



Mesothelioma and asbestos

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Abstract

The current state of knowledge concerning mesothelioma risk estimates is reviewed. Estimates of the risk of mesothelioma exist for the commercial asbestos fiber types chrysotile, amosite and crocidolite. Data also exist on which to assess risks for winchite (sodic tremolite) and anthophyllite asbestos. Uncertainty in estimates is primarily related to limitations in measurements of exposure. Differences in the dimensions of the various fiber types and of the same fiber types at different stages of processing add a further complication. Nevertheless, in practical terms, crocidolite presents the highest asbestos related mesothelioma risk. The risk associated with sodic tremolite (winchite) appears to be similar.

In chrysotile miners and millers, the mesothelioma risk has been linked with exposure to asbestiform tremolite. Exposure to chrysotile in a pure form seems likely to present a very low if any risk of mesothelioma. While the majority of mesothelial tumors result from exposure to the asbestos minerals, there are other well established and suspected etiological agents.

While a practical threshold seems to exist for exposure to chrysotile, it is unlikely to exist for the amphibole asbestos minerals, especially for crocidolite. To date there is no indication of an increased risk of mesothelioma resulting from non-commercial fiber exposure in the taconite industry.

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1. Introduction

While there had been isolated reports of primary malignant mesothelial tumors since at least the 18th century, the link between asbestos exposure and mesothelioma was not established until 1960 when Wagner et al. (1960) published their classic paper on the occurrence of this tumor in persons working and living in the vicinity of crocidolite (blue asbestos) mines in Cape province, South Africa. Since that time, research has examined the relationship between this tumor and other asbestos fiber types, certain naturally occurring non-asbestos fibers (e.g., erionite, fluoroedenite), certain synthetic fibers (e.g., vitreous fibers) and to a limited extent potential non-fiber etiological factors (e.g., therapeutic radiation, SV40).

In order to estimate the risk of mesothelioma for workers and the general public, mathematical models have been developed and the risk of mesothelioma associated with each commercial asbestos fiber type estimated. In this paper, we will attempt to answer the questions what are the causes of mesothelioma, is fiber type important, what are the levels of risk, is there a threshold and is there evidence of an increased risk of mesothelioma in taconite miners?

2. Epidemiologically established causes of Mesothelioma

There is little doubt that the amphiboles amosite, crocidolite, anthophyllite and “tremolite” asbestos fibers are associated with increased risks of mesothelioma (Table 1). While it seems clear that chrysotile contaminated with tremolite at the same levels as encountered in the Quebec chrysotile mines and mills in the past is

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Table 1
Mesothelioma in various cohorts^a

Study	Total cohort	Dead	Number of cases and proportional mortality
<i>Crocidolite</i>			
Gas mask manufacture Canada (McDonald and McDonald, 1978)	199	56 (28%)	9 (16.1%)
Gas mask manufacture (Acheson et al., 1982)	757	219 (28.9%)	5 (2.3%)
Mining blue asbestos—Australia (Berry et al., 2004)	6908	2549 (36.9%)	231 (9.1%)
Mining blue asbestos—South Africa (Sluis-Cremer et al., 1992)	3430	423 (12.3%)	20 (4.7%)
Blue asbestos cigarette filter production (Talcott et al., 1989)	35	28 (80%)	5 (17.8%)
<i>Amosite</i>			
Amosite factory (Seidman et al., 1979)	820	528 (64.4%)	14 (2.7%)
Amosite factory UK (Acheson et al., 1984)	5969	422 (7.1%)	5 (1.2%)
Mining amosite asbestos—South Africa (Sluis-Cremer et al., 1992)	3212	648 (20.2%)	4 (0.6%)
Amosite factory—Tyler Texas—USA (Levin et al., 1998)	1130	315 (27.9%)	6 (1.9%)
<i>Mixed fiber types</i>			
Insulation workers—NY—NJ (Selikoff et al., 1979a)	632	478 (75.6%)	38 (7.9%)
Insulators in shipyards—Sweden (Jarvholm and Sanden, 1998)	248	86 (34.7)	7 (8.1%)
Insulation workers—USA and Canada (Selikoff and Seidman, 1991)	17,800	4951 (27.8%)	458 (9.2%)
Dockyards UK (Rossiter and Coles, 1980)	6292	1043 (16.6%)	31 (3.0%)
Insulators in shipyards—USA (Selikoff et al., 1979b)	440	79 (17.9%)	8 (10.1%)
Asbestos factory workers in London—UK (Newhouse et al., 1985)	M 4255 F 684	975 (22.9%) 274 (39.5%)	73 (7.5%) 25 (9.1%)
<i>Tremolite</i>			
Vermiculite mining—USA (McDonald et al., 2002, 2004)	406	285 (70.2%)	12 (4.2%)
<i>Anthophyllite</i>			
Anthophyllite miners—Finland (Karjalainen et al., 1994)	999	503 (50.3%)	4 (0.8%)
Anthophyllite miners—Finland (Meurman et al., 1994)	735	137 (18.6%)	4 (2.9%)
<i>Chrysotile</i>			
Chrysotile miners & millers (McDonald et al., 1997)	Total 9780	8009 (81.9%)	38 (0.47%)
	Thetford 5041	4125	25 (0.61%)
	Asbestos4031	3331	8 (0.2%)
	Factory 708	553	5 (0.9%)
Chrysotile mining chrysotile Italy (Piolatto et al., 1990)	1,058	427 (40.4%)	2 (0.46) ^b
Chrysotile textile plant (Hein et al., 2007)	3072	1961 (63.8%)	3 (0.15%)
Chrysotile products factory (Weiss, 1977)	264	66 (25%)	0
Asbestos cement plant (Thomas et al., 1982)	1,970	351 (17.8%)	0
Chrysotile gas mask filter workers (Acheson et al., 1982)	570	177 (31.1%)	1 ^c
Friction materials manufacture—USA (McDonald et al., 1984)	3,641	1,267 (34.7%)	0
Friction materials manufacture—UK (Newhouse and Sullivan, 1989)	13,450	2577 (19.2%)	0 ^d

^a Not all studies are independent as some involve overlaps and others follow-up of the same or very similar cohorts. The results of the latest follow-up are shown.

^b Amphibole fibers have been milled at this mine.

^c This case was also considered to have been exposed to blue asbestos at another factory. There was also an excess number of persons with cancer of the ovary at the blue fiber plant. These were considered by the authors to possibly be additional mesotheliomas.

^d There were 13 mesotheliomas in total; 11 had contact with crocidolite; of the two working with chrysotile, 1 diagnosis uncertain, 1 work history was not well established.

capable of increasing the risk of mesothelioma, the potential of “pure” chrysotile to induce mesothelioma in humans is still open to debate.

2.1. Crocidolite

Since the first report by Wagner et al. (1960), increased risks of mesothelioma have been demonstrated in Australian crocidolite miners and millers (Armstrong et al., 1988), in manufacturers of crocidolite filters for cigarettes (Talcott et al., 1989), in crocidolite gas mask workers (McDonald and McDonald, 1978; Acheson et al., 1982)

and in crocidolite railroad brake manufacturers (Berry and Newhouse, 1983) among others. The potency of crocidolite is high with a “little crocidolite going a long way”.

2.2. Amosite

Amosite (fibrous grunerite) has been linked to an increased risk of mesothelioma, but, remains a curiosity in that the risk in mining appears to be much lower (Sluis-Cremer et al., 1992) than appears to be the case in downstream manufacturing industries (Seidman et al., 1986; Acheson et al., 1984). However, this may be follow-up per-

iod, difficulties of ascertainment in South Africa or fiber dimension changes with processing.

2.3. Anthophyllite

Anthophyllite has been shown to increase mesothelioma risk, but the risk appears to be far less than with the other amphibole fibers (Table 1).

2.4. Tremolite

In a vermiculite mine in Montana, the mineral winchite, which is soda tremolite, has been linked with a high risk of mesothelioma (McDonald et al., 2002, 2004). The carcinogenic potency (for mesothelioma) of this asbestiform mineral from the Montana vermiculite mine appears to be similar to the potency of crocidolite (McDonald et al., 2002, 2004).

2.5. Chrysotile

There is little doubt that the mesothelioma risk is elevated in Quebec chrysotile miners and millers (McDonald et al., 1997), but this increased risk is associated with mines where workers were also exposed to asbestiform tremolite (Rowlands et al., 1982; McDonald and McDonald, 1995). The likelihood that the mesothelial tumors are related to tremolite fiber exposure is supported by the extremely low rates of mesothelioma in downstream chrysotile only industries where asbestiform tremolite exposure would be expected to be much lower than encountered by the Quebec miners and millers (Gibbs, 2001).

2.6. Non-asbestos fibrous minerals

Mesothelioma has now been shown to be associated with exposure to erionite, a fibrous zeolite (Baris et al., 1987; Wagner et al., 1985) and there is evidence that the tumor is also associated with exposure to the fibrous fluorendenite amphibole (Comba et al., 2003).

3. Experimental production of mesothelioma

Experimentally, many fibers with appropriate dimensions and biopersistence have been shown to be capable of producing mesothelioma. For example, it is now reasonably well established that synthetic vitreous fibers which are respirable, biopersistent and of certain dimensions, can induce mesothelioma (Stanton, 1973; Stanton and Wrench, 1972; Stanton et al., 1977; Davis, 1991; Pott and Roller, 1996). However, the evidence, to date has not shown increased risks of mesothelioma in workers exposed to synthetic vitreous fibers. Other fibers of sufficient biopersistence, if they are respirable, long and thin are also capable of inducing primary malignant mesothelial tumors in experimental animals.

4. Suspected causes of mesothelioma in humans

While there have been several agents postulated as responsible for mesothelioma, they remain to date as suspected links. Therapeutic radiation, on anecdotal evidence seems highly likely to be an occasional cause of mesothelioma (Hoffman et al., 1994), although the limited studies that have been done to date have not supported the association. There is some evidence that thorotrast treatment increases the risk of mesothelioma (Andersson et al., 1995). The virus SV40 has been shown to be capable of inducing mesothelioma experimentally (Carbone et al., 1999) and fragments of DNA from this virus reported in mesothelioma tumor (Gibbs et al., 1998). In spite of claims of synergy with asbestos exposure there is as yet no evidence that the SV40 virus is responsible for mesothelioma in humans. However, research to establish whether or not it does have a role continues although recent evidence suggests that it may not have a role (Manfredi et al., 2005). There are also several chemicals including potassium bromate, plutonium, beryllium and 2:6 dichloro benzonitrile and a virus that have been shown experimentally to induce mesotheliomas or are suspected of being capable of causing mesothelioma (Kurakawa et al., 1983; Sanders, 1992; Oels et al., 1971; Donna et al., 1991; Gold and Kathren, 1998; Peterson et al., 1984).

5. The risk of mesothelioma by fiber-type

There is now little doubt that there are significant differences in the risk of mesothelioma associated with the various asbestos fibers. An indication of the order of magnitude of likely differences was evidenced by the very large differences in the proportional mortality of mesothelioma in various industries using various fiber types (Table 1). A criticism that can be justifiably levelled at proportional mortality ratios (PMRs), as in the case of mesothelioma, is that they increase steeply with increasing length of follow-up. Hence, comparisons must be made at similar periods since first exposure. A further complication is that exposure level influences risk and PMRs. One way to overcome these criticisms is to relate risk to level of estimated exposure as done by Hodgson and Darnton (2000). They produced models to estimate risk which were non-linear.

5.1. Crocidolite, amosite and chrysotile

The risks associated with these fiber types as reported by Hodgson and Darnton (2000) are shown in Table 2. The experiences of workers in other industries shown in Table 1 are supportive of these findings.

5.2. Tremolite asbestos

Hodgson and Darnton did not estimate the risk associated with asbestiform tremolite or with winchite. However,

as shown in Table 1, McDonald et al. (2002) reported 285 deaths in a cohort of 406 vermiculite miners and 12 mesotheliomas for a PMR of 4.12%. The cohort of workers was exposed to an average concentration of 18 f/cc (McDonald et al., 2002).

5.3. Chrysotile

The risk estimates based on Hodgson and Darnton are shown in Table 2. In this table, all the studies are of workers with known exposure to chrysotile only (with the exception of the Carolina textile plant) where crocidolite yarn was used for some years and the Balengero mine where it has been reported (Gruber, 1999) that some crocidolite was milled. Recently it has been suggested that crocidolite may have played a role in the occurrence of mesothelioma in chrysotile miners from Thetford Mines, Que. (Egilman et al., 2003). In fact, there is good evidence that this was not the case, as studies of the lung tissue of workers from the Thetford Mines area have not shown the presence of crocidolite, only chrysotile and tremolite (McDonald et al., 1997). This is not the result of an analytical problem as crocidolite was found in the lungs of workers at Asbestos where crocidolite was used in a factory (McDonald et al., 1997). As the claimed source of the crocidolite is a riebeckite granite at one mine only, it would not explain the distribution of the mesotheliomas described by McDonald and McDonald (1995) as the mine in question would have been in the peripheral lower risk of mesothelioma mines.

It can be seen from Table 2 that the mesothelioma risks in the chrysotile mining industry are very different from

Table 2
Risk of mesothelioma per fiber/ml-year as reported by Hodgson and Darnton (2000) (adjusted for age at first exposure)

	Percentage total expected mortality per f/ml-year
<i>Crocidolite</i>	
Massachusetts	0.68
Wittensoom	0.48
South Africa crocidolite mines	0.59
Total crocidolite	0.51
<i>Amosite</i>	
Paterson	0.12
South Africa amosite mines	0.06
Total amosite	0.10
<i>Chrysotile</i>	
Carolina (Men) ^a	0.0130
Balengero!	0.0025
Quebec	0.0009
Carolina (Women)	0
New Orleans	0
Connecticut	0
Total chrysotile	0.0010 (<0.0009) ^a

^a Excluding industries where some crocidolite used.

those in the crocidolite mining industries. Indeed, many of the chrysotile studies had an expected mesothelioma mortality of zero. The total expected number of mesotheliomas based on the Hodgson and Darnton (2000) approach, but eliminating all studies in which crocidolite was a potential issue was less than 0.0009/f/ml-year. If we further consider the evidence put forth by McDonald and McDonald (1995) that the mesothelioma risks are higher in the mines with tremolite exposure (demonstrated by tissue burden studies) the findings would suggest that “pure” chrysotile (ie: tremolite free) would pose an even lower risk.

Based on their analysis, Hodgson and Darnton report that the relative potency for causing mesothelioma by the commercial asbestos types, crocidolite, amosite and chrysotile is in the ratio of 500:100:1 respectively. This estimate assumes that the commercial chrysotile may be contaminated by tremolite. In a final draft document prepared for the US EPA, it was suggested that the best estimate for the potency of chrysotile for causing mesothelioma may be less than 1/750th of that of the amphiboles and “the possibility that pure chrysotile is non-potent for causing mesothelioma cannot be ruled out by the epidemiology data” (Berman and Crump, 2004). Yarbrough (2006) in a detailed review of concluded that: “The review of 71 asbestos cohorts exposed to free asbestos does not support the hypothesis that chrysotile, uncontaminated by amphibolic substances, causes mesothelioma.”

6. Estimates of risk

Camus et al. (1998) reported a study of women living in two chrysotile asbestos mining areas in Quebec, over the period 1970–1989. The average cumulative exposure was estimated as 25 fibers/ml years, with a plausible range from 5 to 125 fibers/ml years, equivalent to 105 fibers/ml working yrs, after converting to the measure used for occupational exposure over 40 h a week.

Based on the EPA model of risk for mesothelioma, Camus et al. (2002) predicted that there should be 150 (range 30–750) mesothelioma in the Town of Asbestos. In fact there was 1 peritoneal mesothelioma. Based on the same model, 500 (range 500–2500) mesotheliomas were predicted to occur in the town of Thetford Mines. In fact 10 pleural mesothelioma were found. These models of prediction were based on risk parameters derived from mixed asbestos fiber type exposures and were clearly wrong. Based on the risk of 0.0009/f/ml-yr from Hodgson and Darnton (2000), the relative risk of mesothelioma, assuming linearity in this range would have been $(1 + 0.0009 \text{ cum exp}) = 1.09$. Therefore the number of mesothelioma that would have been predicted in Thetford Mines would have been 9 deaths and at Asbestos would have been just less than 1 which is quite close to the observed numbers. Clearly the EPA model is incorrect and the Hodgson and Darnton estimates much closer to reality.

6.1. Uncertainties

Unfortunately, as with virtually all studies involving humans, there are uncertainties. The main uncertainties relate to the exposure estimates which of necessity often depend on extrapolation into the past. It has been necessary to convert measurements made with midge impingers (Gibbs and LaChance, 1974) and thermal precipitators (HEI-AR, 1991) to membrane filter phase contrast microscopy equivalents with the associated limitations on the conversions. The shape of the relationship between mesothelioma and asbestos exposures at very low doses is also subject to some debate.

In spite of the limitations, it can be seen in Tables 1 and 2 that there is a fair degree of consistency in the risk estimates for the various fiber types.

6.2. Threshold of risk

It is scientifically impossible to prove the negative. Never-the less, the evidence does exist that supports the existence of at least a practical threshold, that is a level at which for practical purposes the risk of mesothelioma is undetectable (Browne and Gibbs, 1998). In addition to the studies in which the risks were 0 in Table 2, there are several other studies where there is no evidence of chrysotile related mesothelioma (Table 1). Berry and Newhouse (1983) and Newhouse and Sullivan (1989) found no chrysotile related mesothelioma in a study involving friction product manufacturing workers followed from 1946 to 1986. The study clearly found crocidolite-related mesothelioma even though crocidolite had only been used for two short periods at the plant to manufacture railroad brakes. Studies of automobile brake mechanics (Table 3) show no increased risk of mesothelioma in studies in the USA, Spain, Germany and Canada. Further the UK proportional mortality study by Hodgson et al. (1997) shows no increased risk of mesothelioma in garage mechanics (PMR approx. 0.33). A more recent study by McElvenny et al. (2005) reported on mesothelioma in males aged 16–74 in Great Britain for the years 1980–2000 (excluding 1981). They found the PMR for motor mechanics was 0.48 (CI 37–62). Registry studies in Scandinavia (Malker et al., 1985; Jarvholm and Brisman, 1988) also failed to show any increased risks. It has been claimed that the experience of brake mechanics in Australia demonstrates an

increased risk (Leigh and Driscoll, 2003), but to date a systematic controlled study has not been carried out. The postulated increased risk is based on a series of cases from the Australian Mesothelioma Register. This contains extensive details on cases over about a 20-year period but, like most cancer registries, it does not have details on a comparison group of those without mesothelioma. This limits the conclusions that can be drawn.

Wong (2001) carried out a meta-analysis on the studies in Table 3 and found an overall RR of 0.90 (CI 0.66–1.23). While this does not reach significance, the consistency of the independent studies from various countries is highly significant statistically. The meta-analysis of Wong may perhaps be criticized on the grounds that in some of the studies the comparison was of vehicle mechanics compared to not being a vehicle mechanic that is the risk is relative to the average risk over all other occupations, including some occupations with a high mesothelioma risk. However, for three of the six studies (McDonald, Teschke, Agudo) there is an analysis that excludes those who had exposure to asbestos in high-risk occupations, and so this criticism is certainly invalid as far as these three studies are concerned. For the other three studies more information is necessary to be definite either way. If the analysis was restricted to the former three studies, the combined estimate would be 0.80 with 95% confidence interval of 0.44–1.49. While this estimate does not rule out a small increased risk it certainly rules out a large one. Wong (2006) reported further on the issues to consider in interpreting the automotive mechanic study result and concluded that the epidemiology of mesothelioma in auto mechanics was “consistent and overwhelming” and that automechanics do not have an increased risk of mesothelioma as a result of their brake and clutch work. A similar conclusion has been reached by other researchers (Laden et al., 2004; Goodman et al., 2004).

The absence of a single mesothelioma in workers employed for less than 2 years in the Quebec asbestos mining industry where exposures were high is indicative of a threshold. In that industry, out of a total cohort of about 11,000 men born 1891–1921, 8000 had died by 1992, so the pattern of results is unlikely to change significantly.

Another argument that might be made concerning a threshold for asbestos relates to fiber size. The International Agency for Research on Cancer did not classify attapulgite with fibers of length less than 5 μm in length as carcinogenic. Studies by Stanton and Wrench (1972), Stanton (1973), Stanton et al. (1977) and Stanton and Layard (1978) showed that fibers greater than 8 μm in length and less than 0.25 μm in diameter had a higher probability of producing tumors than did shorter and larger diameter fibers. They also demonstrated that reducing the length of fibers by pulverization decreases the carcinogenicity as far as mesothelial tumor production is concerned. They concluded that pulverized blue asbestos of length less than 1.25–3.75 μm could be discounted in mesothelioma production.

Table 3

Studies of friction product repair workers (from Wong et al., 2001) showing no increased risk of mesothelioma

Study	Relative risk
US garage workers (McDonald and McDonald, 1980)	0.9 (0.39–2.13)
Canada (Teschke et al., 1997)	0.8 (0.20–2.30)
US Connecticut (Teta et al., 1983)	0.65 (0.08–5.52)
Germany (Woitowitz and Rodelsperger, 1994)	0.87 (0.46–1.64)
Spain (Agudo et al., 2000)	0.62 (0.17–2.25)
US (Spiras et al., 1994)	1.00 (0.90–1.60)

6.3. Pleural vs. peritoneal mesothelioma

In the study of chrysotile miners and millers in Quebec, there were 38 cases of mesothelioma, none of which was a primary peritoneal mesothelioma and only one of which invaded the peritoneum. In other chrysotile only industries, peritoneal mesothelioma rarely if ever occur. Thus, it appears that chrysotile may not cause peritoneal mesotheliomas. This would be quite consistent with the observation that mesotheliomas in the mining industry are related to asbestiform tremolite exposure. A very large exposure to chrysotile contaminated with chrysotile would be necessary to give adequate tremolite exposure to increase the pleural mesothelioma risk. Further analysis shows that the ratio of the slopes for peritoneal and pleural mesotheliomas is between 2.4 and 3.2, with the risks of peritoneal mesothelioma and pleural mesothelioma being identical at 90 f/ml-yr for crocidolite and 55 f/ml-yr for amosite (Hodgson and Darnton, 2000). This means that at lower concentrations, there is a predominance of pleural mesothelioma with peritoneal mesotheliomas occurring more frequently only when the exposure is higher. In the chrysotile mines, the tremolite as a contaminant is rarely if ever adequate to cause the peritoneal mesothelioma.

7. Predicting incidence

The risk of mesothelioma depends on the nature of the fiber to which the person is exposed (fiber type and dimensions), duration of exposure, time since first exposure, age at exposure and rate of elimination of fibers from the lung. It is now reasonably well established that the risk of mesothelioma increases with time since first exposure to the power of 3–4. Equations expressing the relationship between mesothelioma incidence and exposure level, exposure duration and time since first exposure have been derived and can even take into account the rate of elimination of fibers from the body as shown below (Berry, 1999). This depends on the constants k which has been developed, based on various studies by various authors. The simple model is shown below (a). The models taking account of elimination are shown in (b and c).

(a) Simple model

$$I(t) = KC[t^{3.2} - (t-d)^{3.2}] \quad \text{where } t > d.$$

Table 4

Mortality from mesothelioma in workers exposed to cummingtonite-grunerite and “fibers” in taconite mines

Study	Deaths	Mesothelioma
^a Homestake (McDonald et al., 1978)	631	1 (did not work in mine; dubious pathology + other exposures)
^a Homestake gold miners (Steenland & Brown, 1996)	1551	0
Reserve (Higgins et al., 1983)	298	0
^b Two taconite mines (Cooper et al., 1992)	1058	1 (pleural)—taconite exposure began only 11 years before death.

^a These cohorts have some overlap so cannot be considered as independent studies.

^b There were two follow-up periods. Results for latest follow-up shown.

K = constant; C = fiber concentration; t = time since start of exposure; d = duration of exposure (Hughes, 1989).

(b) Elimination model

$$I(T) = ce^{-L(T-w)}(T-w)^3 \quad \text{for } T > w.$$

$I(T)$ = incidence at time T ; $c = afd$ where a is a constant; f is the fiber concentration and d = duration of exposure. L = elimination rate. T = time since the start of exposure and w is a lag period (Berry, 1999).

(c) Simplified elimination model

$$I(T) = ce^{-LT}T^3.$$

$I(T)$ = incidence at time T ; $c = afd$ where a is a constant; f is the fiber concentration and d = duration of exposure. L = elimination rate. T = time since the start of exposure (Berry, 1999).

8. Taconite mining

The studies that have been conducted in the taconite mining industry are shown in Table 4. The table includes the results of studies conducted at the Homestake Mine where workers were exposed to non-asbestiform cummingtonite-grunerite. There were three studies at this mine (McDonald et al., 1978; Steenland and Brown, 1995; Gilliam et al., 1976; Brown et al., 1986) but a single case of mesothelioma, not considered to be associated with the mining exposure was reported in only one of the studies (McDonald et al., 1978). That study included persons with more than 20 years of service, so there was definitely adequate latency to detect mesothelioma. While the study by Higgins might be criticized for inadequate latency, the studies by Cooper et al. (1988, 1992) did allow an adequate time from first exposure to permit the detection of mesothelioma. To date there is no evidence of an increased risk of mesothelioma associated with taconite exposure.

A recent study by Brunner et al. (2007) found that between 1984 and 1998 there were 17 cases of mesothelioma that had ever worked as a taconite miner in Minnesota. All but one had had exposure to commercial asbestos.

9. Conclusions

Risk estimates exist for each of the main asbestos fiber types. The main limitation in these estimates is the mea-

surements of exposure. There are large differences in mesothelioma risks associated with the different fiber types and it seems probable that chrysotile in a pure form may not cause mesothelioma in humans. Because, experimental evidence suggests that different lengths of fibers pose different mesothelioma risks, comparisons should be done on a size basis, but in practice such comparisons are not possible. However, it is possible that some of the differences in risk between industries using the same fiber type may be due to differences in fiber dimensions. A practical threshold seems to exist for exposure to chrysotile, but is unlikely for amphiboles.

Existing taconite studies are limited for evaluation of mesothelioma risks, but to date do not suggest any increased risk of mesothelioma resulting from exposure to non-commercial fibers or cleavage fragments encountered in this industry.

References

- Acheson, E.D., Gardner, M.J., Pippard, E.C., Grime, L.P., 1982. Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40 year follow-up. *Br. J. Ind. Med.* 39, 344–348.
- Acheson, E.D., Gardner, M.J., Winter, P.D., Bennett, C., 1984. Cancer in a factory using amosite asbestos. *Int. J. Epidemiol.* 13, 3–10.
- Agudo, A. et al., 2000. Occupation and risk of malignant pleural mesothelioma: a case-control study in Spain. *Amer. J. Ind. Med.* 37, 159–168.
- Andersson, M., Carstensen, B., Storm, H.H., 1995. Mortality and cancer incidence after cerebral arteriography with or without thorotrast. *Radiat. Res.* 142, 305–320.
- Armstrong, B.K., De Klerk, N.H., Musk, A.W., Hobbs, M.S.T., 1988. Mortality in miners and millers of crocidolite in Western Australia. *Br. J. Ind. Med.* 45, 5–13.
- Baris, I., Simonato, L., Artvinli, M., Pooley, F., Saracci, R., Skidmore, J., Wagner, C., 1987. Epidemiological and environmental evidence of the health effects of exposure to erionite fibres: a four year study in the Cappadocian Region of Turkey. *Int. J. Cancer* 39, 10–17.
- Berman, D.W., Crump, K.S., 2004. Final draft: Technical support document for a protocol to assess asbestos related risk. Prepared for the Office of Solid Waste and Emergency Response. US Environmental Protection Agency, Washington.
- Berry, G., Newhouse, M.L., 1983. Mortality of workers manufacturing friction materials using asbestos. *Br. J. Ind. Med.* 40, 1–7.
- Berry, G., 1999. Models for mesothelioma incidence following exposure to fibres in terms of timing and duration of exposure and the biopersistence of the fibres. *Inhal. Toxicol.* 11, 101–120.
- Berry, G., de Klerk, N.H., Reid, A., Ambrosini, G.L., Fritschi, L., Olsen, N.J., Merler, E., Musk, A.W., 2004. Malignant pleural and peritoneal mesotheliomas in former miners and millers of crocidolite at Witteboom, Western Australia. *Occup. Environ. Med.* 61, e14.
- Brown, D.P., Kaplan, S.D., Zumwalde, R.D., Kaplowitz, M., Archer, V.E., 1986. Retrospective cohort mortality study of underground gold mine workers. In: Goldsmith, D., Winn, D., Shy, C. (Eds.), *Silica, Silicosis, and Lung Cancer*. Praeger, New York, pp. 335–350.
- Browne, K., Gibbs, G.W., 1998. Chrysotile asbestos-thresholds of risk. In: Chiyotani, K., Hosoda, Y., Aizawa, Y. (Eds.), *Advances in the Prevention of Occupational Respiratory Diseases*. Elsevier Science BV, pp. 304–309.
- Brunner, W., Williams, A. N., Bender, A.P., 2007. Investigation of exposures to commercial asbestos in northeastern Minnesota iron miners who developed mesothelioma. *Toxicol. Pharmacol.*, in press.
- Camus, M., Siemiatycki, J., Meek, B., 1998. Non-occupational exposure to chrysotile asbestos and the risk of lung cancer. *N. Engl. J. Med.* 338, 1565–1571.
- Camus, M., Siemiatycki, J., Case, B.W., Desy, M., Richardson, L., Campbell, S., 2002. Risk of mesothelioma among women living near chrysotile mines versus US EPA asbestos risk model: preliminary findings. *Ann. Occup. Hyg.* 46 (Supplement 1), 95–98.
- Carbone, M., Fisher, S., Powers, A., Pass, H.I., Rizzo, P., 1999. New molecular and epidemiological issues in mesothelioma: role of SV40. *J. Cell. Physiol.* 180, 167–172.
- Comba, P., Gianfagno, A., Paoletti, L., 2003. Pleural mesothelioma cases in Biancavilla are related to a new fluoroedenite fibrous amphibole. *Arch. Environ. Health* 58, 229–232.
- Cooper, W.C., Wong, O., Trent, L.S., Harris, F., 1992. An updated study of taconite miners and millers exposed to silica and non-asbestiform amphiboles. *J. Occup. Med.* 34, 1173–1180.
- Cooper, W.C., Wong, O., Graebner, R., 1988. Mortality of workers in two Minnesota taconite mining and milling operations. *J. Occup. Med.* 30, 506–511.
- Davis, J.M.G., 1991. Information obtained from fibre-induced lesions in animals. In: Liddell, F.D.K., Miller, K. (Eds.), *Mineral Fibers and Health*. CRC, Boca Raton, pp. 250–263.
- Donna, A., Betta, P-G., Robutti, F., Bellingeri, D., 1991. A one year carcinogenicity study with 2,6-dichlorobenzonitrile (Dichlobenil) in male Swiss mice: preliminary note. *Cancer Detection and Prevention* 15, 41–44.
- Egilman, D., Fehnel, C., Bohme, S.R., 2003. Exposing the “myth” of ABC, “anything but chrysotile”: a critique of the Canadian asbestos mining industry and McGill University chrysotile studies. *Am. J. Ind. Med.* 44, 540–557.
- Gibbs, G.W., 2001. Health effects associated with mining and milling chrysotile asbestos in Quebec and the role of tremolite. In: *The Health Effects of Chrysotile Asbestos: Contribution of Science to Risk-Management Decisions*. Can. Mineral, (Spec. Publ. 5), pp. 165–175.
- Gibbs, G.W., LaChance, M., 1974. Dust exposure in the chrysotile mines and mills of Quebec. *Arch. Environ. Health* 24, 189–197.
- Gibbs, A.R., Jasani, B., Pepper, C., et al., 1998. SV40 DNA sequences in mesotheliomas. In: Brown, E., Lewis, A.M. (Eds.), *A Possible Human Polyomavirus*. Karger, Basel, Dev. Biol. Stand. 94, 41–45.
- Gilliam, J., Dement, J., Lemen, R., Wagoner, J., Archer, V., Blejer, H., 1976. Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. *Ann. N. Y. Acad. Sci.* 271, 344–366.
- Gold, B., Kathren, R.L., 1998. Causes of death in a cohort of 260 plutonium workers. *Health Phys.* 75, 236–240.
- Goodman, M., Teta, M.J., Hessel, P.A., et al., 2004. Mesothelioma and lung cancer among motor vehicle mechanics: A meta-analysis. *Ann. Occup. Hyg.* 48, 309–326.
- Gruber, U.F., 1999. Unpublished communication, Medicem Symposium, Vienna.
- HEI-AR, 1991. Asbestos in public and commercial buildings. Health Effects Institute, Cambridge MA.
- Hein, M.J., Stayner, L.T., Lehman, E., Dement, J.M., 2007. Follow-up study of chrysotile textile workers: cohort mortality and exposure-response. *Occup. Environ. Med.* 64, 616–625.
- Higgins, I.T., Glassman, J.H., Oh, M.S., Cornell, R.G., 1983. Mortality of reserve mining company employees in relation to taconite dust exposure. *Am. J. Epidemiol.* 118, 710–719.
- Hodgson, J.T., Darnton, A., 2000. The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure. *Ann. Occup. Hyg.* 44, 565–601.
- Hughes, J.M., 1989. The Derivation and use of Asbestos Risk estimates. In: *Proceedings—Symposium on Health Aspects of Exposure to Asbestos in Buildings*, Harvard University, Cambridge December 14–16 1988. pp 267–277.
- Hodgson, J.T., Peto, J., Jones, J.R., Matthews, F.E., 1997. Mesothelioma mortality in Britain: patterns by birth cohort and occupation. *Ann. Occup. Hyg.* 41, 129–133.

- Hoffman, J., Mintzer, D., Warhol, M.J., 1994. Malignant mesothelioma following radiation therapy. *Am. J. Med.* 97, 379–382.
- Jarvholm, B., Brisman, J., 1988. Asbestos associated tumours in car mechanics. *Br. J. Ind. Med.* 45, 645–646.
- Jarvholm, B., Sanden, A., 1998. Lung cancer and mesothelioma in the pleura and peritoneum among Swedish insulation workers. *Occup. Environ. Med.* 55, 766–770.
- Kurakawa, Y., Hayashi, Y., Maekawa, A., Takahashi, M., Kokubo, T., Odashima, S., 1983. Carcinogenicity of potassium bromate administered orally to F344 rats. *J. Natl. Cancer Inst.* 79, 965–971.
- Karjalainen, A., Meurman, L.O., Pukkala, E., 1994. Four cases of mesothelioma among Finnish anthophyllite miners. *Occup. Environ. Med.* 51, 212–215.
- Laden, F., Stampfer, M.J., Walker, A.M., 2004. Lung cancer and mesothelioma among male automobile mechanics: a review. *Rev. Environ. Health* 19, 39–61.
- Leigh, J., Driscoll, T., 2003. Malignant mesothelioma in Australia, 1945–2002. *Int. J. Occup. Environ. Health* 9, 206–217.
- Levin, J.L., McLarty, J.W., Hurst, G.A., et al., 1998. Tyler asbestos workers: mortality experience in a cohort exposed to amosite. *Occup. Environ. Med.* 55, 155–160.
- Malker, H.S., McLaughlin, J.K., Malker, B.K., Stone, B.J., Winer, J.A., Erickson, J.L., Blot, W.J., 1985. Occupational risks for pleural mesothelioma in Sweden. *J. Natl. Cancer Inst.* 74, 561–566.
- Manfredi, J.J., Dong, J., Liu, W.-j., et al., 2005. Evidence a role for SV40 in human mesothelioma. *Cancer Res.* 65, 2602–2609.
- McDonald, A.D., McDonald, J.C., 1978. Mesothelioma after crocidolite exposure during gas mask manufacture. *Environ. Res.* 17, 340–346.
- McDonald, J.C., Gibbs, G.W., Liddell, F.D.K., McDonald, A.D., 1978. Mortality after long exposure to cummingtonite–grunerite. *Am. Rev. Resp. Dis.* 118, 271–277.
- McDonald, J.C., McDonald, A.D., 1995. Chrysotile, tremolite and mesothelioma. *Science* 267, 775–776.
- McDonald, A.D., McDonald, J.C., 1980. Malignant mesothelioma in North America. *Cancer* 46, 1650–1656.
- McDonald, A.D., Fry, J.S., Woolley, A.J., McDonald, J.C., 1984. Dust exposure and mortality in an American chrysotile asbestos friction products plant. *Br. J. Ind. Med.* 41, 151–157.
- McDonald, A.D., Case, B.W., Churg, A., Dufresne, A., Gibbs, G.W., Sebastien, P., McDonald, J.C., 1997. Mesothelioma in Quebec chrysotile miners and millers: epidemiology and aetiology. *Ann. Occup. Hyg.* 41, 707–709.
- McDonald, J.C., Harris, J., Armstrong, B., 2002. Cohort mortality study of vermiculite miners exposed to fibrous talc: an update. *Ann. Occup. Hyg.* 46 (Supplement 1), 93–94.
- McDonald, J.C., Harris, J., Armstrong, B., 2004. Mortality in a cohort of vermiculite miners exposed to fibrous amphibole in Libby, Montana. *Occup. Environ. Med.* 61, 363–366.
- McElvenny, D.M., Darnton, A.J., Price, M.J., Hodgson, J.T., 2005. Mesothelioma mortality in Great Britain from 1968 to 2001. *Occup. Med. (Lond.)* 55, 79–87 (supplement data).
- Meurman, L.O., Pukkala, E., Hakama, M., 1994. Incidence of cancer among anthophyllite asbestos miners in Finland. *Occup. Environ. Med.* 51, 421–425.
- Newhouse, M.L., Berry, G., Wagner, J.C., 1985. Mortality of factory workers in east London 1933–80. *Br. J. Ind. Med.* 42, 4–11.
- Newhouse, M.L., Sullivan, K.R., 1989. A mortality study of workers manufacturing friction materials; 1941–86. *Br. J. Ind. Med.* 46, 176–179.
- Oels, H.C., Harrison, E.G., Carr, D.T., Bernatz, P.E., 1971. Diffuse malignant mesothelioma of the pleura: a review of 37 cases. *Chest* 60, 564–570.
- Peterson, J.T., Greenberg, S.D., Buffler, P.A., 1984. An asbestos-related mesothelioma. A review. *Cancer* 54, 951–960.
- Piolatto, G., Negri, E., La Vecchia, C., et al., 1990. An update of cancer mortality among chrysotile asbestos miners in Balangero, Northern Italy. *Br. J. Ind. Med.* 47, 810–814.
- Pott, F., Roller, M., 1996. Carcinogenicity of synthetic fibres in experimental animals: its significance for workers. *J. Occup. Health Safety—Aust. N. Z.* 12, 333–339.
- Rossiter, C.E., Coles, R.M., 1980. HM Dockyard, Devonport, 1947 mortality study. In: Wagner, J.C., (Ed.), *IARC Biological effects of Mineral Fibres*, vol. 30, pp. 713–721.
- Rowlands, N., Gibbs, G.W., McDonald, A.D., 1982. Asbestos fibres in the lungs of chrysotile miners and millers—a preliminary report. *Ann. Occup. Hyg.* 26, 411–415.
- Sanders, C.L., 1992. Pleural mesothelioma in the rat following exposure to ²³⁹PuO₂. *Health Phys.* 63, 695–697.
- Seidman, H., Selikoff, I.J., Hammond, E.C., 1979. Short-term asbestos work exposure and long term observation. *Ann. N. Y. Acad. Sci.* 330, 61–89.
- Seidman, H., Selikoff, I.J., Gelb, S.K., 1986. 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.* 10, 479–514.
- Selikoff, I.J., Hammond, C.E., Seidman, H., 1979a. Mortality experience of Insulation workers in the United States and Canada, 1943–1976. *Ann. N. Y. Acad. Sci.* 330, 91–116.
- Selikoff, I.J., Lilis, R., Nicholson, W.J., 1979b. Asbestos disease in United States shipyards. *Ann. N. Y. Acad. Sci.* 330, 295–311.
- Selikoff, I.J., Seidman, H., 1991. Asbestos-associated deaths among insulation workers in the United States and Canada, 1967–1987. *Ann. N. Y. Acad. Sci.* 643, 1–14.
- Sluis-Cremer, G.K., Liddell, F.D.K., Logan, W.P.D., Bezuidenhout, B.N., 1992. The mortality of amphibole miners in South Africa 1946–1980. *Br. J. Ind. Med.* 49, 566–575.
- Spirtas, R., Heineman, E.F., Bernstein, L., Beebe, G.W., Keehn, R.J., Stark, A., Harlow, B.L., Benichou, J., 1994. Malignant mesothelioma: attributable risk of asbestos exposure. *O.E.M.* 51, 804–811.
- Stanton, M.F., 1973. Some etiological considerations of fiber carcinogenesis. In: Bogovski, P., Gilson, J.C., Timbrell, V., Wagner, J.C. (Eds.), *Biological Effects of Asbestos*, vol. 8. IARC Scientific Publications, Lyon, pp. 289–294.
- Stanton, M.F., Wrench, C., 1972. Mechanisms of mesothelioma induction with asbestos and fibrous glass. *J. Natl. Cancer Inst.* 48, 797–821.
- Stanton, M.F., Layard, M., 1978. The carcinogenicity of fibrous minerals. In: Gravatt, C.C., Lafleur, P.D., Heinrich, K.F.J. (Eds.), *Workshop on Asbestos, Definition and Measurement Methods (NBS Special Publication 506)*. National Measurements Laboratory, Washington DC, pp. 143–151.
- Stanton, M.F., Layard, M., Tegar, A., Miller, E., May, M., Kent, E., 1977. Carcinogenicity of fibrous glass: pleural response in the rat in relation to fiber dimension. *J. Natl. Cancer Inst.* 58, 587–597.
- Steenland, K., Brown, D., 1995. Mortality study of gold miners exposed to silica and non-asbestiform amphibole minerals: an update with 14 more years of follow-up. *Am. J. Ind. Med.* 27, 217–229.
- Talcott, J., Thurber, W., Kantor, A., et al., 1989. Excess lung cancers and mesotheliomas in a cohort of manufacturers of asbestos-containing cigarette filters. *N. Engl. J. Med.* 321, 1220–1223.
- Teschke, K., Morgan, M.S., Checkoway, H., Franklin, G., Spinelli, J.J., van Belle, G., Weiss, N.S., 1997. Mesothelioma surveillance to locate sources of exposure to asbestos. *Can. J. Public Health* 88, 163–168.
- Teta, M.J., Lewinsohn, H.C., Meigs, J.W., Vidone, A., Mowad, L.Z., Flannery, J.T., 1983. Mesothelioma in Connecticut. *J.O.M.* 15, 749–756.
- Thomas, H.F., Benjamin, I.T., Elwood, P.C., Sweetnam, P.M., 1982. Further follow up study of workers from an asbestos cement factory. *Br. J. Ind. Med.* 39, 273–276.
- Wagner, J.C., Sleggs, C.A., Marchand, P., 1960. Diffuse pleural mesothelioma and asbestos exposure in the northwestern Cape Province. *Br. J. Ind. Med.* 17, 260–271.
- Wagner, J.C., Skidmore, J.W., Hill, R.J., Griffiths, D.M., 1985. Erionite exposure and mesothelioma in rats. *Br. J. Cancer* 51, 727–730.
- Weiss, W., 1977. Mortality of a cohort exposed to chrysotile asbestos. *J.O.M.* 19, 737–740.

- Woitowitz, H.-J., Rodelsperger, K., 1994. Mesothelioma among car mechanics? *Ann. Occup. Hyg.* 38, 635–638.
- Wong, O., 2001. Malignant mesothelioma and asbestos exposure among auto mechanics: appraisal of scientific evidence. *Regul. Toxicol. Pharmacol.* 34, 170–177.
- Wong, O., 2006. The interpretation of occupational epidemiologic data in regulation and litigation: Studies of auto mechanics and petroleum workers. *Regul. Toxicol. Pharmacol.* 44, 191–197.
- Yarborough, C.M., 2006. Chrysotile as a cause of mesothelioma: An assessment based on epidemiology. *Crit. Rev. Toxicol.* 36, 165–187.