhelming evidence is that chrysotile asbestos was the primary or only asbestos exposure. It has been almost 10–15 years since similar review efforts
There have been many new cases and studies of chrysotile asbestos-associated mesothelioma. Although it is clear to most agencies and scientists that all types of asbestos are causative for mesothelioma, there are still some remaining detractors (19), and thus the need for this review.

There is legitimate controversy in the scientific community as to the relative potency of differing types of asbestos in causing mesothelioma. The hypothesized fiber gradient potency in mesothelioma causation ranges between South African crocidolite (an amphibole type), other amphiboles, and chrysotile fibers from 500 to 1 (9) to 200 to 1 (20) to 10 to 1 (5) to 1 to 1 (15). Potency difference assertions will not be easily resolved, but even if chrysotile is much less potent than other types of asbestos, it is now the only type being used in many countries around the world, and thus it is of extreme public health importance to stop its use if it leads to fatal malignant mesothelioma. This review emphasizes studies and cases in which chrysotile asbestos was the only, or overwhelming, asbestos exposure, and thus seeks to reclarify the issue that chrysotile asbestos is capable of being the associated asbestos exposure in malignant mesothelioma causation. It is of paramount importance to elucidate the chrysotile asbestos–mesothelioma connection because of its obvious implications for preventive medicine and public health. This review will begin with the U.S. epidemiology studies, and then will branch out to Canada, Mexico and then Europe, Asia, and Australia.

Selected Abbreviations and Acronyms

| SMR = standardized mortality ratio |
| CI = confidence interval |
| OR = odds ratio |

Chrysotile asbestos was the primary material processed at the plant for textile production. The chrysotile asbestos used by the plant was received from Quebec, British Columbia, and Rhodesia. Small quantities of crocidolite were also used at the plant to make tape or braided packing from the 1950s to 1975. However, only 2000 pounds of total crocidolite was used, compared with the 6–8 million pounds per year of chrysotile used during the same period (23). The crocidolite was never carded, spun, or twisted, so Dement et al. (24) concluded that the predominant exposure to workers at this plant was to chrysotile asbestos. On the basis of this conclusion, the fraction amphibole in the workplace atmosphere is estimated to be at most 0.5% (0%–2%). Dement et al. (22) studied the cohort who worked at least 1 month during 1940–1967, including 1247 white men, 1229 white women, and 546 black men. Follow-up was carried out through 1990. Hein et al. (25) extended follow-up for mortality through 2001. Twenty-one nonwhite women were added to the cohort, and 29 workers for which updated demographic information who had previously been excluded from analysis were added for a total of 3072 workers with vital status follow-up through 2001. Two deaths were certified as caused by mesothelioma on the death certificates of two white men who had latency periods of 37 and 34 years and who worked in the plant for 25 and 32 years (22). Both of these workers had primarily worked in the spinning operations part of the plant. Hein et al. (25) add a third mesothelioma to the two certified by Dement et al. (22). This third mesothelioma occurred in 1995, nearly 50 years after the employee began working in the mule spinning department for approximately 2.5 years (25).

North Carolina Textile Plants

Workers employed for at least 1 day between January 1, 1950, and December 31, 1973, in any of four plants in North Carolina, that produced asbestos textile products were enumerated by Loomis et al. (26). Vital status was ascertained through December 31, 2003. Historical exposures to asbestos fibers were estimated from work histories and 3578 industrial hygiene measurements taken 1935–1986. Mortality of the cohort of 5770 workers was compared with that of the national population via standardized mortality ratios (SMRs). Approximately 90% of the asbestos came from Canada, with smaller amounts from the United States and South Africa, and occasionally from Russia and Australia. According to available records, only chrysotile was used except for a separate operation in Plant 3, where a limited amount of amosite was carded, twisted, and woven between approximately 1963 and 1976. The other plant (Plant 2) produced friction products and other finished goods from purchased asbestos yarn and tape. Eight mesotheliomas were found in total, 4 pleural

U.S. STUDIES

Illinois

Wolf et al. (21) examined clinical, radiologic, pathologic, and epidemiologic data on 32 patients with diffuse malignant mesothelioma diagnosed between 1968 and 1984 at a community hospital in Berwyn, Illinois. Thirty patients had a history of exposure through work (n = 15) and/or residence near an asbestos facility (n = 27). Two large chrysotile asbestos product manufacturing plants were within 4.8 km of the hospital. This case series of 32 patients had a clear high exposure to chrysotile because of where they lived or worked.

South Carolina Textile Plant

This asbestos manufacturing plant was located in Charleston, South Carolina (22), starting in 1896, and production of asbestos textiles (yarn and cloth) was 1909–1978.
and 4 peritoneal. This study provides evidence that workers exposed to chrysotile are at increased risk of mesothelioma, with an SMR of approximately 11 based on 4 deaths observed and 0.37 expected after mesothelioma began to be coded as a separate cause of death in 1999 with the 10th revision of the *International Classification of Diseases*.

**U.S. Railroad Machinists**

Mancuso (27, 28) reported on a cohort of 181 railroad machinists who worked 1920–1929 and were alive as of 1945 and were followed through 1986. Mancuso (29, 30) made a strong case that their railroad occupational exposures to asbestos were only to chrysotile. Fourteen mesotheliomas were found as of 1986 in this group. The mortality rate of 88.1 per 1000 deaths is one of the highest rates ever found for mesothelioma.

**Plastics Manufacturing New Jersey**

Dell and Teta (31) studied mortality through 1988 for 5932 male employees who worked for at least 7 months between January 1, 1946, and December 31, 1967, at a New Jersey plastics manufacturing and research and development plant. The cohort was followed through 1988. There were 1859 deaths. Among them were nine pleura mesothelioma deaths (five listed on the death certificate as underlying and four listed as contributory), which occurred with an average latent period of 33.4 years in this cohort who were primarily making phenolic resins. Asbestos, "usually chrysotile" (31) was used as a filler in the plastic molding process.

**U.S. Brake Repair Workers**

Langer and McCaughey (32) describe a case of diffuse pleural mesothelioma in a man whose sole exposure to asbestos was to the chrysotile during brake maintenance and repair. This 55-year-old man was admitted to hospital 1980 and died in 1981. Since the age of 19 he had serviced automobiles, including the replacement of brake linings. He had no other occupational history of exposure to asbestos or residential history near an asbestos plant. Postmortem digestion of tissue and electron diffraction revealed chrysotile fibrils. 10% of the fibrils were longer than 10 μm. No amphibole fibers were found. The authors estimate that only chrysotile had been used in brake pads since the 1940s.

Lemen (33) reviewed possible asbestos exposure from its use in brakes. Molded brake linings with chrysotile asbestos were introduced in 1927 (33) and were in virtually every car by 1940 and continued to be used in rear brake drums even after the introduction of disk brakes in the era of 1965–1975. Chrysotile comprised 40% to 50% of the brake lining. Most of the chrysotile fibers did not escape to the environment during driving brake use. The fibers ended up as a nonfibrous material called fosterite formed by the heat of the braking process (approximately 600°F). However, some fibers remain unchanged and escape into the environment. Also, during repair and maintenance of brakes, there is potential for chrysotile exposure to the garage mechanics or those in the vicinity. There is a possibility that fosterite has the potential to affect health, but this has not been adequately investigated. The remaining fibers are short (<5 μm in length). There is some evidence that short fibers are less toxic than longer, thinner fibers—longer than 10 microns (34), which is been disputed by Dodson et al. (35) more recently. However, Lemen (33) emphasizes that even if short fibers are less toxic, that they are not without carcinogenic hazard. There was heightened interest in the chrysotile short fiber carcinogenicity question after the collapse of the World Trade Towers on September 11, 2001. Lemen's (33) greatest concern was exposure to mechanics removing brakes or installing new brakes, including the practices of manipulation of brake pads with compressed air blowout, wire brushing or other methods of cleaning out old pads.

**Connecticut Friction Plant**

Finkelstein and Meisenkothen (36) describe six mesothelioma cases in the Connecticut Raybestos plant that made brake linings, transmission and other automotive friction disks, bands, and other materials. Workers in the plant were exposed to chrysotile asbestos during the period of 1940s to the 1980s.

**Pennsylvania Textile**

O'Donnell et al. (37) studied 55 asbestos cases in workers who had worked in a Pennsylvania chrysotile textile factory who were patients in the Lancaster General Hospital 1940–1965. Five of the cases developed mesothelioma (three peritoneum, one pleura, and one both). The interval from initial exposure until the neoplasms were diagnosed in this series was 20–40 years. Mann et al. (38), in a previous study of these asbestosis cases, and three of the O'Donnell et al. (37) mesothelioma cases, found that the factory was using chrysotile.

**California Naturally Occurring**

California has large amounts of serpentine rock in the northern and central part of the state in the Sierra Nevada Coast and Klamath mountain ranges. Serpentine is the base mineral of chrysotile asbestos. Pan et al. (39) conducted a case-control study comparing 2908 incident malignant mesothelioma cases as compared with the same number of pancreatic controls matched by 5-year age group and sex from the California Cancer Registry. Occupational and residential histories were determined and compared. Both occupational exposure and proximity to asbestos sources was associated with mesothelioma incidence. The authors conclude that they confirmed their hypothesis of proximity
to nonoccupational asbestos (serpentine) was associated with malignant mesothelioma.

## CANADA

### Quebec Miners and Millers

McDonald et al. (40) surveyed the Canadian Association of Pathologists and the Quebec Association of Laboratory Physicians for fatal cases of primary malignant tumors of the pleura or peritoneum between 1959 and 1967. They found a total of 165 cases: 113 pleural, 45 peritoneal, 3 pleural, and peritoneal and 4 pericardial. A case-control study was conducted in which they compared the mesothelioma cases with two control groups, one composed of primary lung cancer and one composed of secondary lung cancer cases. Relatives and friends of the deceased filled out questionnaires on occupation, residence, family history, smoking habits, and household dust exposure. An association between mesothelioma and definite or probable occupational exposure to asbestos was demonstrated, but could only be confirmed in 20% of the male cases and in one female case. The documented occupational exposure was more in the manufacturing and industrial application than in mining, indicating to the authors that chrysotile was less associated than other forms of asbestos. Although the authors' hypothesis is possible, the overwhelming occupational Quebec exposure to asbestos in this region was from extremely large chrysotile mines (Thetford and Asbestos) and its subsequent use in manufacture of products. In addition, residential exposure would be to chrysotile from general environmental contamination from the mines (ie, leakage from trucks, washing of workers clothes at home).

McDonald et al. (41) reported on the mesotheliomas in a widely reported study of a cohort of 9780 men who worked as chrysotile miners and millers in Quebec at the Thetford mines. Thirty-three mesotheliomas were observed in miners and millers whose work was with chrysotile asbestos. The overwhelming asbestos exposure to these men was chrysotile. Twenty-one autopsy lung specimens were examined on electron microscope, which showed the amphibole tremolite at about 8 times as chrysotile in 14 of the lungs specimens and 1.7 times greater in 5 of the specimens. The authors ran several statistical analyses attempting to attribute the distribution of mesothelioma cases to exposure to nonchrysotile tremolite instead of the cases' overwhelming exposure to chrysotile in time and space, calling it the tremolite hypothesis. The geographic and time statistical analyses had mixed results even though the authors conclude quite enthusiastically concerning their tremolite hypothesis. Whether it was the chrysotile or the chrysotile-tremolite combination that caused the mesothelioma cases is irrelevant, because the two occurred together, ie, Thetford chrysotile often has roughly 1% tremolite, and if McDonald et al. (41) are correct that it is the 1% tremolite—99% chrysotile combination that is responsible for the mesotheliomas, then Thetford asbestos (99% chrysotile, 1% tremolite) is still the asbestos exposure to these cases of mesothelioma (whatever its exact geologic formula).

### Canadian Case Reports

In 2010, there was a case report of peritoneal mesothelioma in a mill worker from a tremolite-free Canadian asbestos mine (42). He worked for 25 years as a mill worker in two different Carey mines and then 15 years additional as yield maintenance foreman. Born in 1923, he died 1990. There was no other known exposure to asbestos except chrysotile. Samples from this mining area have been consistently tremolite free.

Champion (43) reported on two cases of mesothelioma in two young men. One was the 31-year-old son of a pipe lagger in Scotland; there is no way to tell which fiber type was responsible. However, the second case, a 32-old-year man, had been born in Fulford, Quebec and had moved to Asbestos, Quebec, at age 3, where he lived for 23 years. For 10 years he worked “…as an asbestos mine prospector in Quebec and elsewhere in Canada….The patient in Case 2 had worked for many years in the Canadian mining industry and had lived in a mining town. He had been exposed only to chrysotile” (43).

### Canadian Environmental Exposures from Quebec Chrysotile Mines

Camus et al. (44) described female mesothelioma cases first diagnosed from 1970 to 1989 from the area of the Quebec chrysotile mines of Thetford and Asbestos Canada. Ten pleural and one peritoneal mesothelioma cases were found in a survey of 817 female residents.

## MEXICO

Aguilar-Madrid et al. (45) carried out a case-control study of 119 pleural malignant mesothelioma workers insured by the Mexican Institute of Social Security and 353 age-, sex-, and city-matched controls with the same type of insurance. The cases were immunohistopathologically confirmed by two certified pathologists. Occupational and sociodemographic histories were obtained. Asbestos used in Mexico is overwhelmingly chrysotile imported from Canada. Odds ratios for occupational exposure to asbestos for cases compared with controls were 3.7 (95% confidence interval [95% CI], 1.3–10.4) for the whole group and 14.3 (95% CI, 8–26) for the 96 cases as compared with 111 controls with the most certain data. The authors forecast an epidemic of
future mesothelioma cases if there is continued use of imported chrysotile asbestos in Mexico.

**EUROPE**

**British Women Who Manufactured Gas Masks**

Acheson et al. (46) reported on a 40-year follow-up of two groups of women who manufactured gas masks, one at Blackburn (n = 570) out of chrysotile for civilians working in 1939, and the other factory in Leyland and Preston (n = 757) working in 1939 manufacturing respirators for soldiers out of crocidolite and some chrysotile. Five death certificates mentioned mesothelioma, four in the crocidolite group, but one in the chrysotile-only Blackburn group as the underlying cause of death.

**Italy**

There is an open air chrysotile mine located in Balangero, Italy, which is located in the foothills of the Alps (near Turin, northern Italy). The mine and its associated milling, crushing, screening, and bagging plant began production of chrysotile asbestos in 1916 and, with the exception of the war years from 1939 to 1945, production increased each year. By the time it closed in 1990, the mine was producing 500 tons of chrysotile asbestos per day from the crushing of 9000 tons of serpentine rock (47). In an examination of several air samples using scanning electron microscopy, researchers did not find amphibole fibers at detectable concentrations. In addition to the asbestos being at least 99% chrysotile, a fibrous silicate known as balangeroite, accounted for 0.2%–0.5% of the total mass of samples as commercialized from the Balangero mine. Two mesothelioma deaths were observed, both in workers whose first exposure had occurred at least 20 years earlier. In continuing study of the same facility (2009), Pira et al. (48) found four pleura mesotheliomas as compared with 0.9 expected (4.67 SMR; 95% CI. 1.27–11.96) and 5 pleura and peritoneal mesotheliomas as compared with 1.6 expected (3.16 SMR; 95% CI, 1.02–7.36).

Mirabelli et al. (49) searched the Registry of Malignant Mesotheliomas of Piedmont and found four cases of pleural mesothelioma among blue-collar workers in the mine in addition to the original two reported (6 observed vs 1.5 expected; p < .01). They found three mesothelioma cases among white-collar workers in the mine, and five additional mesotheliomas in workers hired by subcontractors. In addition, three more cases were found among workers processing chrysotile outside the mine. Ten additional cases were found who had not worked in the mine (who might have been exposed to nonoccupational exposures such as mine tailings). In total, 14 mesothelioma cases were found among active workers in the mine and 13 exposed to Balangero chrysotile outside the mine. Mirabelli et al. (49) consider the cluster of 14 mesothelioma cases they found among workers active in the mine and 13 among others “...exposed to Balangero chrysotile adds further evidence to the carcinogenicity of tremolite-free chrysotile” (49).

As to the balangeroite contaminant of chrysotile, a study was conducted Turci et al. (50). They incubated fibers in simulated phagolysosomal fluids with pure chrysotile, pure balangoroite, one sample chrysotile contaminated with balangeroite, and two chrysotile samples contaminated with tremolite. The authors concluded that the balangeroite cannot be considered solely responsible for the mesothelioma cases in Balangero.

A historical cohort study of the largest Italian asbestos textile factory that was in operation 1865–1986 in Grugliasco, Italy, was conducted by Mamo and Costa (51). The study cohort consisted of 1653 workers who were followed through the national mortality registry 1981–1995. SMRs were calculated using for comparison a workforce of manual workers in Turin. Statistically significant excesses for pleural mesothelioma (4 in males, SMR = 3322 men, 10 in women, 13248 females) were observed. This textile plant used the chrysotile mined in Balangero. The textiles were mostly composed of medium and long-fiber chrysotile asbestos, generally mixed with rubber, various resins and additives, and at times with metallic netting.

**East Germany**

Sturm et al. (52) describe the uses of asbestos and asbestos related diseases in the former East Germany. Applications included asbestos construction materials, sheets, boards, tiles, pipes, textiles, filters, seals, putties, filling and joint compounds, plastics, friction materials, and talcum powder. Almost all of the asbestos was chrysotile from the former Soviet Union and smaller quantities of “long-fibred grades” chrysotile from Canada and small amounts of crocidolite from Mozambique and Italy. Chrysotile asbestos from Russia was introduced into East Germany in the early 1960s to establish an asbestos-cement industry. Occupational diseases from 1970 to 1988 in the region were analyzed. 812 mesothelioma cases were investigated and “…due to the exact knowledge of the conditions of production it is possible for 481 cases exposed to asbestos to provide detailed information about the relevant grades of asbestos….On this basis sole exposure to chrysotile asbestos was determined to be the cause of disease in 67 cases…This clearly points to the mesothelioma-inducing potential of chrysotile asbestos from Russia…” (52).

**Lithuania**

Smäilytė et al. (53) described the asbestos situation in Lithuania, where asbestos was used on industrial sites at very high levels until 1990. There were two factories that
have manufactured asbestos-cement pipes and plates in Lithuania from the 1950s. In both plants only chrysotile asbestos was used, and the asbestos came from mines in the Ural area of Russia and Kazakhstan. The content of tremolite fibers in Russian asbestos is much lower than in Canadian chrysotile (54). The asbestos consumption in both factories remained at the same level up to 1990, when it started to decline. Included in the study (53) were all the workers employed 3 months or more before 1986, from 1956 in one plant and from 1963 in the other. The year 1985 was chosen as the last year for entry because asbestos-related cancers have a long induction period, seldom less than 15 years. The authors studied complete data on 1887 workers. The study population (53) was followed from 1978 to the end of 2000. One case of pleural mesothelioma was found and the study showed no deaths from pneumoconiosis. No amphiboles were added to the Lithuanian asbestos-cement production; so the study is informative concerning chrysotile asbestos exposure and mesothelioma risk, with one observed case and 0.3 expected.

Everatt et al. (55) investigated retrospective occupational exposures to asbestos for 298 lung cancer and 4 mesothelioma patients admitted to the Institute of Oncology, Vilnius between November 1, 2003 and May 15, 2005. Occupational histories and lung burden studies were carried out. From the lung burden studies, only chrysotile fibers were found in Lithuania specimens as compared with specimens from other countries in Europe. This agrees with the importation of chrysotile asbestos from Russia for use in Lithuania. Of the four mesothelioma cases (3 men and 1 woman), the diagnosis was confirmed histologically or cytologically. The mean age of the three males was 60.7 and the one woman patient was 43 years of age. One of the male mesothelioma patients had an occupational exposure to chrysotile. The other three did not have documentable asbestos exposures. The authors emphasize the lack of recognition by physicians of occupational etiology of cancer in Lithuania, so over time there may have been many missed cases of mesothelioma.

Zimbabwe

Cullen and Baloyl (57) reported on a study of 51 individuals who had been compensated for pneumoconiosis and who had exposure to chrysotile asbestos in Zimbabwe’s mines or mills since that country’s independence in 1980. A sample of more than 300 who had been compensated for pneumoconiosis were examined for occupational history and availability of complete medical and occupational records to select the sample of 51 for the study. The exposure period of the 51 included workers encompassing 1932–1986 and they were certified between 1980 and 1987. X-rays, demographic data, medical and occupational histories, and laboratory reports were examined in the 51 individuals. There were two cases of pathologically confirmed malignant mesothelioma (pleural), one of these found among 18 asbestos cases.

Australia

Rogers et al. (58) reported on their study of the lung tissue of 221 definite and probable cases of malignant mesotheliomas reported to the Australian Mesothelioma Surveillance Program 1980–1985 and age-sex frequency matched control series of 359 postmortem cases. A total of 697 definite or probable mesotheliomas were diagnosed during the period, and lung tissue material for fiber analysis was available for 221. A total of 207 were pleural, and 14 were peritoneal. The postmortem lung tissue specimens were examined by light microscope and analytical transmission electron microscope and energy dispersive x-ray analysis. Fiber type and length greater or less than 10 μm were reported and only fibers larger than 2 μm were counted.
TABLE 1. Chrysotile asbestos mesothelioma studies

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<td>Yano et al. 2001 (61)</td>
<td>Chongquing, Chinas textile, cement and friction and heat-resistant materials</td>
<td>Cohort</td>
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<td>Yano et al. 2009 (62)</td>
<td>Chongquing, China</td>
<td>Case report</td>
<td>1 peritoneal</td>
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<tr>
<td>Huilan and Zhiming 1993 (63)</td>
<td>China, 8 factories</td>
<td>Cohort</td>
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<td>Baumann et al 2007(64), 2010 (65)</td>
<td>New Caledonia Cancer Registry</td>
<td>Case-control</td>
<td>109</td>
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</tbody>
</table>

There was a subgroup of 25 cases (23 pleural and 2 peritoneal) where only chrysotile was found in the lungs. There was a significant trend in odds ratio with increasing chrysotile fiber content. Two of the cases had a definite history of exposure only to chrysotile, 11 had a history of mixed exposure, and 10 had no documented history of asbestos exposure, and 2 had no available history. “Analysis of a small group of cases and controls with only chrysotile found in the lungs also showed a statistically significant trend (p < .005) of an increasing relative risk of mesothelioma with increasing fiber content in lungs” (58).

China

Three cases of mesothelioma were observed in workers in a chrysotile plant located in Chongquing, Hebei Province in China in a retrospective mortality study covering the years of 1972–1981 (59). The plant opened in 1939 and continued to grow and expand the variety of products it produced, including textiles, asbestos cement products, friction materials, rubber products, and heat-resistant materials. In 1996, 6000 tons of raw chrysotile asbestos obtained from two mines in Sichuan, China, were used in this plant and through its history, chrysotile was the only type of asbestos used in the plant. Commercial samples from the two mines at Sichuan exclusively used in the Chongjin chrysotile plant were analyzed by x-ray diffraction and transmission electron microscopy. The results showed the samples to contain less than 0.001% of tremolite fiber. The cohort comprised male workers employed before January 1972. A total of 515 men were selected for this cohort and followed up for 25 years through 1996. There were two reported cases of malignant mesothelioma, one pleural and the other peritoneal.

In a review of asbestos exposed miners in another region in China, Laiyuan, Cai et al. (60) report on a cohort study of 9950 chrysotile miners from five different mines. Four mesothelioma deaths were found from the workers for the Laiyuan miner after 15 years of follow-up.

Yano et al. (61) conducted a 25-year longitudinal study (1972–1996) in Chongquin, China. The study cohort comprised 515 male asbestos plant workers exposed to chrysotile only. The control cohort included 650 workers from an electronics plant. Two cases of malignant mesothelioma, one pleural and the other peritoneal, were found in the asbestos cohort.

Yano et al. (62) report the case of a 35-year-old chrysotile asbestos worker in Chongquing, China, who developed
Mesothelioma after only 4 years of employment in an asbestos textile plant. In addition to the adult work, he had been "born and bred in a company residence of an asbestos plant and manually spun asbestos during school age." (62). Only chrysotile was used in the plant.

Huilan and Zhiming (63) report the results of a retrospective cohort study of eight chrysotile factory workforces in China. A total of 5893 workers in the eight plants who had retired or left the plants between 1972 and 1986 were traced to 1986 for cause of death. The rate of follow-up was 97.1%. Two pleural mesothelioma deaths were documented in this chrysotile-only exposed cohort.

New Caledonia

Very high incidences of malignant mesothelioma have been found in the Island of New Caledonia (64). The age-standardized incidence rate for mesothelioma for men was 4.6 per 100,000 per year in the 1996–2005 period and 3.1 for women. Baumann et al. (64) studied the possible association between pleural mesothelioma and a traditional lime, called "Po," to cover houses. 68 pleural mesothelioma cases were studied from the tumor registry from 1984 to 2002. For each case, two controls were selected from the cancer registry matched by gender, age, and date of diagnosis. Po, ethnicity, serpentine in the soil, and other factors were investigated. The only significant factor in a linear regression of ethnicity, Po, and other factors, was serpentine (the base rock of chrysotile asbestos) in the soil p = .017.

Baumann et al. (65) further studied all mesothelioma cases (109) from the New Caledonia Cancer Registry from 1984 to 2008. Factors that were investigated were demographic variables, residential history, school, and occupational history. The most significant finding was the association with living near roads covered by serpentine, followed by the number and proximity of serpentine quarries and the size of the surface area containing serpentines. There are also locations on the island with a tremolite-actinolite type of asbestos. The odds ratio (OR) for the serpentine (antigorite) area was great (OR, 20.667; 95% CI, 4.028–106.03) as compared with the tremolite-actinolite area (OR, 1.714; 95% CI 0.664–4.423).

**DISCUSSION**

This review sought to search the world epidemiology literature on mesothelioma to catalogue the case-series, cohort, and case-control studies in which the asbestos exposure appeared to be overwhelmingly to the chrysotile type. Mesothelioma is a rare cancer, but as illustrated in Table 1 (21, 22, 25–28, 31, 32, 36–38, 41–49, 51–53, 55–65), there have been cases in which chrysotile is the exclusive or overwhelming asbestos exposure from all over the world. Many members of the mainstream scientific community have concluded from the evidence that there is no "safe" level of exposure to asbestos of any type. "...an occupational history of brief or low-level exposure should be considered sufficient for mesothelioma to be designated occupationally related..." to asbestos exposure (66).

In addition to the "amphibole hypothesis," there have been scientific disagreements about the biopersistence of chrysotile in the pleura and its capability to cause mesothelioma, and the capability of fibers less than 10 µm to cause cancer (34). The review by Dodson et al. (35) describes the work of Pott et al. (67) and others that makes it clear that small fibers are capable of carcinogenicity, and the work of Suzuki and Yuen (68) that chrysotile migrates to the pleura from the lung.

An occupational history of brief or low level exposure to asbestos is considered sufficient for mesothelioma to be considered as occupationally related, although many times the exposure is not documented because of mixed exposures to different substances in the construction trades or other work environments and the imperfect nature of retrospective recall of either the worker or the surviving relatives. We do know that many asbestos exposed individuals do not know they have been exposed when they have actually been exposed in the workplace or in the community. Thus, a mesothelioma labeled as "idiopathic" may be due to the fact that the victim's exposure to asbestos is not known or documented.

The authors of multiple studies have shown that all levels of exposure to asbestos can increase the risk of mesothelioma. Because there is no known threshold, then current regulatory levels for asbestos may be capable of mesothelioma carcinogenicity. Brief or low exposures to asbestos are capable of mesothelioma carcinogenicity. It is universally accepted that it takes a greater exposure to asbestos to cause asbestosis than the amount needed for mesothelioma carcinogenicity. Thus, in worker groups, like brake workers, where there has been excess asbestosis, these workers have definitely been exposed to asbestos levels enough for mesothelioma carcinogenicity.

It is clear that all types of asbestos are capable of malignant mesothelioma carcinogenicity. Chrysotile asbestos may be less potent in this regard than certain types, for instance South African crocidolite, but given the widespread use and continuing exposure to chrysotile in many countries of the world, there have been projections of a continuing epidemic of mesothelioma (69).

**SUMMARY**

There are many well-documented cases of mesothelioma from chrysotile asbestos in case-reports and epidemiology studies from all over the world. The published studies most
certainly missed many cases of mesothelioma that have occurred from chrysotile asbestos exposure because of the difficult nature of the pathologic definitive diagnosis, the difficulty in documenting work exposures of the past, the absence of study of many workers who were exposed and left the industry without being included in the studies, and the environmental exposure that occurred to nonworkers. Thus, it is reasonable to assume that the total numbers of cases that are documented is just the tip of the iceberg of a potential world-wide environmental cancer epidemic of mesothelioma from asbestos, including chrysotile asbestos. There is general agreement among many scientists and health agencies that exposure to any type of asbestos (chrysotile or amphibole) can increase the likelihood of lung cancer, mesothelioma, and nonmalignant lung and pleural disorders (70–79).

Given the continued use of chrysotile asbestos in many countries worldwide, there have been projections of a continuing and increasing mesothelioma epidemic. In addition there are many safer, cheaper substitute materials available for each asbestos use, including plastic, cellulose, plant fibers, clay and wood fibers (80). Consequently, a number of the members of the scientific community have repeatedly called for a universal ban on the use of all types of asbestos as a mandatory measure to protect the public health (80). An analysis (81) of trends in global mesothelioma mortality rates over time, comparing countries that have banned asbestos to countries that have continued use, showed reduction in mortality in countries after adopting a ban. It is long past the time for a worldwide asbestos ban.

REFERENCES