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**Supplement: International Symposium on the Health Hazard
Evaluation of Fibrous Particles Associated with Taconite and
the Adjacent Duluth Complex**

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Regulatory Toxicology and Pharmacology

*Official Journal of the International Society of
Regulatory Toxicology and Pharmacology*

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International Symposium on the Health Hazard Evaluation of Fibrous Particles Associated with Taconite and the Adjacent Duluth Complex

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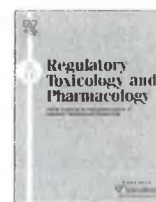
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W. Clark Cooper, MD, and Irving J. Selikoff, MD,
in recognition of their enormous contributions
to occupational and environmental medicine



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Introduction

International symposium on the health hazard evaluation of fibrous particles associated with taconite and the adjacent duluth complex

This international symposium was convened to assess the current state of knowledge concerning the health hazards that might be associated with the ingestion and inhalation of fibrous particles produced from the processing of taconite ore.

Concern about fibrous particles in taconite arose from their similarities to amphibole asbestos minerals that are known to be human carcinogens. The mineralogical characteristics of asbestos fibers are reviewed and compared with the fibrous particles known to be present in taconite ore from the eastern end of the Iron Range. The epidemiological and experimental animal studies for asbestos-related disease (including gastrointestinal cancer from asbestos in drinking water) were critically evaluated and compared to those of the fibrous minerals in the taconite. The focus was on the amphiboles in the cummingtonite–grunerite and tremolite–ferroactinolite series and other fibrous particles in both the Iron Range and the Duluth Complex. This included examination of the reported occurrence of any asbestiform ferroactinolite, crocidolite asbestos, chrysotile asbestos, etc. In addition, an effort was made to provide a scientific framework to address fibrous minerals, which may be associated with nonferrous mineral deposits in the Duluth Complex.

State-of-the-art risk assessment models for asbestos were presented. Risk assessment scenarios were developed for taconite-derived fibers at environmental exposure levels related to the operation of the Silver Bay taconite processing facility. These calculated risks were found to be trivial even after it was assumed that all mineral fibers were as carcinogenic as amphibole asbestos.

Questions addressed by the scientific program of the Symposium

1. Concern about the fibrous particles in the taconite originated from what observations? Are they still valid? What do we actually know about the health hazards of the fibrous particles, including the cleavage fragments that result from the processing of taconite ore?
2. What are the physicochemical properties of the fibrous particles in taconite ore, including crocidolite asbestos and asbestiform ferroactinolite, which indicate a potential for health hazards?
3. How do typical concentrations of airborne and waterborne fibrous particles, determined by state-of-the-art analytical transmission electron microscopy methods, found in the area surrounding the taconite processing plant in Silver Bay compare with background levels reported for asbestos around the world? What do we know about the importance of fiber length? Is there any new evidence regarding the length of fibers and toxicity?

What are the data required for determining if taconite waste rock and coarse tailings from the eastern end of the Iron Range can be used off-site? What considerations about fibrous minerals, if any, should be taken into account in the development of nonferrous mineral deposits in the Duluth Complex rock?

4. What do the experimental animal studies reveal about the differences between the inhalation/injection/ingestion of asbestos and other fibrous mineral particles?
5. Do studies in human populations tell us anything about the potential health hazards that might occur from exposure to fibers similar to those found in taconite?
6. What are the views held by the various federal regulatory agencies (OSHA/EPA/MSHA/CPSC) regarding the distinction between asbestos and the fibrous particles associated with taconite? What is the importance of asbestos fiber type (mineral species), morphology, biopersistence, and surface properties?
7. Using the available risk assessment models for asbestos exposure, what are the lung cancer and mesothelioma risks associated with the environmental taconite exposures? What can be said about noncancer risk of asbestos-related disease?
8. What is the scientific evidence that bears on the question that amphibole-bearing taconite from the eastern most end of the Biwabik Iron Formation if used as aggregate, would pose a public health concern different from that of other widely used aggregate sources? How would one go about doing a risk assessment for the use of taconite waste rock as aggregate? Is there sufficient information available to perform a risk assessment for the use of this taconite waste rock as aggregate?
9. What science, if any, has been developed since 1976 that might have influenced the outcome in the Reserve Mining case? Is it consistent with the scientific information available earlier or does it suggest that some changes should be made?

Two of the papers in Session 5, "An evaluation of the risk of lung cancer and mesothelioma from exposure to amphibole cleavage fragments" and "Assessment of the pathogenic potential of asbestiform vs. nonasbestiform particulates (cleavage fragments) in in vitro (cell or organ culture) models and bioassays," were not presented at the Symposium. These papers were added after the Symposium to further address the above questions.

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Geology of the Biwabik Iron Formation and Duluth Complex

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Abstract

The Biwabik Iron Formation is a ~1.9 billion year-old sequence of iron-rich sedimentary rocks that was metamorphosed at its eastern-most extent by ~1.1 billion year-old intrusions of the Duluth Complex. The metamorphic recrystallization of iron-formation locally produced iron-rich amphiboles and other fibrous iron-silicate minerals. The presence of these minerals in iron-formation along the eastern part of what is known as the Mesabi Iron Range, and their potential liberation by iron mining has raised environmental health concerns. We describe here the geologic setting and mineralogic composition of the Biwabik Iron Formation in and adjacent to the contact metamorphic aureole of the Duluth Complex. The effects of metamorphism are most pronounced within a few kilometers of the contact, and decrease progressively away from it. The contact aureole has been divided into four metamorphic zones—each characterized by the composition and crystal structure of the metamorphic minerals it contains. The recrystallization of iron-formation to iron-rich amphibole minerals (grunerite and cummingtonite) and iron-pyroxene minerals (hedenbergite and ferrohypersthene) is best developed in zones that are most proximal to the Duluth Complex contact.

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Keywords: Iron-formation; Mining; Fibrous; Mineralogy; Metamorphism

1. Introduction

The Biwabik Iron Formation is a layered sequence of iron-rich sedimentary rocks that was metamorphosed by intrusions of the Duluth Complex. The metamorphic recrystallization of iron-formation locally produced iron-rich amphiboles and other fibrous iron-silicate minerals. The presence of these minerals in iron-formation along the eastern Mesabi Iron Range and their potential liberation by iron mining has raised environmental health concerns. As a background to discussion of those concerns, we describe here the geologic setting of the Biwabik Iron Formation and the Duluth Complex, the stratigraphy of the iron-formation, the nature of the contact between the Biwabik Iron Formation and the Duluth Complex, and the general mineralogic and textural changes within iron-

formation related to its progressive metamorphism by the Duluth Complex.

2. Geologic setting

Taconite mines of the Mesabi Iron Range are developed in the Biwabik Iron Formation, which is the type example of Lake Superior-type banded iron-formation. Banded iron-formations are a type of chemical sedimentary rock composed of alternating granular (“cherty”) and laminated (“slaty”) layers that were deposited in nearshore marine environments. All global occurrences of Lake Superior-type iron-formations were formed during the Paleoproterozoic era—a unique time in earth history approximately 2.4–1.6 billion years ago when photosynthesizing organisms are believed to have evolved and caused widespread oxygenation of the world’s oceans and atmosphere. Along the 200-km extent of the Mesabi Iron Range, the Biwabik Iron Formation occurs as a thick (100–250 m), laterally extensive sheet

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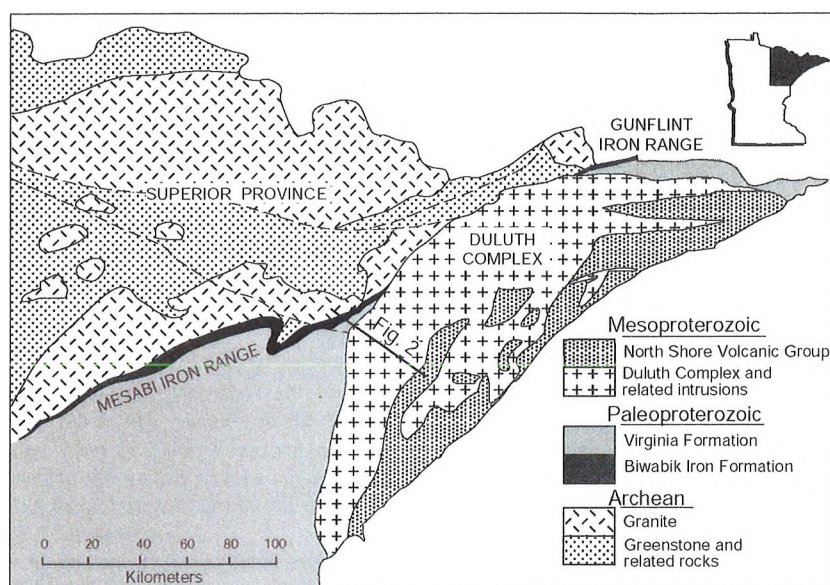


Fig. 1. Simplified bedrock geologic map of the Mesabi Iron Range and adjacent Duluth Complex. The location of the cross-section depicted on Fig. 2 is labeled.

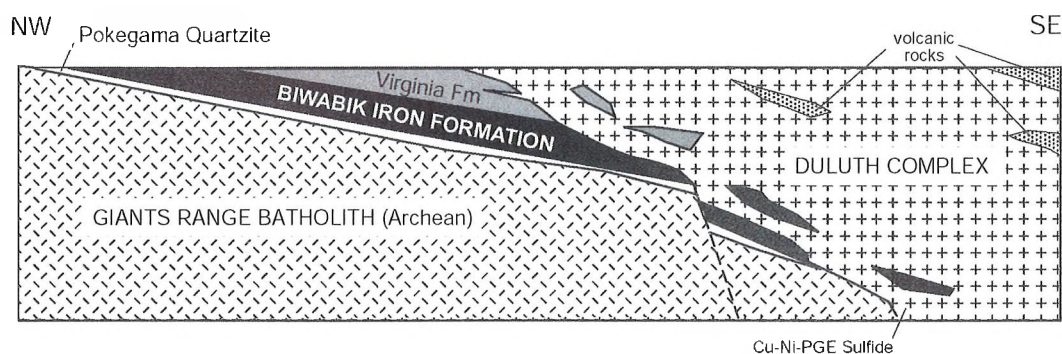


Fig. 2. Schematic geologic section showing the basal contact of the Duluth Complex against older host rocks including the Biwabik Iron Formation, and capped by volcanic rocks of the North Shore Volcanic Group.

that is slightly tilted to the south–southeast (Fig. 1). It conformably overlies the Pokegama Quartzite, a sandstone, siltstone, and conglomerate unit of variable thickness (0–100 meters), and is overlain by the Virginia Formation, a thick, but poorly exposed sequence of shale and graywacke. Collectively, this stratigraphic sequence (Pokegama Quartzite–Biwabik Iron Formation–Virginia Formation) is called the Animikie Group. A U–Pb zircon date from a tuffaceous unit in the nearby Gunflint Iron Formation yielded an age of $1,878.3 \pm 1.3$ million years (Fralick et al., 2002). The Gunflint and Biwabik Iron Formations were continuous prior to emplacement of the Duluth Complex, and thus the date is an approximate age for deposition of the Biwabik Iron Formation and associated Animikie strata. The Animikie Group rests unconformably on granite, greenstone, and other rocks of the Archean (greater than 2.4 billion years old) Superior Province, which constitutes the bedrock in most of northern Minnesota.

At the northeast terminus of the Mesabi Iron Range near Babbitt, the Biwabik Iron Formation and other units

of the Animikie Group are abruptly truncated by gabbroic rocks of the Duluth Complex (Fig. 1). The coarse-grained igneous rocks of the Duluth Complex formed by the slow cooling and crystallization of mafic (dark colored) magmas that were intruded into subvolcanic chambers during a phase of continental rifting and voluminous igneous activity centered on present-day Lake Superior during the Mesoproterozoic era, about 1.1 billion years ago. The magma formed chambers several kilometers in thickness that were emplaced between a floor (or footwall) of Paleoproterozoic and Archean rocks, and a several-kilometers-thick cap of lavas (Fig. 2). Regional tilting to the east and erosion has removed the overlying volcanic rocks and exposed the arcuate lower contact of the intrusions against older footwall rocks.

3. Stratigraphy of the Biwabik Iron Formation

The Biwabik Iron Formation can be classified by texture into two generalized types of iron-formation: cherty mate-

Table 1
Minerals in the Biwabik Iron Formation

<i>Iron oxide minerals</i>	
Hematite	Fe ₂ O ₃
Magnetite	Fe ₃ O ₄
<i>Carbonate minerals</i>	
Ankerite	Ca(Mg, Fe)(CO ₃) ₂
Siderite	FeCO ₃
Dolomite	CaMg(CO ₃) ₂
Kutnohorite-ferroan	Ca(Mn, Mg, Fe)(CO ₃) ₂
Kutnohorite	
Calcite	CaCO ₃
<i>Silicate and iron silicate minerals</i>	
Quartz	SiO ₂
<i>Chlorite group</i>	
Chamosite	(Fe ²⁺ , Al, Mg) ₆ (Si, Al) ₄ O ₁₀ (OH) ₈
Minnesotaite	Mg ₃ (Si ₂ O ₅) ₂ (OH) ₂
Talc	Mg ₃ Si ₄ O ₁₀ (OH) ₁₂
<i>Brittle mica group</i>	
Stilpnomelane	K(Fe ²⁺ , Fe ³⁺ , Al) ₁₀ Si ₁₂ O ₃₀ (O, OH) ₁₂
<i>Mica group</i>	
Biotite	K ₂ (Fe ²⁺ , Mg) ₆₋₄ (Fe ³⁺ , Al, Ti) ₀₋₂ (Si ₆₋₅ , Al ₂₋₃)O ₂₀₋₂₂ (OH, F) ₄₋₂
Muscovite	K ₂ Al ₄ (Si ₆ Al ₂)O ₂₀ (OH) ₄
<i>Serpentine group</i>	
Greenalite	(Fe ²⁺ , Fe ³⁺ , Mg) ₆ Si ₄ O ₁₀ (OH) ₈
<i>Amphibole group</i>	
Grunerite	(Fe ²⁺ , Mg, Mn) ₇ Si ₈ O ₂₂ (OH)
Commingtonite	(Mg, Fe ²⁺) ₇ Si ₈ O ₂₂ (OH) ₂
Hornblende	Ca ₂ Na(Mg, Fe ²⁺ , Fe ³⁺ , Al) ₅ (Si ₆₋₇ , Al ₂₋₁)O ₂₂ (OH, F) ₂
Actinolite	Ca ₂ (Mg, Fe ²⁺) ₅ [Si ₈ O ₂₂](OH) ₂
<i>Pyroxene group</i>	
Hedenbergite	Ca(Mg, Fe)[Si ₂ O ₆]
Enstatite-ferrosilite series	(Mg, Fe ²⁺)[SiO ₃]
Diopside	CaMgSi ₂ O ₆ to Ca(Mg, Fe ²⁺)Si ₂ O ₆
<i>Cordierite group</i>	
Cordierite	(MgFe ²⁺) ₂ Al ₄ Si ₅ O ₁₈
<i>Olivine group</i>	
Fayalite	(Fe, Mg) ₂ SiO ₄ to Fe ₂ SiO ₄
<i>Garnet group (reported in McSwiggen and Morey, this volume)</i>	
Almandine	Fe ₃ Al ₂ Si ₃ O ₁₂
Andradite	Ca ₃ Fe ₂ Si ₃ O ₁₂

rials, which are granular, massive, and typically but not always rich in quartz and iron oxides; and slaty materials, which are generally finely laminated, fine-grained, and composed mostly of iron silicates and iron carbonates (Table 1). Beds or groups of beds having granular or laminated attributes are interlayered on all scales. Despite this heterogeneity, the formation was divided by Wolff (1917) into four entities based on the ratio of "cherty" to "slaty" material present. These informal lithostratigraphic members are, from bottom to top: Lower Cherty, Lower Slaty, Upper Cherty, and Upper Slaty (Fig. 3). Within this classification scheme, slaty members typically contain about 40 percent laminated strata; whereas, the cherty members con-

tain 10 to 30 percent laminated material. Cherty members contain, on average, slightly more silica than the slaty members. Magnetite is the dominant iron mineral in cherty strata (magnetite is 31 percent FeO and 69 percent Fe₂O₃ by weight). Slaty members contain significant Al₂O₃, reflecting the presence of stilpnomelane—the only aluminum-bearing phase.

This stratigraphic scheme (Wolff, 1917) was designed to aid in understanding how various kinds of hematite-rich ores are distributed in the iron-formation. Except for the Intermediate Slate—a tuffaceous unit at the Lower Cherty–Lower Slaty boundary—the contacts between members are gradational and somewhat arbitrary. Therefore, the cherty–slaty nomenclature in itself was not a particularly useful mapping tool. Consequently, Grout and Broderick (1919) developed a modified scheme that created six stratigraphic units that could be easily recognized and mapped throughout the eastern Mesabi district, even where the rocks were appreciably metamorphosed (Fig. 4). The scheme was designed to estimate various resources and support the development of taconite mining at Babbitt in the early 1920 s, and therefore emphasized the distribution of magnetite. Some 40 years later, Gundersen (1960) and Gundersen and Schwartz (1962) re-evaluated the stratigraphic setting in the eastern Mesabi district to further refine estimates of recoverable magnetite. They subdivided the iron-formation into 22 entities (units A–V on Fig. 4), primarily on the basis of magnetite content and metamorphic mineralogy, and to a lesser extent on bedding characteristics. Their classification scheme emphasized small bed-to-bed differences, and consequently is best utilized to evaluate stratigraphy in drill cores. Although most of the 22 entities can be recognized in exposed bedrock, most are too thin to be mapped at a scale of 1:24,000. Therefore, other cartographic schemes, such as those of Griffin and Morey (1969) and Bonnicksen (1975), were developed utilizing bedding attributes as well as texture and mineralogy (Fig. 4).

The demonstrated utility of several stratigraphic classification schemes highlights the considerable heterogeneity that exists in the iron-formation, particularly in the eastern Mesabi district. That heterogeneity is further complicated by metamorphic processes associated with the emplacement of the Duluth Complex, which produced mineralogical changes within an aureole several miles wide.

Mining on the Mesabi Iron Range has been continuous since 1892. The first deposits that were mined—the so-called "natural ores"—consisted of material altered (oxidized and leached) by aqueous solutions along major and minor structures within the iron-formation, such as faults, fractures, folds, and select bedding-planes. More than 500 natural ore mines existed. After about 1955, production shifted to the use of taconite ores, composed of relatively unaltered magnetite-rich iron-formation. Most taconite ores have been and continue to be extracted from the Lower Cherty member of the Biwabik Iron Formation, with lesser amounts from the Upper Cherty and Slaty

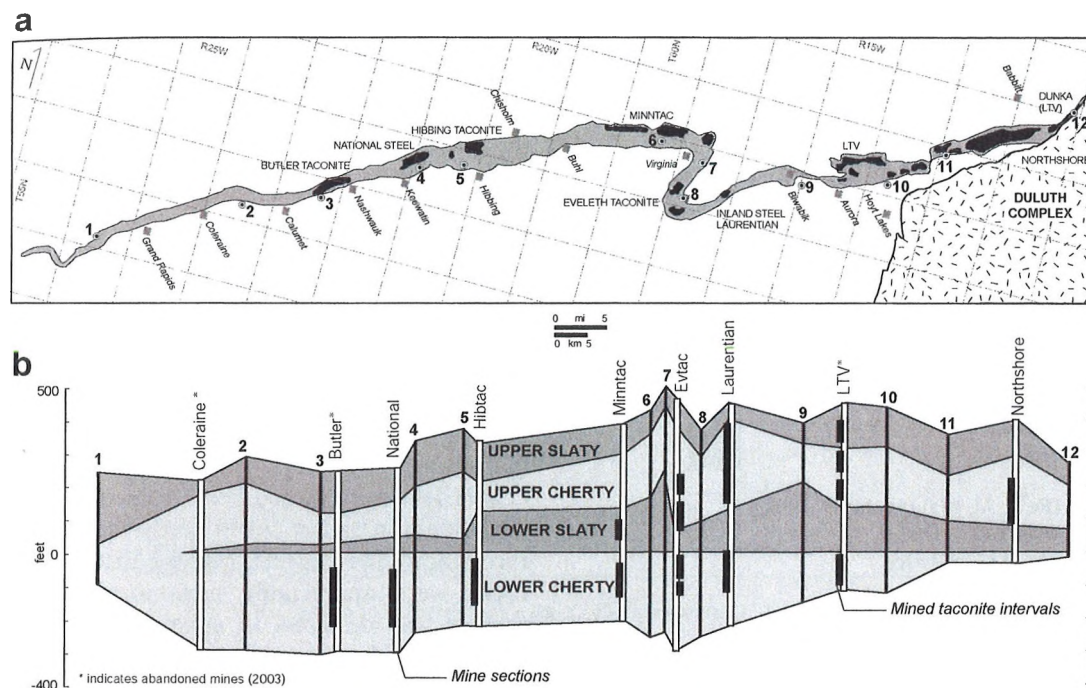


Fig. 3. Simplified geologic map (a) showing locations of taconite mines, drill holes, and contact metamorphic zones from French (1968); and stratigraphic section (b) showing subdivision of the Biwabik Iron Formation and approximate mined taconite intervals at each locality. Stratigraphic units are measured from a horizontal line approximating the position of the Intermediate Slate at the Lower Cherty–Lower Slaty boundary. Modified from a compilation of drill holes by H. Djerlev–Hibbing Taconite (Meineke, 1993); and from mine sections compiled by M. Severson (Zanko et al., 2003).

	CLASSIFICATION SCHEMES						MINERALOGIC CONTENT				
	Wolf 1917	Grout and Broderick 1919	Gundersen and Schwartz 1962	Bornichsen 1975	Griffin and Moe 1969	Approximate Thickness (ft)	Quartz	Magnetite	Iron Silicates	Hematite	Calc-silicates
VIRGINIA FORMATION Shale to slate, siltstone, and graywacke											
ARGILLITE, lesser limestone			A			5					
LIMESTONE, lesser argillite			B			16					
IRON-FORMATION--thin-bedded, laminated, interbedded cherty strata more abundant downward. Septaria structures. Base drag-folded and brecciated	Upper Slaty	Aub ₆	C	US	bus	42					
			D			20-7					
			E			6					
			F			24-15					
						25					
IRON-FORMATION--cherty, conglomeratic, thick magnetite layers Jasper, algal structures	Upper Cherty	Aub ₄	G	UCu	buc ₃	30-12					
			H			3-5					
			I			17-22					
			J			40-30					
			K			45-15					
IRON-FORMATION--cherty, conglomeratic, thick magnetite layers	Upper Cherty	Aub ₄	L	UCm	buc ₂	15-25					
			M			5					
			N			5-26					
			O								
IRON-FORMATION--granular, conglomeratic, thin lenticular layers of magnetite	Upper Cherty	Aub ₄		UCI	buc ₁						
IRON-FORMATION--thin-bedded, obscure granules, minor magnetite	Lower Slaty	Aub ₃	P	LS	bls ₂	58-95					
			Q			26					
			R			12					
			S			22-8					
			T			5-20					
IRON-FORMATION--thin-bedded, minor magnetite	Lower Cherty	Aub ₁	U	LC	blc	4-60					
			V			3-30					
IRON-FORMATION--thick-bedded, magnetite	Lower Cherty	Aub ₁									
IRON-FORMATION--thick-bedded, granular	Lower Cherty	Aub ₁									
IRON-FORMATION--algal structures	Lower Cherty	Aub ₁									
IRON-FORMATION--conglomeratic, quartz pebbles, hematitic	Lower Cherty	Aub ₁									
POKEGAMA QUARTZITE											
ARCHAIC											

Fig. 4. Schematic representation of various stratigraphic classifications of the Biwabik Iron Formation and corresponding relative mineralogic abundance.

members (mined taconite intervals on Fig. 3b). Six taconite mines are currently operating.

4. Contact between the Biwabik Iron Formation and the Duluth Complex

The nature of the intrusive contact between the gabbroic rocks of the Duluth Complex and the Biwabik Iron Formation is fairly well known from exposures in the Dunka Pit and from hundreds of drill holes that penetrated the footwall of the Duluth Complex. The corresponding drill cores have been acquired over the past 50 years in support of exploration for copper–nickel–platinum group element (Cu–Ni–PGE) sulfide deposits in the basal part of the complex. Most of this core, which is stored at the Minnesota Department of Natural Resources core repository in Hibbing, has been relogged and analyzed by geologists at the University of Minnesota's Natural Resources Research Institute. These subsurface data indicate that the contact between the gabbroic rocks of the Duluth Complex and the Animikie Group sedimentary rocks has a southeasterly dip that is steeper than the dip of bedding in the sedimentary rocks. Thus, the gabbro has cut progressively downward across the Virginia Formation, Biwabik Iron Formation, and Pokegama Quartzite, and ultimately down to Archean rocks (predominantly granite). This sequential crosscutting is also evident at the surface along the northwestern basal contact of the gabbro (Fig. 1). In areas of closely spaced drilling, it is clear that downcutting occurred in a stair-step fashion, with some of the major declines corresponding to faults in the footwall rocks (Fig. 2).

On a more detailed scale, the nature of the contact is locally complex. As observed in some surface exposures and areas of detailed drilling, strongly recrystallized and intensely deformed sedimentary rocks are complexly interdigitated with the gabbro. Some partial melting of the sedimentary rocks is also common. The complexities of the contact likely resulted from the intense heating of the sedimentary rocks, which not only resulted in their recrystallization, but also caused the rocks to become ductile, and thus easily deformed with minor magmatic and tectonic stresses. In the basal zone of the gabbro, inclusions of sedimentary rocks are abundant and commonly so strongly recrystallized and partially melted that they are difficult to distinguish from the host gabbro. Remnants of Biwabik Iron Formation inclusions are recognized locally only by the abundance of iron oxide in the gabbro. The assimilation of sulfide-bearing sedimentary rocks is thought to be the main process responsible for the Cu–Ni–PGE mineralization locally within the basal gabbro.

5. Progressive metamorphism of the Biwabik Iron Formation

Conductive cooling of the gabbroic magma resulted in thermal metamorphism of the Biwabik Iron Formation and associated rocks underlying the Duluth Complex. The effects of this metamorphism are most pronounced

within a few kilometers of the contact zone, and progressively decrease southwestward away from the contact. Four generalized metamorphic zones can be delineated west of the Duluth Complex (French, 1968). These are shown on Fig. 3 and summarized below.

- Zone 1 “Unaltered” taconite extends westward from the first appearance of metamorphic minerals and textures. It is generally considered protolith to more metamorphosed rocks to the east. The unaltered rocks contain quartz, magnetite, hematite, siderite, ankerite, talc, and iron-silicates (chamosite, greenalite, minnesotaite, stilpnomelane, and talc). The minerals quartz, hematite, siderite, chamosite, greenalite, and some magnetite are considered primary minerals. Textures of the others—talc, minnesotaite, stilpnomelane, and most magnetite—indicate crystallization from secondary diagenetic processes or early metamorphism unrelated to emplacement of the Duluth Complex.
- Zone 2 Transitional taconite contains mineral assemblages that are similar to unaltered taconite, but differs by the extensive replacement of quartz and ankerite and the reduction of hematite to magnetite in the iron-formation, and the appearance of clinozoisite in the subjacent Pokegama Quartzite.
- Zone 3 Moderately metamorphosed taconite is characterized by the development of the iron-rich amphiboles grunerite and cummingtonite, at the expense of original iron carbonates and silicates, and the associated production of calcite.
- Zone 4 Highly metamorphosed taconite is completely recrystallized to a metamorphic fabric composed mainly of quartz, iron amphiboles (grunerite-cummingtonite, hornblende), iron pyroxenes (hedenbergite, ferrohypersthene), magnetite, and rare fayalite and calcite.

Despite the heterogeneity of the iron-formation, some of the stratigraphic framework established from exposures and drilling in the relatively unaltered rocks of Zone 1 can be correlated with more metamorphosed equivalent strata in zones closer to the Duluth Complex. Remarkably, even in the highest metamorphic grade, the iron-formation locally retains relics of original sedimentary textures. Small intrusive dikes and veins in the contact zone may represent introduction of magma and some volatiles from the adjacent Duluth Complex (Gundersen and Schwartz, 1962); however, studies by French (1968), Morey et al. (1972), and Bonnichsen (1975) indicate that metamorphism was isochemical, involving the loss of H₂O and CO₂, but no significant introduction of components from the adjacent gabbro. The loss of volatiles during late stages of metamorphism produced minor and localized, hydrous, retrograde minerals including cummingtonite.

It is generally assumed that the magma associated with the Duluth Complex was approximately 1200 °C at the

time of emplacement. However, the temperatures attained by the Animikie Group during that event in the various metamorphic zones are difficult to estimate. Diopside occurs in some of the carbonate-rich rocks at the top of the iron-formation just east of Mesaba (Griffin and Morey, 1969), and Gundersen and Schwartz (1962) reported wollastonite near Babbitt, about 4 miles to the east. Experimental work reported in French (1968) indicated that these phases formed at 500–600 °C for diopside, and 600–700 °C for wollastonite, in the pressure range of 1000–3000 bars (P_{H_2O}). Non-calcareous rocks in the Virginia Formation containing cordierite, biotite, muscovite, and quartz also indicate a temperature in the range of 500–700 °C at about 1000 bars (P_{H_2O} ; Labotka et al., 1981). Temperatures in this order of magnitude are further indicated by the work of Perry and Bonnichsen (1966, p. 525), who suggested on the basis of oxygen-isotope fractionation in magnetite-quartz pairs that the maximum temperature attained by the iron-formation at the east end of the district near Dunka River was about 700–750 °C. Mineralogic zoning described by French (1968) indicated that metamorphic temperatures progressively decreased to the west in a general direction away from the present location of the contact with the Duluth Complex. He concluded that grunerite formed at temperatures below 400 °C, probably in the range of 300–400 °C (French, 1968, p. 87).

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- Bonnichsen, B., 1975. Geology of the Biwabik Iron Formation, Dunka River area. *Minnesota: Economic Geology* 70 (2), 319–340.
- Fralick, P., Davis, D.W., Kissin, S.A., 2002. The age of the Gunflint Formation, Ontario, Canada. Single zircon U-Pb age determinations from reworked volcanic ash. *Canadian Journal of Earth Sciences* 39 (7), 1085–1091.
- French, B.M., 1968. Progressive contact metamorphism of the Biwabik Iron-formation, Mesabi range, Minnesota. *Minnesota Geological Survey Bulletin* 45, 103.
- Griffin, W.L., Morey, G.B., 1969. The geology of the Isaac Lake quadrangle, St. Louis County, Minnesota: *Minnesota Geological Survey Special Publication SP-8*, 57, 1 pl.
- Grout, F.F., Broderick, T.M., 1919. The magnetite deposits of the eastern Mesabi range, Minnesota. *Minnesota Geological Survey Bulletin* 17, 58, p. 1.
- Gundersen, J.N., 1960. Stratigraphy of the eastern Mesabi district, Minnesota. *Economic Geology* 55 (5), 1004–1029.
- Gundersen, J.N., Schwartz, G.M., 1962. The geology of the metamorphosed Biwabik iron-formation, eastern Mesabi district, Minnesota. *Minnesota Geological Survey Bulletin* 43, 139.
- Labotka, T.C., Papike, J.J., Vaniman, D.T., Morey, G.B., 1981. Petrology of contact metamorphosed argillite from the Rove Formation, Gunflint Trail, Minnesota. *American Mineralogist* 66, 70–86.
- Meineke, D., 1993. Geology and taconite mines of the Mesabi range, Field Trip 1: Institute on Lake Superior Geology, 39th Annual Meeting, Eveleth, Minn., *Proceedings* 39 (pt. 2), pp. 1–66.
- Morey, G.B., Papike, J.J., Smith, R.W., Weiblen, P.W., 1972. Observations on the contact metamorphism of the Biwabik Iron-Formation, east Mesabi district, Minnesota, In: Doe, B.R., and Smith, D.K., (Eds.), *Studies in mineralogy and Precambrian Geology: Geological Society of America Memoir* 135, pp. 225–264.
- Perry Jr., E.C., Bonnichsen, B., 1966. Quartz and magnetite: Oxygen-18–oxygen-16 fractionation in metamorphosed Biwabik Iron Formation. *Science* 153, 528–529.
- Wolff, J.F., 1917. Recent geologic developments on the Mesabi Iron Range, Minnesota: *American Institute of Mining and Metallurgical Engineers. Transactions* 56, 229–257.
- Zanko, L.M., Severson, M.J., Oreskovich, J.A., Heine, J.J., Hauck, S.A., and Ojakangas, R.W., 2003. Oxidized taconite geological resources for a portion of the western Mesabi range (west half of the Arcturus Mine to the east half of the Canisteo Mine), Itasca County, Minnesota—A GIS-based resource analysis for land-use planning: *Natural Resources Research Institute Technical Report NRRI TR-2001/40*, 130 p.



Overview of the mineralogy of the Biwabik Iron Formation, Mesabi Iron Range, northern Minnesota

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Abstract

The mineralogy of the Biwabik Iron Formation changes dramatically from west to east as the formation nears the basal contact of the Duluth Complex. This reflects a contact metamorphism that took place with the emplacement of the igneous Duluth Complex at temperatures as high as 1200 °C. However, the mineralogy of the Biwabik Iron Formation also varies vertically through the stratigraphy of the unit. This variability in both the vertical and horizontal dimensions makes it difficult to predict exact horizons where specific minerals will occur. The iron-formation has been subdivided into four broad stratigraphic units (lower cherty, lower slaty, upper cherty, and upper slaty) and into four lateral mineralogical zones (1–4). Zone 1, the westernmost zone, is characterized by quartz, magnetite, hematite, carbonates, talc, chamosite, greenalite, minnesotaite, and stilpnomelane. The silicate mineralogy in Zone 2 of the Biwabik Iron Formation changes very little. However, the minerals begin to change dramatically in Zone 3. Most significantly, Zone 3 is characterized by the appearance of grunerite in both a tabular form and a fibrous form. In Zone 4, the original silicate minerals have completely reacted, and a new suite of minerals occupies the iron-formation. These include grunerite, hornblende, hedenbergite, ferrohypersthene (ferrosilite), and fayalite.

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Keywords: Biwabik Iron Formation; Duluth Complex; Mineralogy

1. Introduction

The Biwabik Iron Formation occurs as a northeast-trending outcrop belt, 2.5–3.0 miles wide and 122 miles long (Fig. 1a). The outcrop belt defines the “Mesabi Iron Range”, a world-class iron-ore deposit. Over 3.5 billion tons of ore have been shipped from the range. Much has been written about the magnetite and its transformation into taconite ore, but less information is available concerning other components in the iron-formation that typically end up in the over 7 billion tons of waste materials commonly referred to as tailings. This report focuses on the mineralogy of those parts of the Biwabik Iron Formation.

2. Regional setting

As described by Jirsa et al. (2008), the Biwabik Iron Formation is underlain by a thin basal quartz arenitic sequence called the Pokegama Quartzite and overlain by a thick graywacke-shale sequence named the Virginia Formation (Fig. 1b). Contacts between the iron-formation and underlying and overlying clastic strata are conformable and gradational. Strata within the Biwabik have been classified by texture into two fundamentally different kinds of iron-formation; (1) cherty materials, which are seemingly coarse-grained, thick bedded, and typically, but not always, rich in quartz and iron oxides, and (2) slaty materials, which are generally fine-grained, finely laminated to very thin bedded, and composed mostly of iron silicates and iron carbonates. Beds or groups of beds having cherty or slaty attributes are interlayered on all scales. Despite the heterogeneity, the Biwabik can be divided into four lithostratigraphic entities,

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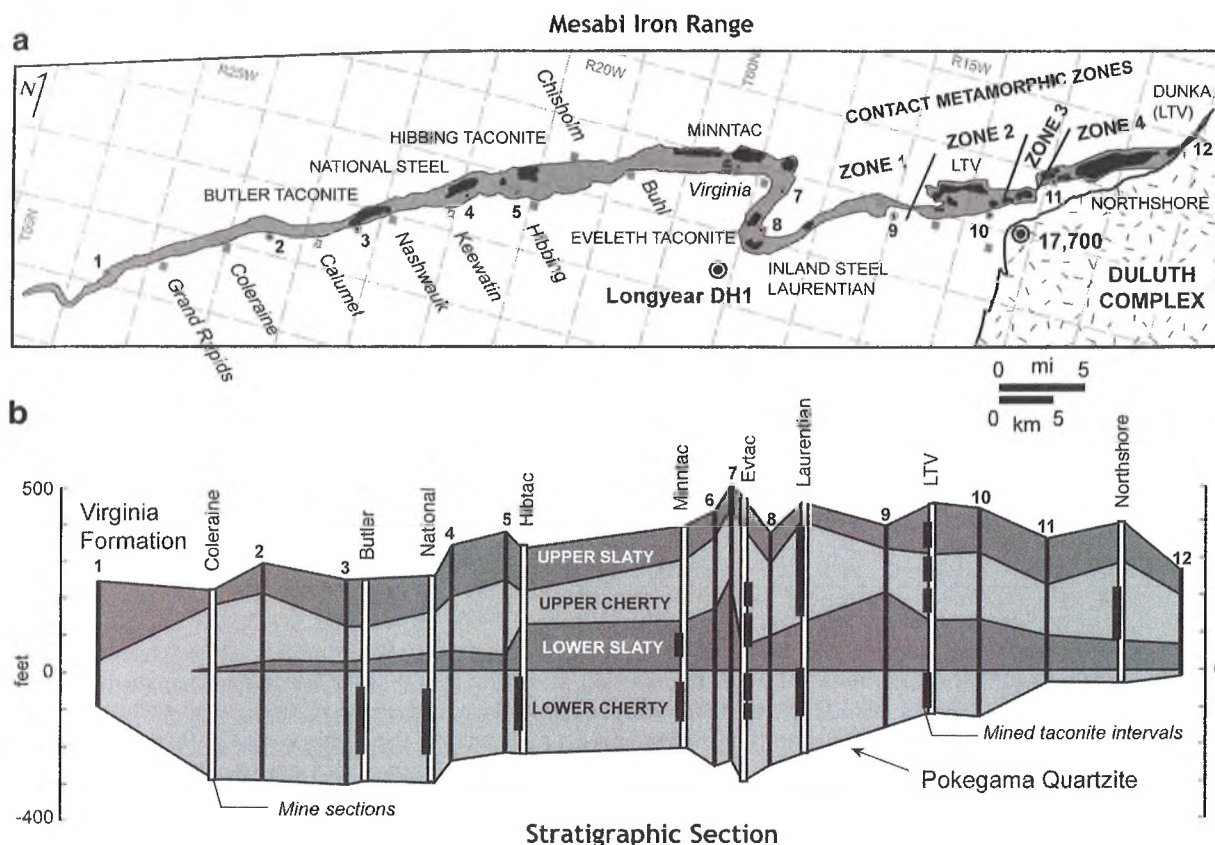


Fig. 1. Simplified geologic map and stratigraphic section of the Mesabi Iron Range. The main geologic unit is the Biwabik Iron Formation (shown in gray). The stratigraphic section shows the lateral distribution of the units of the iron formation, the Upper Slaty, Upper Cherty, Lower Slaty, and Lower Cherty [after Jirsa et al. (2008)].

which are from bottom to top, (1) Lower Cherty, (2) Lower Slaty, (3) Upper Cherty, and (4) Upper Slaty. Wolff (1917) originally defined these entities and coined them “divisions”, and this usage is still adhered to by some of the mining companies operating along the range. Subsequent studies by White (1954) showed that the divisions were mappable entities and therefore have been considered as members.

Most of the Biwabik Iron Formation has not been metamorphosed to any extent and contains mineral assemblages indicative of low-grade diagenetic processes (Morey, 2003). However, on the east end of the range, a thermal metamorphic event associated with the emplacement of the Duluth Complex produced a metamorphic aureole some 2–3 miles wide. Although quartz- and magnetite-bearing assemblages within the aureole were thoroughly recrystallized and although a significant number of metamorphic silicates, such as grunerite-cummingtonite, fayalite, ferro hypersthene, hedenbergite, hornblende, and actinolite, were produced, the cherty and slaty members and their associated attributes can still be recognized.

3. Petrographic overview

French (1968) provided a broad overview of the iron-formation at the east end of the range. He distinguished

a broad zone of “unmetamorphosed” iron-formation, his Zone 1, and three metamorphic zones marked by mineralogic changes along the strike of the iron-formation toward the contact with rocks of the Duluth Complex. Zone 2 includes transitional taconite, Zone 3, moderately metamorphosed taconite, and Zone 4, highly metamorphosed taconite.

Comparatively, little information regarding mineralogic aspects of the iron-formation in Zone 1 has been published since the work of Gruner (1946) and French (1968, 1973). In contrast, various aspects of the metamorphic aureole have been described extensively by Gundersen (1960), Gundersen and Schwartz (1962), French (1968), Griffin and Morey (1969), Bonnichsen (1969, 1975) and Morey et al. (1972). According to Gundersen and Schwartz (1962), the thermal metamorphic processes associated with emplacement of the Duluth complex were manifested largely by simple recrystallization and the development of fayalite-, magnetite-, and quartz-bearing assemblages. Assemblages containing other metamorphic silicates formed by metasomatic processes involving the injection of magnesium- and calcium-bearing igneous solutions. Subsequent workers, however, view mineralogic change as being essentially isochemical except for the loss of water and carbon dioxide.

4. Zone 1: Unmetamorphosed iron formation

Unmetamorphosed iron-formation of Zone 1 is characterized by textural attributes strikingly similar to those associated with limestone of the Phanerozoic age. The basic distinction between cherty and slaty varieties of iron-formation is one that has been recognized for a long time by geologists studying the Biwabik Iron Formation (Wolff, 1917). Mengel (1965) recognized that the cherty varieties are marked by sand-size grains, locally called granules, but including pebbles of admixed chert and carbonates, angular fragments of algal structures, ooids, oncolites, and detrital quartz and feldspar. The admixed material commonly occurs in strata having graded bedding or cross bedding showing that the clasts behaved as particulate detritus as in arenaceous clastic rocks. On the other hand, LaBerge (1967) showed that the slaty varieties have textural attributes similar in many respects to those in siltstone or shale.

Textural elements in cherty strata include; (1) granules, (2) oolites and pisoliths, (3) oncolites, and (4) cements. Granules greatly predominate over the other kinds of clasts that are generally associated with intergranular cement. Most granules are internally structureless. They range in length from about 0.5 mm to 1 mm and are irregularly rounded or ovoid in shape. The granules typically consist of extremely fine-grained monomineralic or polyminerallc aggregates. Boundaries between granules and cement are typically sharp, but may be diffuse because of recrystallization. Many granules commonly exhibit fractures that represent shrinkage or syneresis cracks presumably formed by expulsion of water from a gel.

Although they differ in size, oolites and pisoliths are typically concentrically laminated. Some oolites have only a few concentric rims and are akin to structures in limestone known as superficial oolites. Other oolites, grapestones, are formed from clusters or aggregates of smaller oolites or granules held together by concentric rims that impart an overall botryoidal shape. Still other oolites have eccentric rims suggestive of an oncolitic origin. Regardless, oolites and pisoliths are formed *in situ* by a combination of chemical and physical processes.

Distinctly different rim and pore cements are a marked feature of the cherty rocks. Older rim cement generally consists of fine-grained fibrous or bladed chert oriented perpendicular to the surfaces of the granules or oolites. This cement is paragenetically followed by pore-filling quartz that typically is blocky and coarse-grained.

Textural relationships in slaty varieties of iron-formation are complex and difficult to interpret because of the generally fine grain size of the constituent minerals. The principal textural elements include varying proportions of very fine-grained chert, carbonate or iron silicate. A few less well defined textural elements may include possible volcanic shards.

Matrices in slaty rocks differ from cements in cherty rocks only in their presumed mode of origin. Matrices were

probably deposited *in situ* as ooze or muds whereas cements were precipitated in interstitial voids after granules and oolites were deposited. Consequently, matrices tend to occur as thin, undisturbed laminae that have regular-sharp contacts. However, isolated granules are not uncommon, particularly in matrices dominated by chert.

4.1. Mineral associations

Particular stratigraphic units in the Longyear Drill Hole 1 (see location map, Fig. 1a) have distinct mineral associations that may in some cases approximate mineral assemblages (Fig. 2). Shaly rocks of the Virginia Formation are dominated by a septeclorite (chamosite) + sericite $\pm$ albitic plagioclase $\pm$ quartz. Slaty rocks in the uppermost part of the Upper Slaty interval consist predominantly of calcite $\pm$ dolomite $\pm$ chamosite $\pm$ stilpnomelane $\pm$ quartz $\pm$ an iron oxide, mainly magnetite. Iron-formation a few feet below the transition contains siderite $\pm$ ankerite $\pm$ chamosite $\pm$ stilpnomelane $\pm$ quartz $\pm$ an iron oxide, mainly hematite. Magnetite appears to be confined to scattered beds or laminae. Rocks assigned to the Upper Cherty member contain chamosite $\pm$ stilpnomelane $\pm$ siderite $\pm$ quartz $\pm$ hematite, along with scattered thin beds of monomineralic magnetite. Lower Slaty beds also consist predominantly of chamosite $\pm$ stilpnomelane $\pm$ siderite $\pm$ quartz, but appear to lack a discrete iron oxide phase. Chamosite disappears from the upper part of the Lower Cherty interval and is replaced by minnesotaite $\pm$ talc. Other mineral phases include stilpnomelane $\pm$ siderite $\pm$ ankerite $\pm$ quartz $\pm$ iron oxide (hematite). Midway in the member, stilpnomelane disappears and the strata are dominated by minnesotaite $\pm$ talc $\pm$ siderite $\pm$ ankerite $\pm$ quartz. Ultimately talc disappears and typical mineral associations contain greenalite $\pm$ minnesotaite $\pm$ siderite $\pm$ ankerite $\pm$ quartz $\pm$ hematite. The basal red taconite consists of chert $\pm$ hematite $\pm$ chamosite $\pm$ ankerite. Grains of detrital quartz and potassium feldspar are scattered throughout the interval. Quartz and potassium feldspar $\pm$ greenalite $\pm$ calcite define mineral associations in quartz arenitic strata typical of the Pokegama Quartzite.

4.2. Quartz and chert

The most abundant mineral in the iron-formation in Drill Hole 1 is quartz. It is by far the dominant constituent of granules, oolites, and pisoliths, cements, and matrices. Morphological varieties include microcrystalline quartz (micritic quartz), fibrous quartz (chalcedony), and coarse-grained quartz (megaquartz). Some of the micritic quartz has undergone considerable recrystallization.

Most granules consist entirely of micritic quartz or of micritic quartz admixed with lesser amounts of silicates, carbonates or iron oxides. Chalcedony, or less commonly, megaquartz, fills internal shrinkage cracks and fractures. Early chalcedonic cement typically forms a radial fringe surrounding many of the intraclasts. Chalcedonic rim

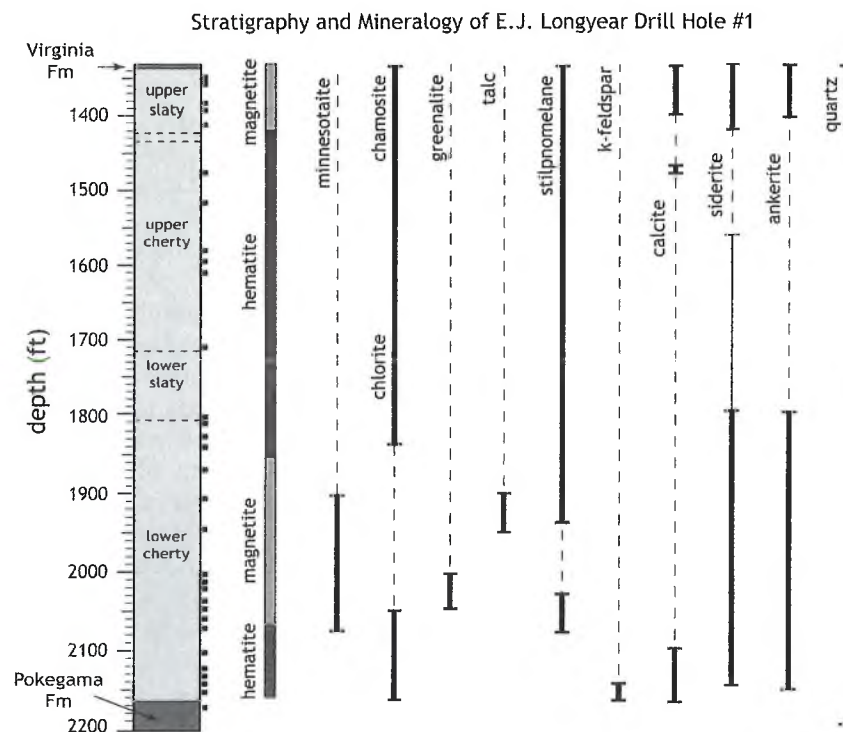


Fig. 2. Stratigraphic section and mineralogy of the E.J. Longyear Drill Hole #1. It was drilled as a long stratigraphic test hole and was finished in 1910. Its location is shown in Fig. 1. The small squares on the right side of the stratigraphic column are the sampling intervals.

cement is followed paragenetically by pore-filling cement consisting mostly of megaquartz.

In slaty iron-formation, micritic quartz occurs within layers admixed with various proportions of iron silicates or less commonly as monomineralic laminae. Many such laminae are content graded and pass into silicate- and carbonate-rich layers as the proportions of these phases increases.

4.3. Silicate minerals

4.3.1. Chamosite and greenalite

Because the silicates in unmetamorphosed iron-formation have not been described previously in any detail, their morphological and chemical attributes are discussed in the following sections. Fig. 3a–d shows that the compositions of individual phases, measured in Drill Hole 1, deviate substantially from the ideal compositions reported in the literature.

Pale-green chamosite is a widely distributed phase in Drill Hole 1. It occurs within both granules and oolites as rim cement and matrix material between granules (Fig. 4). Chamosite also pseudomorphically replaces shard-like structures of possible volcanic origin found within thinly layered packets of slaty iron-formation scattered about within thicker intervals of cherty iron-formation. Similar shard-like structures, also involving chamosite, occur within silicate-bearing carbonate laminae in stratigraphic intersects dominated by slaty varieties of iron-formation.

Ideal chamosite [$\text{Fe}_6(\text{Al},\text{Si})_4\text{O}_{10}(\text{OH})_8$] is an iron chlorite. It differs mainly from greenalite in containing larger amounts of alumina (Fig. 5). Although chamosite in Drill Hole 1 has a variety of habits, average microprobe analyses are broadly similar and approximate the average composition of chamosite found in Phanerozoic ironstone (Klein, 1983). Chamosite in the Upper Slaty differs mainly in having somewhat more Al_2O_3 and MgO . However, in the Upper Cherty, the chamosite composition has changed considerably and the Mg/Fe ratio is now about 50:50. In the Lower Slaty, chamosite contains more Fe than Mg whereas in the Lower Cherty it is more Mg rich.

Greenalite is restricted to the Lower Cherty where it has textural attributes similar to those of chamosite. Most greenalite-bearing granules are aggregates of bright green, pale green or pale brown material typically intergrown with micritic quartz, stilpnomelane, and minor minnesotaite. Many oolites have cores that are composed primarily of greenalite and rimmed by greenalite interlayered with chalcidonic quartz.

According to Gruner (1936), the structure of greenalite [$\text{Fe}_6\text{Si}_4\text{O}_{10}(\text{OH})_8$] is the ferrous analog of antigorite [$\text{Mg}_6\text{Si}_4\text{O}_{10}(\text{OH})_8$]. It always contains at least some magnesium. Variations in composition are illustrated graphically in Fig. 6. Many of the analyzed samples lie close to the ideal greenalite composition; substitutions are minor and typically involve replacement of FeO and SiO_2 by small quantities of MgO and Al_2O_3 , respectively. However, some samples contain almost 8 wt% Al_2O_3 and tend to plot along a join line that extends between an ideal greenalite compo-

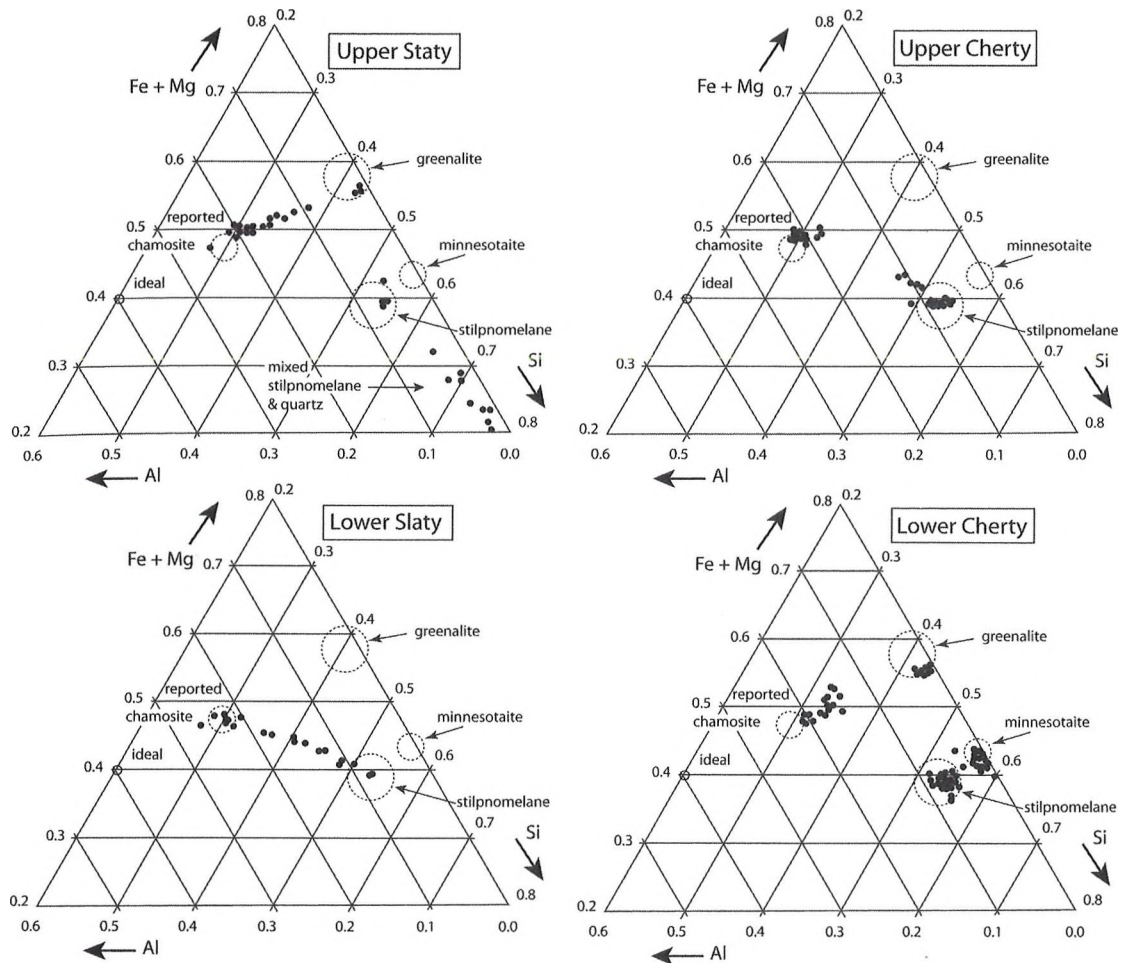


Fig. 3. Compositional relationships between the main silicate minerals of Zone 1 in the Biwabik Iron-Formation.

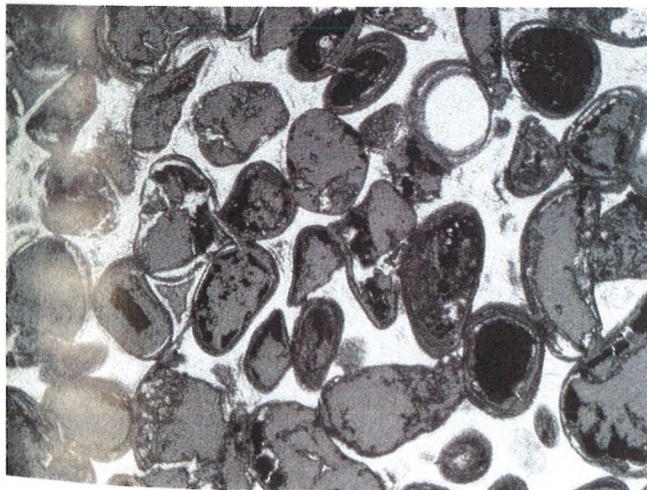


Fig. 4. Optical image of chamosite granules in a quartz matrix. Field of view is 900 μm across.

sition and an ideal chamosite composition. Even single granules contain variable quantities of Al_2O_3 and there appears to be a correlation between Al_2O_3 content and color. Bright green greenalite typically contains 5 wt% or less Al_2O_3 ; pale green to pale brown greenalite contains

Compositional Relationships Between Chamosite, Clinocllore, Greenalite and Serpentine

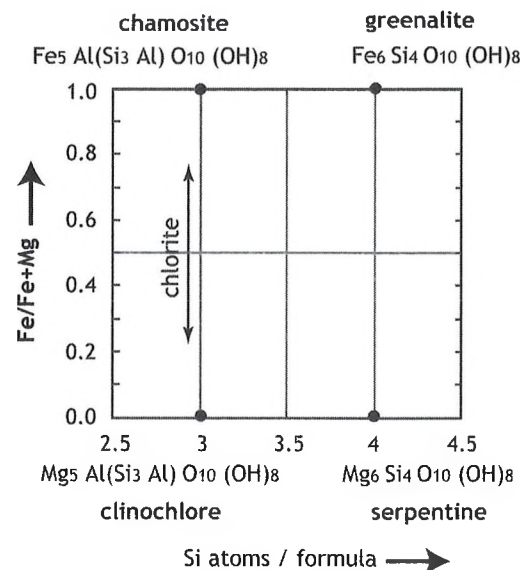


Fig. 5. Relationships between the ideal compositions of chamosite, clinocllore, greenalite, and serpentine (antigorite).

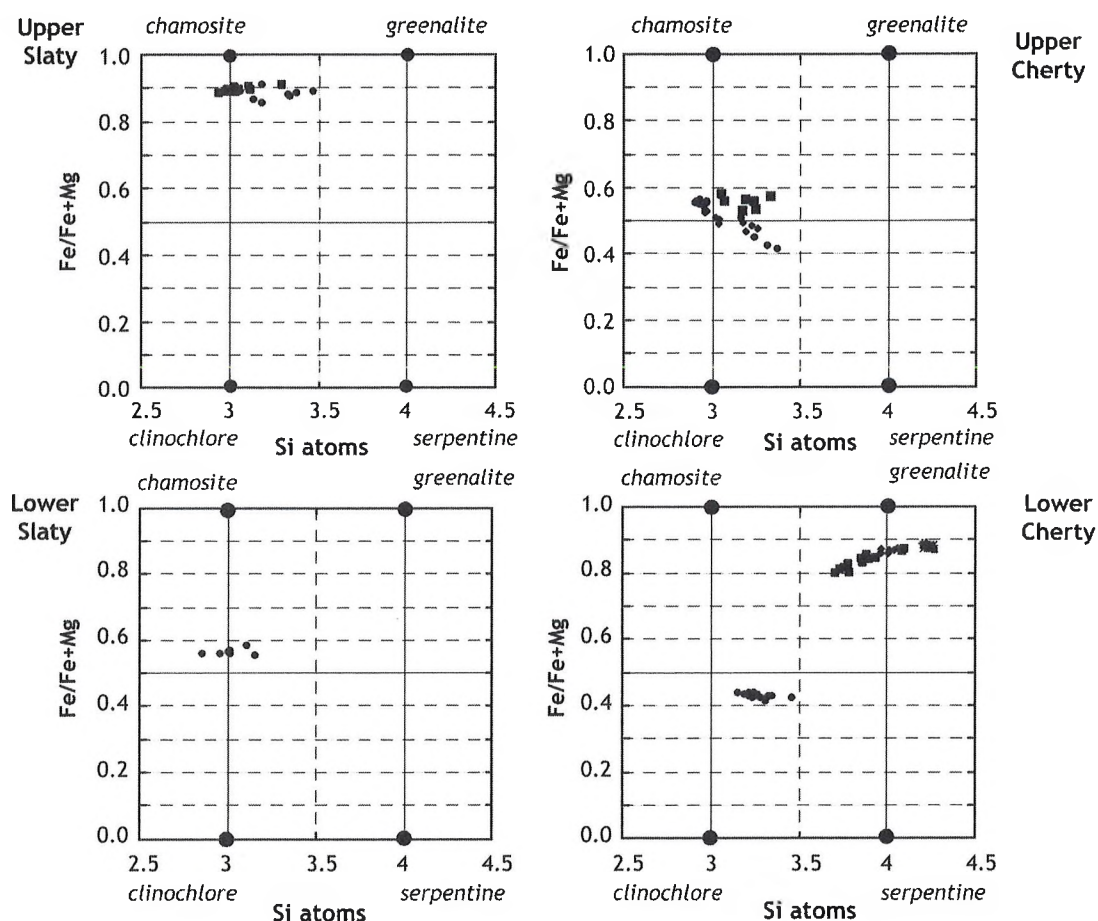


Fig. 6. Variations in the compositions of clinochlore (chlorite), chamosite and greenalite as a function of stratigraphic division.

4.8–6.3 wt% Al_2O_3 whereas dark brown granules contain 7.0–7.8 wt% Al_2O_3 . According to Klein (1974), typical greenalite should contain no more than around 5 wt% Al_2O_3 . He suggests that some of the greenalite having 6 to nearly 8 wt% Al_2O_3 may in fact be berthierine, a 7 Å chamosite. Careful X-ray work will be needed to determine if the alumina-rich phases reported here are indeed berthierine (7 Å), or chamosite (7 Å), or an iron-rich chlorite (14 Å).

Because the chamosite analyzed in this study has a composition that lies along a join line between greenalite and chamosite, these two phases may be structurally related, or they may be intergrown on a submicron scale. Given that the two have similar paragenetic histories, it is likely that chamosite served as a sink for alumina and the two therefore reflect heterogeneities in bulk composition.

4.3.2. Minnesotaitite

Minnesotaitite is a minor constituent; mainly in granules admixed with greenalite (Fig. 7), or with greenalite and stilpnomelane. It is somewhat more abundant in slaty varieties where it is associated with stilpnomelane.

Pale brownish-green to colorless minnesotaitite occurs as felt-like masses or as fine- to medium-grained acicular crystals arranged in sprays of acicular bundles (Fig. 7) or “bowties”. Both habits are scattered haphazardly, but the

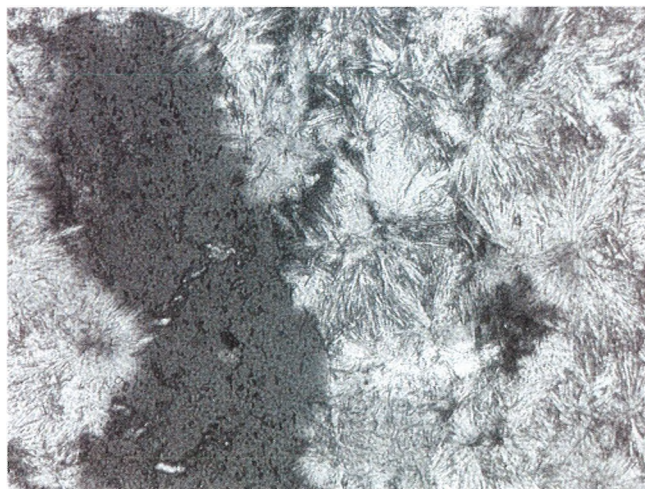


Fig. 7. Optical image of a greenalite granule surrounded by minnesotaitite matrix. Field of view is 900 μm across.

bowties especially occur along the greenalite granules (Fig. 8). Felt-like, disseminated masses of greenalite and minnesotaitite also seem to replace micritic chert, both in granules and in matrix material. Many granules of minnesotaitite are fractured, and the fractures are filled with calcedonic quartz (Fig. 9).

Minnesotaite [$\text{Fe}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$] is the iron analog of talc [$\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$], although the two have different structures. It differs from greenalite in containing more silica, but like greenalite and chamosite, it always contains some magnesium. In Drill Hole 1, it differs from an ideal end-member composition in containing almost 6 wt% MgO.

4.3.3. Talc

Talc occurs in the Lower Cherty division, almost always intergrown with minnesotaite. It has a habit similar to minnesotaite, but tends to be more sheaf-like. Microprobe analyses (Fig. 10) yield compositions intermediate between ideal talc [$\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$] and minnesotaite [$\text{Fe}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$] implying either the presence of ferroan talc (Miyano, 1987) or the presence of intimately admixed talc and minnesotaite.

4.3.4. Stilpnomelane

Stilpnomelane is a typically cryptocrystalline, highly pleochroic (yellowish-brown to dark brown) sheaf-like silicate found in a variety of textural settings. Commonly, it has a pale brown or reddish brown color, but some varieties have a greenish brown color. The range of colors implies a range of $\text{Fe}^{2+}/(\text{Fe}^{2+} + \text{Fe}^{3+})$ ratios on a microscopic scale.

Although granules composed entirely of stilpnomelane may occur (Fig. 11), stilpnomelane more commonly occurs as individual laths (Fig. 12) or radiating sheaves (Fig. 13) in subordinate amounts within granules of micritic chert or carbonate (Fig. 14). Crosscutting relationships imply that the stilpnomelane is the youngest phase. It is noteworthy that many stilpnomelane-bearing granules are broken by

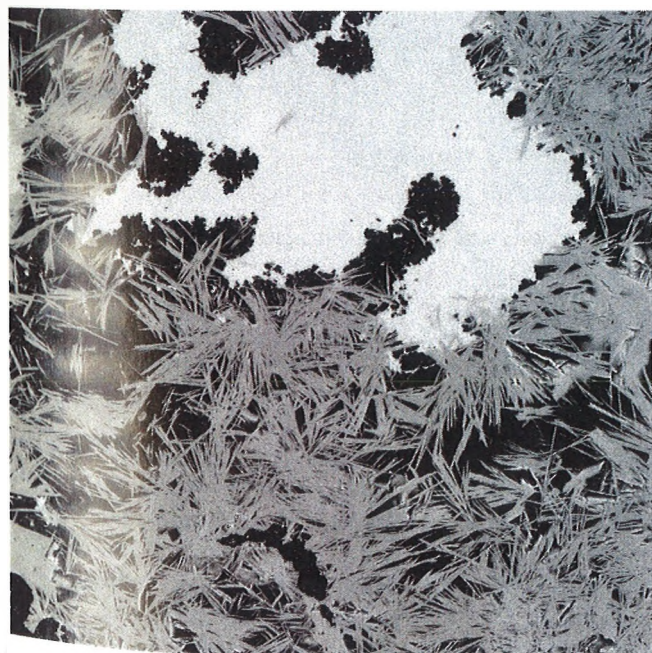


Fig. 8. Backscattered electron image of a greenalite granule surrounded by minnesotaite matrix. Field of view is about 240 μm across.

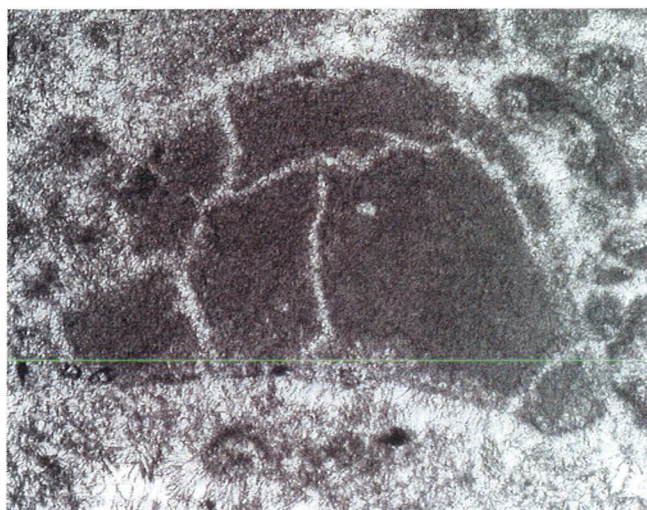


Fig. 9. Optical image of a minnesotaite granule in minnesotaite matrix. The granule exhibits shrinkage cracks. Field of view is 400 μm across.

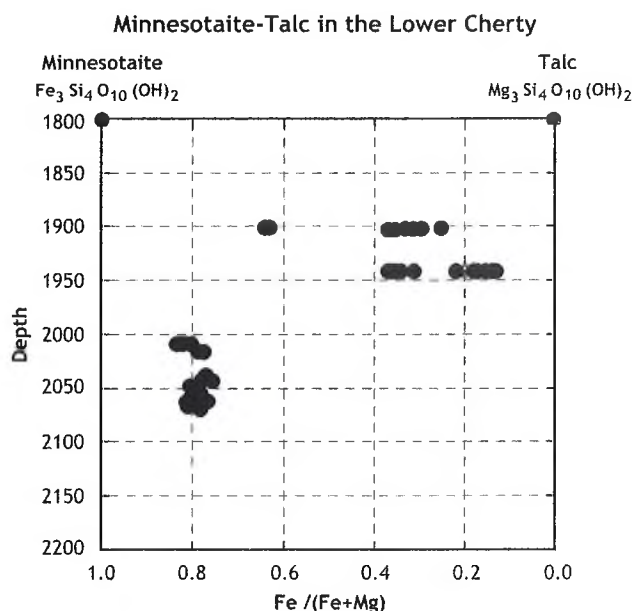


Fig. 10. Compositional plot of minnesotaite and talc as a function of depth.

shrinkage cracks that are filled with chalcedony. The stilpnomelane must be an early-formed diagenetic phase. Rarely, stilpnomelane also may be found within the cores of oolites along with fine-grained chamosite and minnesotaite. Monomineralic rims of stilpnomelane surround many of these oolites. The oolites also are cut by chalcedony-filled shrinkage cracks.

Lastly, granules of admixed stilpnomelane and micritic chert may be found floating within siderite, either as matrix or as cement. Margins of the granules have been partially replaced by the siderite, implying that it is paragenetically later than phases within the granules.

Stilpnomelane in slaty varieties of iron-formation is not easily discernable because of a very fine grain size and a

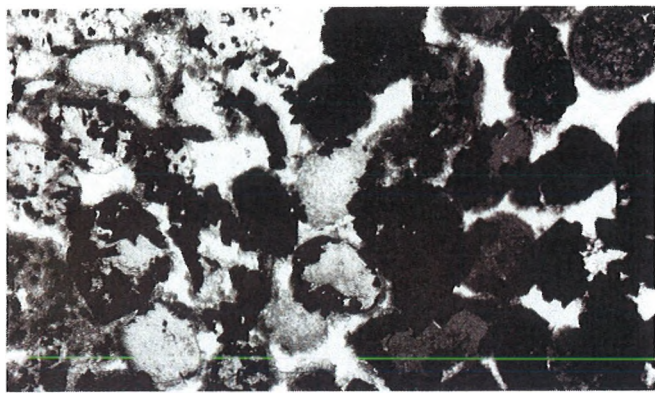


Fig. 11. Optical image showing granules of chamosite (on the left) and stilpnomelane (on the right). Field of view is 1800 μm across.

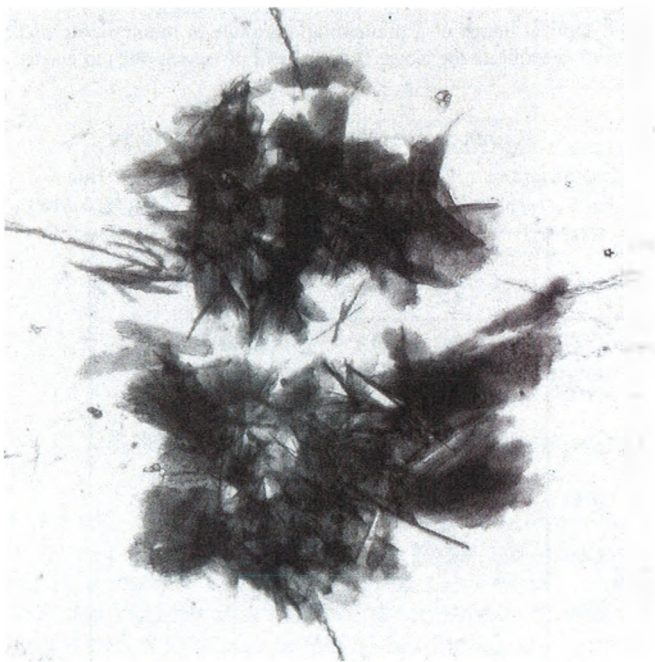


Fig. 12. Optical image of stilpnomelane blades in a quartz matrix. Field of view is 600 μm across.



Fig. 13. Backscattered electron image of stilpnomelane needles in a carbonate matrix.

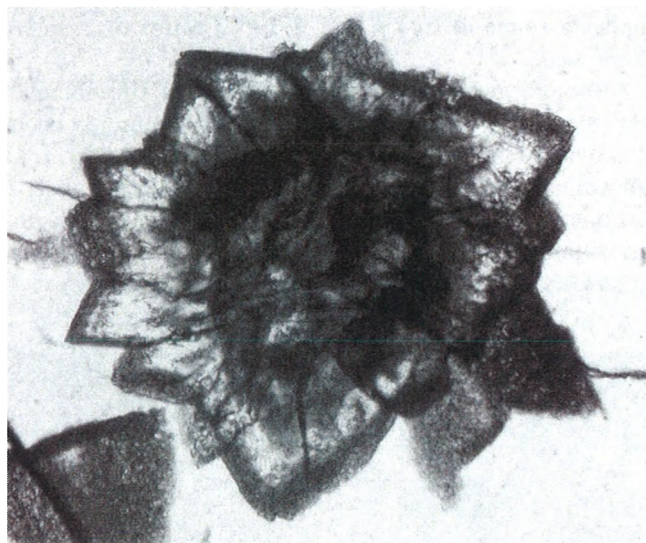


Fig. 14. Optical image of siderite with a stilpnomelane core. Field of view is 500 μm across.

semi-opaque nature of many of the individual layers. In places, it occurs as circular grains (“microgranules”) set within a felt-like matrix of admixed minnesotaite and greenalite. Stilpnomelane also appears to replace elongate shard-like structures of possible volcanic origin embedded within a siderite matrix. There it generally forms cryptocrystalline aggregates that have preferred orientations perpendicular to shard boundaries.

The composition of stilpnomelane is more complex than that of greenalite or minnesotaite, mainly in containing small and variable, but essential, amounts of K_2O and Na_2O , as well as larger amounts of Al_2O_3 (Fig. 15).

Although the structure of stilpnomelane has not been fully established, Gruner (1944) suggested that it is fundamentally talc-like. Similarly, a precise chemical formula remains uncertain; nonetheless, a simplified formula is use-

ful for comparative purposes $[(Ca,Na,K)(Fe,Mg)_3Si_4O_{10}(OH)_2]$. Many of the analyzed samples have that approximate composition (Fig. 15). However, some analyzed grains have compositions along a mixing line that extends between stilpnomelane and chamosite. These two phases are either structurally related or are finely intergrown. Similarly in one sample, a stilpnomelane-like phase appears to be admixed with two other phases, an alumina-poor chamosite, and an unidentified phase that is both silica-rich and alumina-rich. Although it is possible that the analyzed silica values reflect the presence of very fine chert, that alone would not explain the atypical alumina values. Additional analyses did nothing to clarify this point.

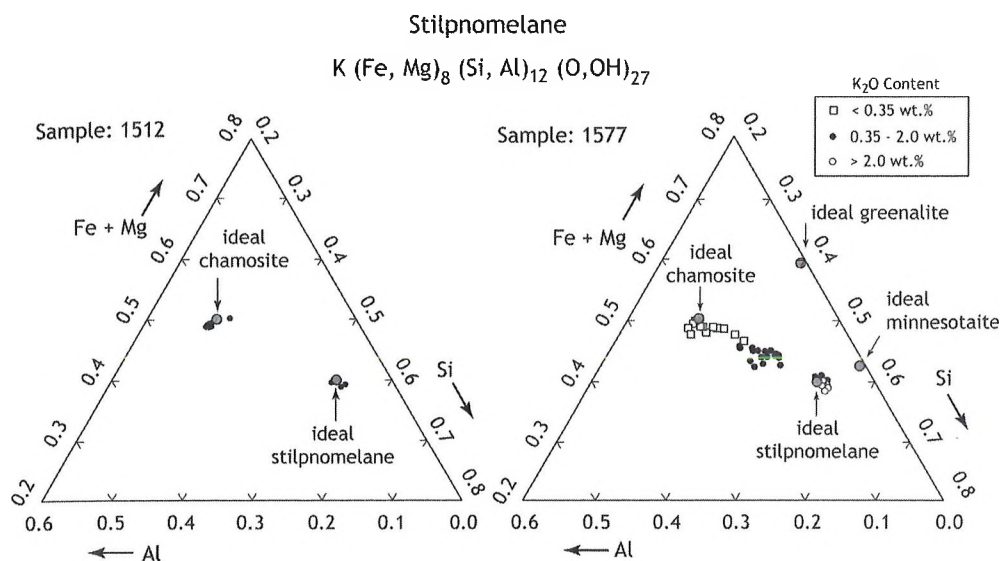


Fig. 15. Compositional plots of stilpnomelane and chamosite.

4.4. Carbonate minerals

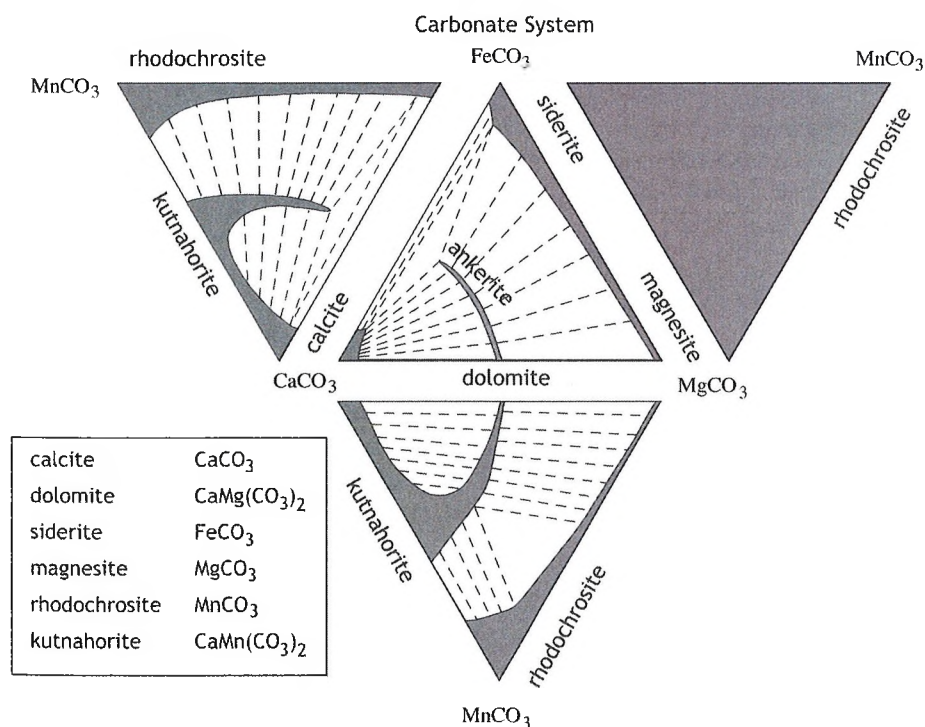
Samples of both cherty and slaty varieties of iron-formation contain three or four carbonate species: calcite, siderite, and members of the dolomite-ankerite and the kutnahorite/ferroan kutnahorite series (Fig. 16).

4.4.1. Siderite

Siderite ($FeCO_3$) occurs in cherty varieties of iron-formation in several ways. Primary siderite occurs in granules as aggregates of rounded to anhedral grains cemented together by rhombic overgrowths (Fig. 14). Many of the

rounded grains have spherulitic structures and are set in coarsely crystalline siderite marked by interlocking rounded and rhombic grains. Textural relationships imply that the granules and the enclosing matrix are more-or-less contemporaneous in origin.

Secondary siderite occurs as coarse, zoned and/or twinned rhombohedra that replace granules composed of micritic chert and their associated cements. Relict granules form ghosts that are preserved within grains of rhombic siderite. Secondary siderite also occurs in mottled areas as aggregates of fine-grained anhedral grains. The mottles enclose phases such as chert and the several iron silicates.

Fig. 16. Compositional relationships within the carbonate system $CaCO_3$ - $MgCO_3$ - $MnCO_3$ - $FeCO_3$.

Siderite in slaty varieties of iron-formation typically occurs as small spheres cemented together by rhombic overgrowths. The spheres have cryptocrystalline cores that are turbid or semi-opaque. Individual carbonate-rich laminae may consist entirely of spherical siderite or of spherical siderite and associated rhombic overgrowths, or entirely of interlocking rhombic grains. Rhombic siderite also occurs as disseminated grains in calcite-rich laminae. The two phases are more-or-less contemporaneous. Other carbonate-rich laminae are typically interlayered with dark-colored greenalite- or stilpnomelane-rich laminae that have various proportions of admixed spherical siderite. Many of these laminae are recrystallized as evidenced by patchy mixtures of fine-grained silicates and granoblastic clusters of rhombohedral or subhedral siderite.

The composition of siderite can be expressed in terms of four components: FeCO_3 , MnCO_3 , MgCO_3 , and CaCO_3 , which are in solid solution. Some samples from the Lower Cherty division contain as much as 20–25 mol% MnCO_3 (Fig. 17). Microprobe analyses from the Upper Slaty, Upper Cherty, and Lower Slaty divisions (Fig. 17) are broadly similar, and average around $\text{Fe}_{.88-.84}\text{Mg}_{.03-.11}\text{Ca}_{.02-.03}\text{Mn}_{.02-.07}\text{CO}_3$. Some substitution of Fe by Mg occurs locally, and most samples contain <5 wt% MnCO_3 , but a few samples from the Upper Cherty division contain as much as 10 wt% MnCO_3 , generally at the expense of MgCO_3 .

These measured compositions are considerably more iron-rich than an average composition of 68–83 mol% FeCO_3 (French, 1968). In contrast, the average composition of siderite from the Lower Cherty (Fig. 17) differs considerably from that of the remainder of the iron-formation. There, both magnesium and manganese substitute for iron yielding an average composition of $(\text{Fe}_{.60-.78}\text{Mg}_{.15-.19}\text{Ca}_{.02-.03}\text{Mn}_{.04-.22})\text{CO}_3$.

4.4.2. Dolomite-ankerite series

Pure dolomite $[\text{CaMg}(\text{CO}_3)_2]$ has a restricted stratigraphic distribution in the transitional interval between the Biwabik and Virginia formations. Much of it has a coarse replacement texture marked by euhedral rhombic crystals that are considerably zoned. Microprobe analyses show that the dolomite has a composition with little or no substitution of FeO or MnO, and has an average composition of $(\text{Ca}_{.54}\text{Mg}_{.41}\text{Fe}_{.04}\text{Mn}_{.01})\text{CO}_3$.

Ankerite $[\text{Ca}(\text{Mg,Fe})(\text{CO}_3)_2]$, in contrast to dolomite, is widely distributed and occurs in both cherty and slaty varieties of iron-formation. It typically forms coarse-grained rhombs that can be extensively zoned (Fig. 18). Replacement by ankerite of earlier-formed phases commonly develops patches of aggregated grains, which give the rocks a mottled appearance. In some samples, the mottles contain remnants of earlier granules, which are outlined by fine mats of later growth (Fig. 19).

Ankerite rarely occurs in carbonate-rich slaty layers where it forms irregular beds and patches of anhedral that surround and apparently replace earlier siderite. Other laminae consist entirely of very fine-grained ankerite. Textural relations are such that it cannot be determined if this ankerite is a primary precipitate or a secondary replacement mineral.

Microprobe analyses of ankerite (Fig. 20) in the Upper Slaty member are quite consistent around $(\text{Ca}_{.52-.55}\text{Mg}_{.20}\text{Fe}_{.25-.26}\text{Mn}_{.01-.02})\text{CO}_3$. It is considerably more iron rich in the Upper Cherty, $(\text{Ca}_{.55}\text{Mg}_{.10}\text{Fe}_{.34}\text{Mn}_{.01})\text{CO}_3$. Some ankerite from the Lower Cherty division contains appreciable manganese that substitutes for iron, $(\text{Ca}_{.51}\text{Mg}_{.21}\text{Fe}_{.23}\text{Mn}_{.05})\text{CO}_3$. As a general rule, samples that have abundant manganese in ankerite also have abundant manganese in siderite.

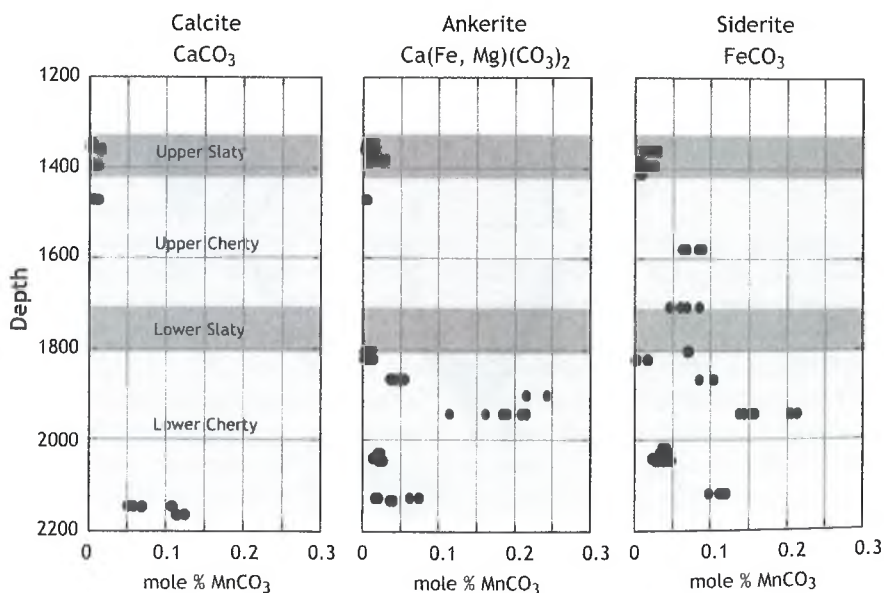


Fig. 17. Manganese-content as a function of depth of the carbonates in the Biwabik Iron Formation.

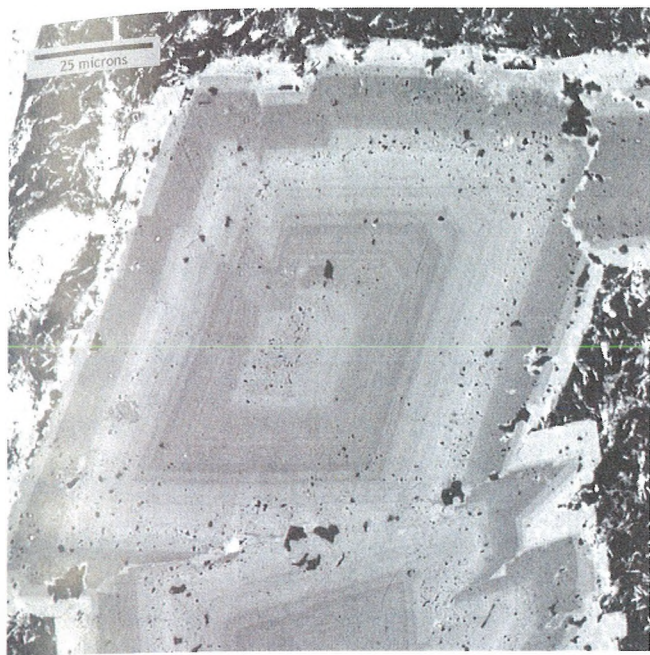


Fig. 18. Backscattered electron image of a zoned ankerite crystal. The dark bands are richer in magnesium and the lighter bands are richer in iron.

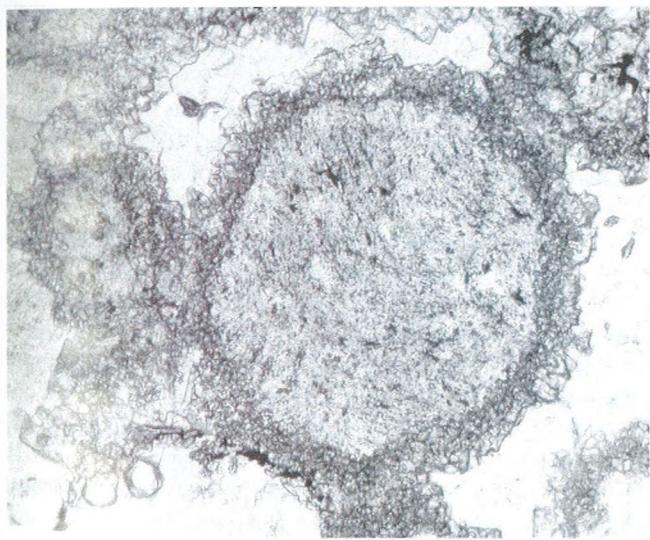


Fig. 19. Optical image of an ankerite granule surrounded by later ankerite growth. Granule is about 600 μm in diameter.

4.4.3. Kutnohorite-ferroan kutnohorite series

Members of the kutnohorite-ferroan kutnohorite series $[(\text{CaMn})(\text{CO}_3)_2\text{-Ca}(\text{Mn,Mg,Fe})(\text{CO}_3)_2]$ occurs in the Lower Cherty member (Fig. 17). They have textural and paragenetic attributes broadly similar to those of the dolomite-ankerite series. However, the term dolomite is restricted to phases that have compositions normally close to pure $\text{CaMg}(\text{CO}_3)_2$ with only small amounts of Fe^{2+} replacing Mg. In Drill Hole 1, there is continuous replacement of Mg by Fe through ankerite towards $\text{CaFe}(\text{CO}_3)_2$. Mn also replaces Mg in the dolomite structure, leading to

the ideal kutnohorite composition $[\text{CaMn}(\text{CO}_3)_2]$. Inasmuch as the kutnohorite in Drill Hole 1 contain considerable iron $[(\text{Ca}_{.48}\text{Mg}_{.19-.25}\text{Fe}_{.10-.15}\text{Mn}_{.12-.23})\text{CO}_3]$, it is the ferroan variety.

4.4.4. Calcite

Finally, crystalline euhedral grains of calcite $[\text{CaCO}_3]$ are a major constituent in dolomitic limestone-bearing intervals at the top of the Biwabik Iron Formation. There it has a composition (Fig. 20) that deviates little from the ideal end-member composition $[(\text{Ca}_{.98}\text{Mg}_{<.01}\text{Fe}_{.01}\text{Mn}_{<.01})\text{CO}_3]$.

Calcite also occurs in slaty varieties of iron-formation in the uppermost part of the Upper Slaty member where it has an average composition $(\text{Ca}_{.97}\text{Mg}_{.01}\text{Fe}_{.01}\text{Mn}_{.01})\text{CO}_3$. Calcite is typically found in cherty varieties, as sparry pore cement that fills voids between silicate granules or within shrinkage cracks that transect silicate granules. It also occurs as mottles consisting of porphyroblasts that have included and replaced micritic chert-rich oololiths, granules, and cement. In both varieties the composition of the calcite deviates little from $(\text{Ca}_{.97}\text{Mg}_{.01}\text{Fe}_{.02}\text{Mn}_{.01})\text{CO}_3$.

Subhedral grains of calcite also occur as interstitial cement in clastic strata interlayered within the basal red taconite toward the bottom of the iron-formation. That calcite is iron-rich and has an average composition $(\text{Ca}_{.85}\text{Mg}_{.01}\text{Fe}_{.13}\text{Mn}_{.01})\text{CO}_3$. Interstitial cement in the underlying Pokegama Quartzite contains appreciable manganese-rich calcite, $(\text{Ca}_{.90}\text{Mg}_{.01}\text{Fe}_{.02}\text{Mn}_{.07})\text{CO}_3$.

5. Zone 2: Transitional iron-formation

Transitional iron-formation as defined by French (1968) contains mineral assemblages similar to those observed in unmetamorphosed iron-formation, but exhibits evidence of extensive recrystallization of quartz and magnetite and the widespread replacement of the iron silicates by quartz and ankerite. Such features include granules of very fine-grained acicular minnesotaite $\pm$ trace amounts of micritic chert and magnetite that are typically fractured. The fractures are in turn filled with tabular grains of minnesotaite $\pm$ quartz and $\pm$ ankerite. Although these replacement features are quite pronounced, they in themselves are not necessarily related to emplacement of the Duluth Complex. Nonetheless, French (1968) placed the rocks of Zone 2 within the metamorphic aureole because of the partial reduction of hematite to magnetite in the lower red taconite and the appearance of clinozoisite in the underlying Pokegama Quartzite.

6. Zones 3 and 4: Moderately and highly metamorphosed iron-formation

The boundary between Zone 2 and the moderately metamorphosed iron-formation of Zone 3 occurs about 2.3 miles from the contact with the Duluth Complex. It is marked by the appearance of a variety of amphibole phases

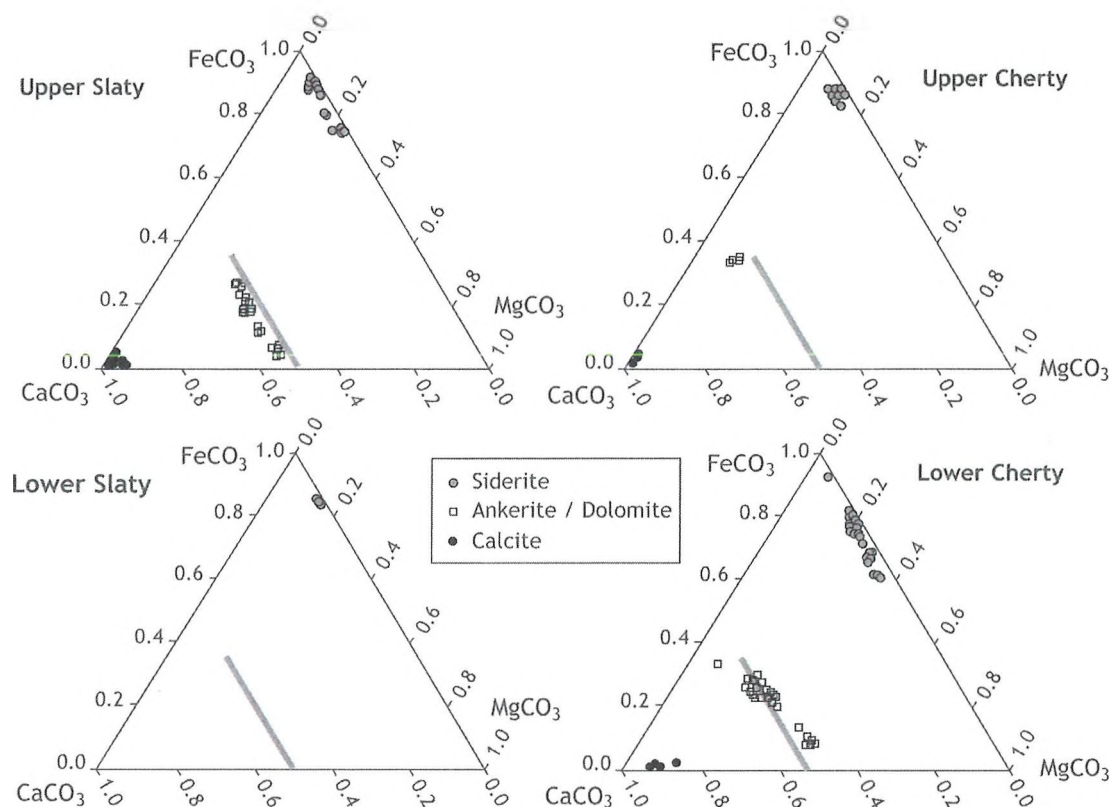


Fig. 20. Compositional plots of the carbonates in the Biwabik Iron Formation.

and by the disappearance of original iron carbonates and silicates (Fig. 21). The development of grunerite-cummingtonite is pervasive throughout the zone and appears to have formed simultaneously in all rock types from both earlier iron silicates and iron carbonates.

Textual aspects similar to those in Zones 1 and 2 persist into Zone 3. However, the iron-formation throughout Zone 4 is completely recrystallized; most rock types are finely granular or hornfelsic. Some specific layers, however, are locally medium to very coarsely granular. These coarser-grained rocks are not foliated or lineated but have been described as granoblastic hornfels (Gundersen, 1960). Despite the considerable recrystallization, the original layered and laminated fabric is preserved and emphasizes the differences in the original bulk compositions.

6.1. Cummingtonite-grunerite series

Since the Reserve controversy of the 1970s, morphological attributes of the cummingtonite-grunerite series have attracted considerable attention, primarily because of their general resemblance to some asbestos-like minerals. However, to our knowledge, no detailed studies regarding specific stratigraphic, compositional, and structural attributes of these phases in the Biwabik Iron Formation have been completed. There is a general consensus, however, that these amphiboles formed under both prograde conditions, or as metamorphic temperatures increased

and under retrograde conditions as temperatures decreased, in the metamorphic aureole.

The ideal end-member composition of cummingtonite is $\text{Mg}_7\text{Si}_8\text{O}_{22}(\text{OH})_2$ and for grunerite it is $\text{Fe}_7\text{Si}_8\text{O}_{22}(\text{OH})_2$. However, French (1968), following the convention of Deer et al. (1963), subdivided the series using the ratio, $R = \text{Fe}^{2+}/(\text{Fe}^{2+} + \text{Fe}^{3+} + \text{Mn} + \text{Mg})$. In that scheme, amphiboles with an R -value of greater than 0.7 are termed grunerite. The term cummingtonite is applied to those with a more magnesium-rich ratio. Despite the data having considerable scatter, French (1968) concluded that there is a general increase in Mg content with proximity of the Duluth Complex (Fig. 22). Values of $R < 0.7$ (or cummingtonite) typically appear within one mile of the contact. French, however, did not give enough textural information to determine which of the amphiboles he analyzed were prograde or retrograde. Nonetheless, these data agree with the observations of Gundersen and Schwartz (1962) who identified prograde cummingtonite near the gabbro, and those of Morey et al. (1972) who established the presence of prograde grunerite well away from the gabbro.

Prograde grunerite first occurs in Zone 3 as small, tabular crystals surrounded by radiating fibrous sheaves composed of fine needles (Fig. 23). Prograde grunerite in Zone 4 forms well developed acicular grains (Fig. 24), which gave way to the east to medium-size prismatic grains that are colorless and display evidence of well developed polysynthetic twinning (Gundersen and Schwartz, 1962).

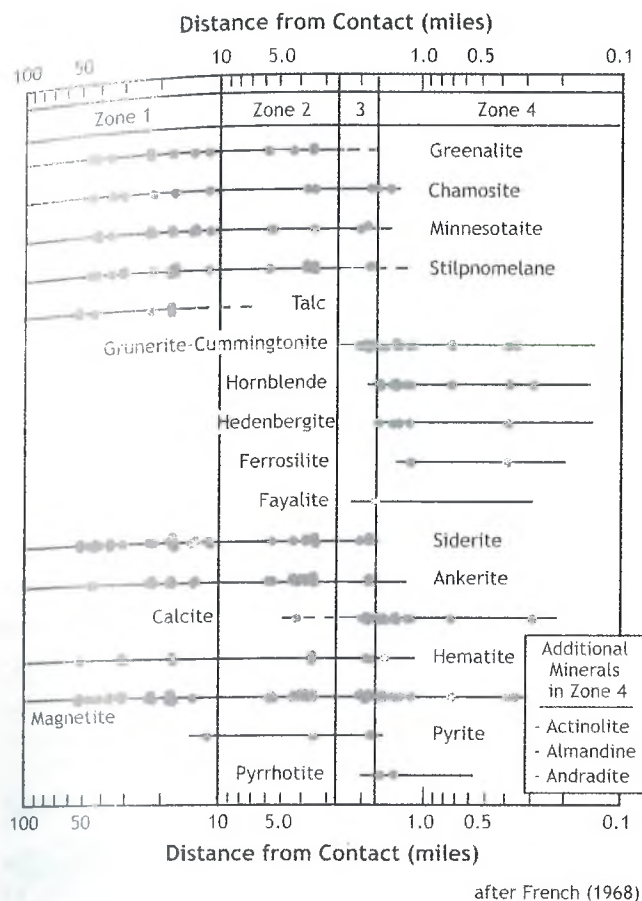


Fig. 21. Mineral occurrences in the Biwabik Iron Formation as a function of distance from the contact with the Duluth Complex.

Still farther to the east and immediately adjacent to the Duluth Complex, paragenetic relationships are complicated by the presence of retrograde cummingtonite that is medium to coarse-grained and prismatic. For example, virtually all of the prismatic cummingtonite at the Dunka River locality appears to be paragenetically late, having formed partly from fayalite, but mainly from ferrosilite/pigeonite (Bonnichsen, 1969). At somewhat lower temperatures, prismatic cummingtonite may be replaced by more magnesium-rich phases that have an acicular habit. At still lower temperatures prograde acicular grunerite may be replaced by acicular or fibrous cummingtonite. Many of

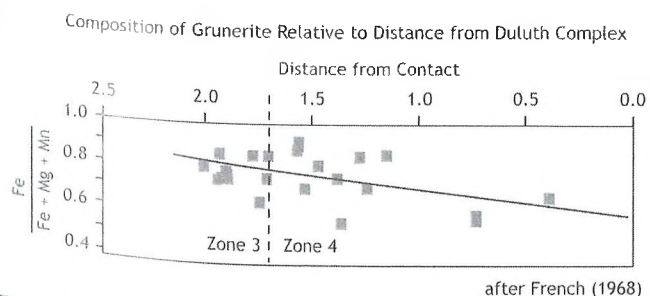


Fig. 22. Composition of cummingtonite-grunerite in the Biwabik Iron Formation relative to distance from the Duluth Complex.

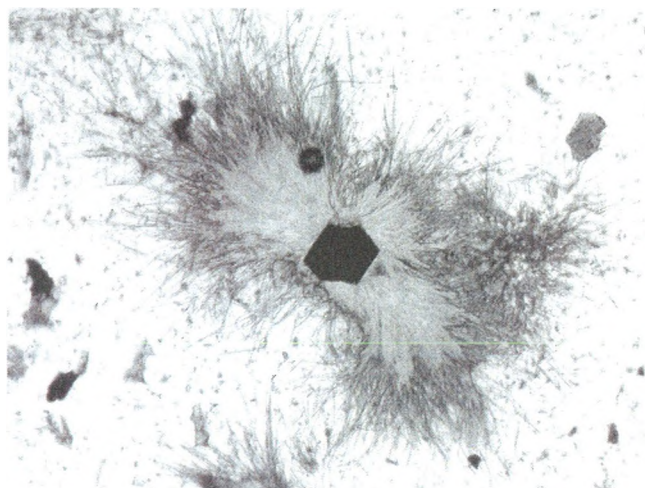


Fig. 23. Optical image of fibrous grunerite in a matrix of quartz from the metamorphic contact zone with the Duluth Complex. Field of view is about 1000 μm across.

these retrograde reactions seem to involve the development of secondary magnetite (Gundersen and Schwartz, 1962).

6.2. Other silicates

Zones 3 and 4 also contain a variety of other iron silicates. The clinopyroxene, hedenbergite, first appears as a prograde phase in the metamorphic aureole about 1.7 miles from the contact with the Duluth Complex. It defines the outer fringe of Zone 4. Other mineralogic changes that occur as the contact with the Duluth Complex is approached include the disappearance of hematite and its replacement by magnetite and the appearance of fayalite, and immediately adjacent to the contact, ferrosilite.

Fayalite is restricted to cherty divisions within Zone 4. Typically, it occurs as small anhedral grains that contain included grains of older-formed minerals (Fig. 25). The origin of the fayalite is somewhat equivocal. Textural features

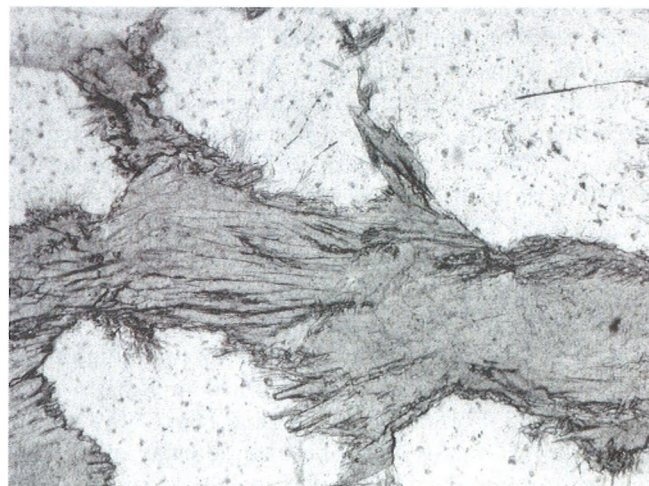


Fig. 24. Optical image of acicular grunerite in a matrix of quartz from Zone 4. Field of view is about 1000 μm across.

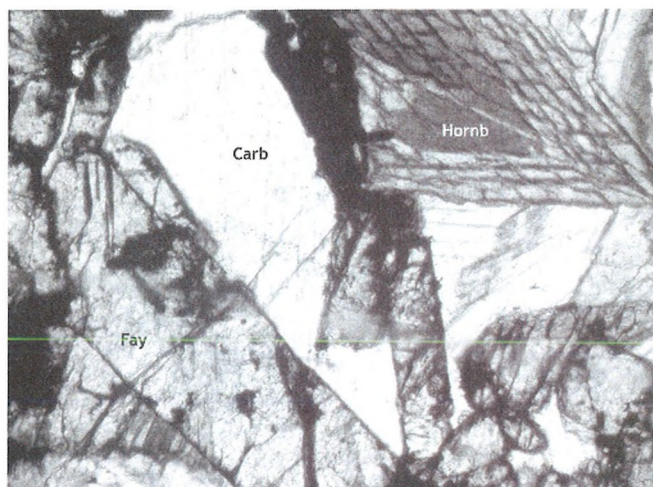


Fig. 25. Optical image of fayalite (Fay) intergrown with hornblende (Hornb) and carbonate (Carb). Field of view is about 600 μm across.

imply that it formed by a reaction involving quartz and magnetite (Gundersen and Schwartz, 1962). Other textural evidence implies that it evolved from siderite like that seen in Zone 1 (Morey et al., 1972) or by a reaction involving quartz and grunerite as in Zone 2 (French, 1968). Regardless of textural attributes, the fayalite occurs over a very restricted iron-rich compositional range.

A calcium pyroxene, hedenbergite, is abundant throughout the iron-formation in Zones 3 and 4. It is medium to coarse-grained and generally forms interlocking aggregates, layers, or mottles. Analyzed grains from Zone 3 display a wide range of compositions marked by substitution of magnesium for iron (Morey et al., 1972). Textural evidence implies that hedenbergite takes the place of the ankerite found in unmetamorphosed iron-formation (Morey et al., 1972). The amphibole hornblende occurs as both prograde and retrograde phases. Prograde hornblende occurs intergrown with hedenbergite in the lower part of Zone 4 (Fig. 26). More commonly, however, very fine acicular to fibrous hornblende is a retrograde phase that replaces hedenbergite, mainly at grain margins. Retrograde, acicular grunerite is also commonly found surrounding grains of hedenbergite (Fig. 27).

Phases of the enstatite-ferrosilite series (Deer et al., 1992) originally identified as ferrohypersthene (Gundersen and Schwartz, 1962; Bonnichsen, 1975) are widespread and abundant throughout Zone 4; they are the most abundant silicate at the Dunka River locality (Bonnichsen, 1975) at the far eastern end of the range. It occurs primarily as large, tabular crystals that in part initially crystallized as pigeonite and then inverted to ferrosilite during cooling. As previously noted it has been extensively replaced by cummingtonite.

Two garnet varieties were identified in Zone 4 of the Biwabik Iron Formation, almandine ($\text{Fe}_3\text{Al}_2\text{Si}_3\text{O}_{12}$) and andradite ($\text{Ca}_3\text{Fe}_2\text{Si}_3\text{O}_{12}$). The almandine is more abundant and is found to be present in the lower part of the Lower Slaty member and the lower part of the Lower Cherty member (Morey et al., 1972). The garnet occurs

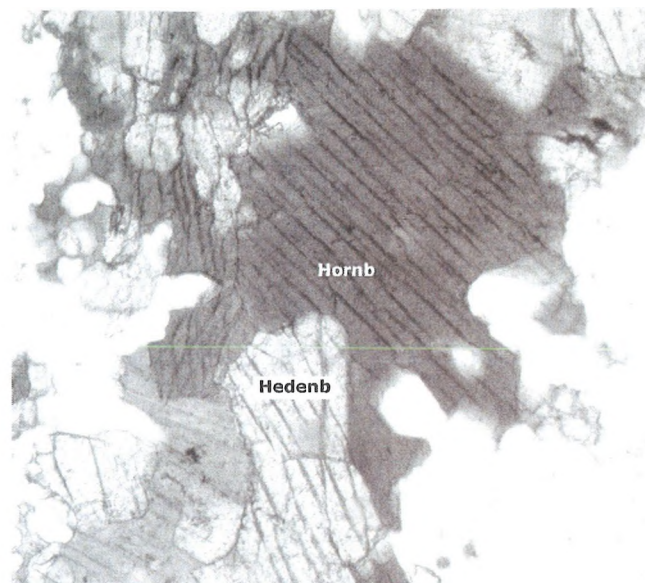


Fig. 26. Optical image of hornblende (Hornb) and hedenbergite (Hedenb) from Zone 4. Field of view is about 1000 μm across.

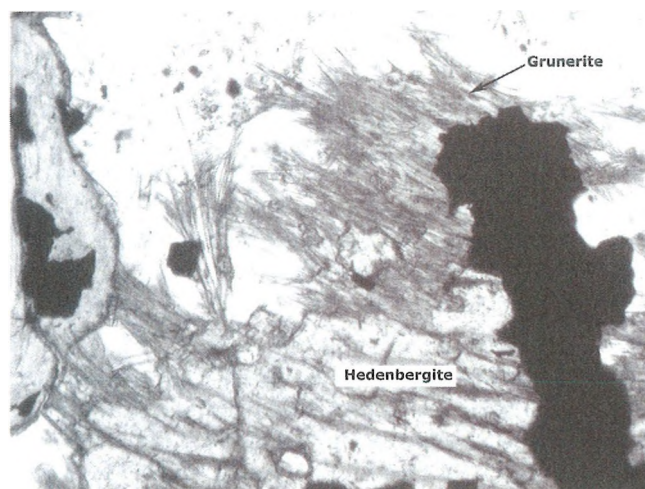


Fig. 27. Optical image of retrograde grunerite surrounding hedenbergite. Field of view is about 550 μm across.

as euhedral grain typically with cores of earlier minerals (Fig. 28).

7. Conclusions

Textures and mineral compositions associated with both unmetamorphosed and metamorphosed Biwabik Iron Formation are complex. The iron-formation is heterogeneous on a scale of a few inches to a few feet. Thus, any single mineral or mineral assemblage is a function of the bulk composition of the specific bed involved. At the east end of the range, further complexities arise from superimposed metamorphic conditions associated with the emplacement of the Duluth Complex. New minerals formed both under prograde conditions as metamorphic temperatures increased and under retrograde conditions as temperatures

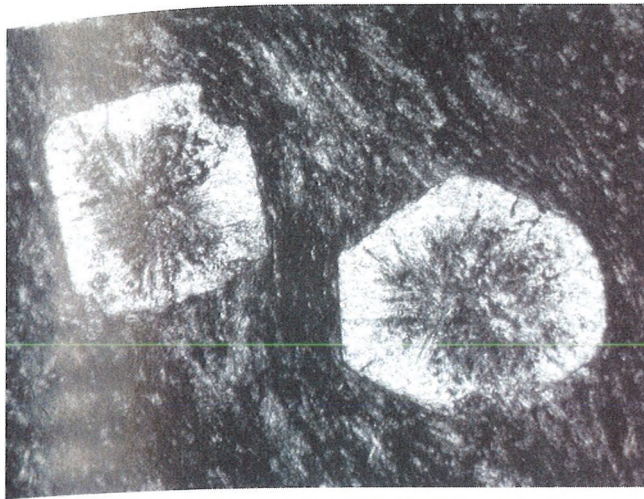


Fig. 28. Optical image of almandine garnet in a matrix of grunerite, magnetite and carbonaceous materials. Field of view is about 600 μm across.

decreased. Therefore, one cannot assume that the mineralogy in one mine or part of the range will be identical in correlative units in other mines or parts of the range.

Conflict of Interest

Analytical work was done, on a consulting basis, for one of the mining companies that is operating on the Mesabi Iron Range, as was analytical work done for one of the State agencies that regulates the mining companies

Acknowledgments

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References

- Bonnichsen, B., 1969. Metamorphic pyroxenes and amphiboles in the Biwabik Iron Formation, Dunka River area, Minnesota, in *Pyroxenes and amphiboles: crystal chemistry and phase petrology*. Mineralogical Society of America Special Paper 2, 217–239.
- Bonnichsen, B., 1975. Geology of the Biwabik Iron Formation, Dunka River area, Minnesota. *Economic Geology* 70, 319–340.
- Deer, W.A., Howie, R.A., Zussman, J., 1963. In: *Rock-Forming Minerals*, vol. 5. Wiley, New York.
- Deer, W.A., Howie, R.A., Zussman, J., 1992. An introduction to rock-forming minerals, second ed. Prentice Hall, London, pp. 696.
- French, B.M., 1968. Progressive contact metamorphism of the Biwabik Iron-formation, Mesabi Range, Minnesota. *Minnesota Geological Survey Bulletin* 45, 103.
- French, B.M., 1973. Mineral assemblages in diagenetic and low-grade metamorphic iron-formation, in Precambrian iron-formations of the world. *Economic Geology* 68 (7), 1063–1074.
- Griffin, W.L., Morey, G.B., 1969. The geology of the Isaac Lake quadrangle, St. Louis County, Minnesota. *Minnesota Geological Survey Special Publication Series SP-8*, 57 p.
- Gruner, J.W., 1936. The structure and composition of greenalite. *American Mineralogist* 21, 449–455.
- Gruner, J.W., 1944. The composition and structure of minnesotaite, a common iron silicate in iron formation. *American Mineralogist* 29, 363–372.
- Gruner, J.W., 1946. The mineralogy and geology of the taconites and iron ores of the Mesabi range, Minnesota. St. Paul, Office of the Commissioner of the Iron Range Resources and Rehabilitation, 127 p.
- Gundersen, J.N., 1960. Stratigraphy of the eastern Mesabi district, Minnesota. *Economic Geology* 55, 1004–1029.
- Gundersen, J.N., Schwartz, G.M., 1962. The geology of the metamorphosed Biwabik Iron-Formation, Eastern Mesabi district, Minnesota. *Minnesota Geological Survey Bulletin* 43, 139.
- Jirsa, M.A., Miller, J.D., Morey, G.B., 2008. Geology of the Biwabik Iron Formation and Duluth Complex. *Regulatory Toxicology and Pharmacology* 52, S5–S10.
- Klein Jr., C., 1974. Greenalite, stilpnomelane, minnesotaite, crocidolite and carbonates in a very low-grade metamorphic Precambrian iron-formation. *Canadian Mineralogist* 12, 475–498.
- Klein Jr., C., 1983. Diagenesis and metamorphism of Precambrian banded iron-formations. In: Trendall, A.S., Morris, R.C. (Eds.), *Iron-Formations. Facts and Problems*. Elsevier, New York, pp. 417–469.
- LaBerge, G.L., 1967. Microfossils and Precambrian iron-formations. *Geological Society of America Bulletin* 78 (3), 331–342.
- Mengel Jr., J.T., 1965. Precambrian taconite iron formation: a special type of sandstone. In: *Geological Society of America, 79th Annual Meeting, Kansas City, Missouri, 1965, Program*, p. 106.
- Miyano, T., 1987. Diagenetic to low grade metamorphic conditions of Precambrian iron-formation. In: Uipterdijk Apple, P.W., LaBerge, G.L. (Eds.), *Precambrian Iron-Formations*. Theophrastus Publications, Athens, pp. 155–186.
- Morey, G.B., 2003. Paleoproterozoic Animiekie Group related rocks and associated iron ore deposits in the Virginia Horn. In: M.A. Jirsa, G.B. Morey (Eds.), *Contributions to the Geology of the Virginia Horn Area, St. Louis County, Minnesota*. Minnesota Geological Survey Report of Investigation 53, 74–102.
- Morey, G.B., Papike, J.J., Smith, R.W., Weiblen, P.W., 1972. Observations on the contact metamorphism of the Biwabik Iron-formation, east Mesabi district, Minnesota. In: Doe, B.R., Smith, D.K. (Eds.), *Studies in Mineralogy and Precambrian Geology*, vol. 135. Geological Society of America, Memoir, pp. 225–264.
- White, D.A., 1954. The stratigraphy and structure of the Mesabi range, Minnesota. *Minnesota Geological Survey Bulletin* 38, 92.
- Wolff, J.F., 1917. Recent geologic developments on the Mesabi Iron Range, Minnesota. *American Institute of Mining and Metallurgical Engineers, Transactions* 56, 229–257.



The mineral nature of asbestos

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Abstract

Fibrous minerals are common in nature but asbestiform minerals are rare. The unique mineralogical characteristic common to all the asbestos minerals is their morphologic form (or habit of crystallization) as polyfilamentous fiber bundles. The individual fibrils within the bundles have a tendency to be very long with a narrow range of diameters and grow with their long fiber axis in parallel orientation to the bundle length. The asbestiform habit imparts to the asbestos minerals sufficient flexibility and tensile strength so that most can be woven into cloth. In the past application has focused on their ability to insulate against the transfer of heat. However, these minerals possess other properties which make them useful in many industrial applications.

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Keywords: Asbestos; Asbestiform; Fibrous

The ancient world made use of the asbestos minerals, invented the names amiantos and asbestos, and developed practical uses for these minerals which continue to the present. The enormous demand for asbestos, currently around 2,000,000 tons per year worldwide, developed over the last 120 years. The asbestiform minerals rarely occur in sufficient abundance to be of commercial importance; only one asbestiform serpentine mineral and five asbestiform amphibole minerals occur in such abundance. These six industrial minerals, known collectively as asbestos, share a unique set of physicochemical properties, although each can be distinguished from another by their chemical compositions and structure. The one serpentine asbestos mineral, chrysotile, crystallizes in the form of rolled up sheets structurally unique in nature and different from the double-chain structure that characterize the five amphibole minerals. The amphibole minerals can occur in habits

which are not polyfilamentous and therefore are not classified as asbestos. These non-asbestos amphiboles occur commonly and represent 5% of the earth's crust.

The various words used in antiquity to denote the asbestos minerals, including asbestos, asbestus, asbestinon, asbest, asbeste, asbeston, abeston, amiantos, amiantus, amianthus, amiant, and amiante, can be traced back to the writings of the ancient Greek philosophers and their use of two words—*αμιαντος* (amiantos) and *ασβεστος* (asvestos). The Greek physician, Pedanius Dioscorides of Cilicia (40–90 A.D.) describes an “undefiled stone”, *αμιαντος λιθος*—transliterated as amiantos lithos, which occurs in Cyprus. In modern Greek usage, the noun *λιθος* (lithos) is omitted and replaced with *αμιαντος* (amiantos). Dioscorides and other ancient Greek writers used the noun *αβσεστος* (asvestos) to mean quicklime; a meaning retained in Modern Greek. However, Pliny the Elder apparently misunderstanding the use of this word by the early Greeks and replaced the Greek noun for quicklime, asvestos, with the Latin word asbestinon, or “asbestos.” The familiar claim that the Romans knew the hazards of

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asbestos has its likely origin in mistranslating asbestos for quicklime, which was used on occasion by the Romans in battle to choke the enemy (Browne and Murray, 1990).

The ancient word took on a new meaning with the development of the science of mineralogy and the commercial use of the asbestos in the 19th Century. The term was used to describe a group of six minerals in commerce having the following desirable industrial properties:

- Long fibrous shape.
- High tensile strength and flexibility.
- Low thermal and electrical conductivity.
- High absorbcency.
- High mechanical thermal stability.
- Resistance to acids and bases.

Fibrous crystals of minerals are fairly common in nature but the formation of asbestiform minerals is rare; generally, minerals crystallize in more isometric shapes. The term fibrous includes other terms such as filiform, acicular, capillary, byssolitic, and asbestiform. Asbestiform fibers are a particularly rare form of fibrous mineral. The unique mineralogical characteristic common to all of the asbestos minerals is that their morphologic form or habit of crystallization as polyfilamentous fiber bundles (see Fig. 1). The one serpentine and five amphibole minerals, which form the various types of commercial asbestos, more commonly, crystallize into other habits. The non-asbestos habits do not possess the desirable industrial properties noted above (see Fig. 2) (Langer et al., 1979; Ross et al., 1984). Asbestos forms in dilated rock either perpendicular (cross-fiber) or parallel (slip-fiber) to the opening in the rock (see Fig. 3). Slip-fiber commonly forms along the compressed limbs of tight fold in the host rock. Minerals other than the commercial asbestos minerals can, albeit rarely, crystallize in the asbestiform habit. While the clay mineral palygorskite occurs naturally, it almost exclusively forms with an asbestiform habit (Zoltai, 1981; Nolan et al., 1991). For example, other amphibole minerals, potassium winchite and richterite occur occasionally in asbestiform habit (Wylie and Huggins, 1980; Verkouteren and Wylie, 2000; Wylie and Verkouteren, 2000). Another amphibole, asbestiform fluoro-edenite has been described from Biancavilla in Sicily (Gianfagna and Oberti, 2001; Gianfagna et al., 2003).

Although the amphibole mineral group accounts for approximately 5% by volume of the earth's crustal mineralogy (Liebau, 1985), deposits of asbestos large enough to be commercially viable are rare. Small quantities of asbestos have been used since ancient times. With the needs of industry in the last decades of the 19th Century, exploitation became important; the fibers have physicochemical properties that made them useful in many applications (Alleman and Mossman, 1997). Since that time, more than 95% of the commercially developed asbestos ore deposits were of chrysotile asbestos, the geologically most abundant type of asbestos (Ross and Virta, 2001). Currently, chrysotile asbestos is mined in Russia, China, Kazakhstan, Can-

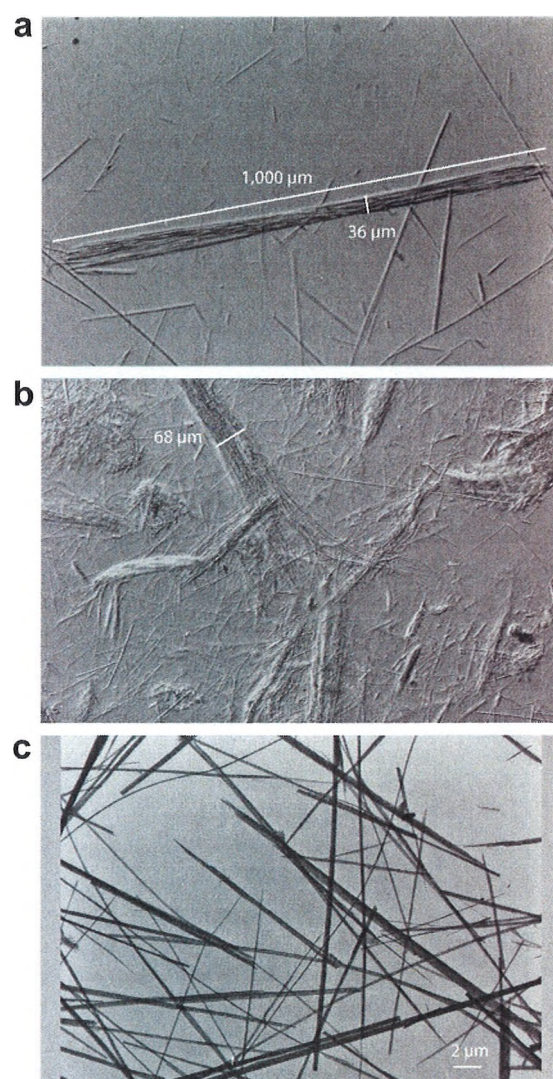


Fig. 1. Light photomicrographs (using Hoffman Optics) of the tremolite asbestos from Jamestown, California (a) and actinolite asbestos from Devon, England (b) note the polyfilamentous nature of the asbestos mineral. The fibers are bundles of much finer individual fibril that are shown in (c) transmission electron photomicrograph of the Devon actinolite asbestos.

ada, and Brazil. The remaining percentage was amphibole asbestos, predominately crocidolite and amosite. Although anthophyllite asbestos and tremolite asbestos have been mined to minor extents, a Finnish anthophyllite asbestos mine at Paakkila operated from 1918 to 1977. Anthophyllite and tremolite have been extensively mined from a number of small deposits across the state of Rajasthan in India (Mansinghka and Ranawat, 1996). Only these six commercial minerals are considered asbestos and are regulated under the various asbestos exposure standards (see Table 1).

With a few exceptions, commercially viable asbestos deposits contain 2–4% asbestos in the ore body. All of the major commercial asbestos fiber types have been mined in the Republic of South Africa although mines operate there today. Crocidolite mining also occurred in Australia

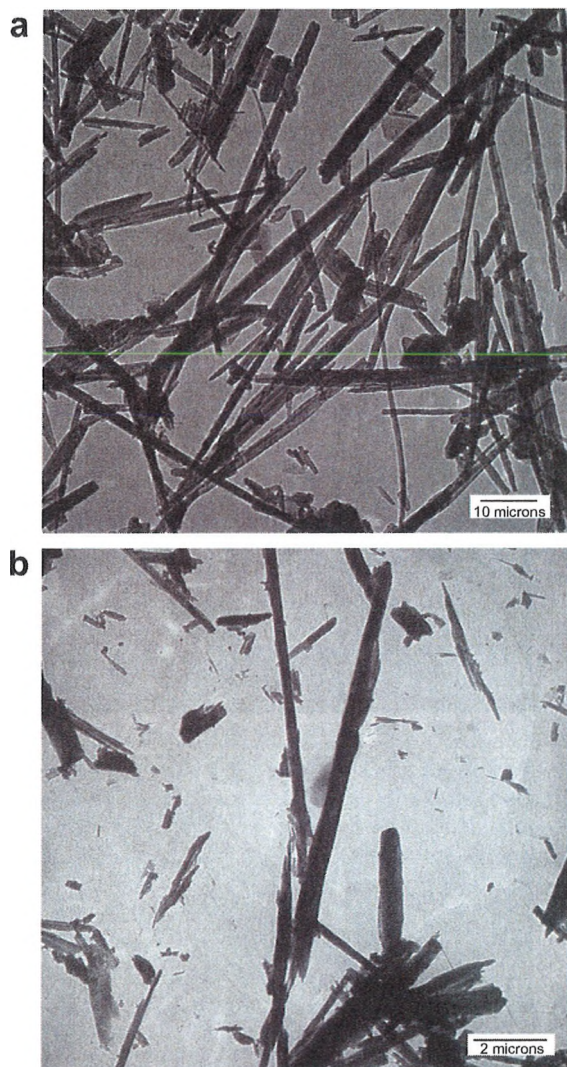


Fig. 2. Transmission electron photomicrograph of the tremolite asbestos from Metsovo, Greece associated with an increase risk of mesothelioma from environmental exposure (a). Note the morphological similarity with the tremolite asbestos found in a home in El Dorado, California (b).

and Bolivia. Current worldwide mining of amphibole asbestos, if it occurs, is on a very limited basis while current worldwide chrysotile asbestos production is approximately 2×10^6 tons per year.

The mention of asbestos in the ancient world most likely referred to chrysotile asbestos and tremolite asbestos (Browne and Murray, 1990; Ross and Nolan, 2003). Prior to the modern scientific age, knowledge of the differences between the various asbestos fiber types would not have been understood in a meaningful way. Interest focused on the remarkable properties of the mineral, the flexibility and tensile strength which allowed it to be spun into cloth. The high temperature stability allowing novel applications such as cremation wrappings made by the Romans to collect the ashes of the Emperors, external wicks for the lamps of the Vestal Virgins and the legendary tablecloth of Charlemagne reportedly cleaned by being placed in the fire after dinner for the amusement of his guests.

Knowledge concerning the elemental compositions and crystal structure of amphibole and serpentine minerals developed in the 19th and 20th Century, respectively. It was known to 19th Century mineralogists that minerals crystallizing in the asbestiform habit had higher tensile strength and flexibility than those crystallizing in the more common acicular or prismatic form (Zoltai, 1978; Langer et al., 1979). By the time of World War I, the elemental composition of many amphiboles had been determined and analysis of the morphology of large single crystals indicated the amphibole crystal class was either monoclinic or orthorhombic. By 1916, the chemical formula of tremolite, one of the simplest and most common of the amphibole group minerals, was well known to be $[\text{Ca}_2\text{Mg}_5\text{Si}_8\text{O}_{22}(\text{OH})_2]$ and belonged to the monoclinic crystal class. With the development of X-ray diffraction methods it was becoming possible to determine the arrangements of the atoms in the cell and therefore the number of chemical formula in the unit. Warren (1929) reported the first crystal structure of an amphibole—tremolite. The similarity of the amphibole structure allowed Warren (1930) to report on four more monoclinic amphiboles—kupferite, actinolite, hornblende, and grunerite. Further research would show that the various amphiboles with the monoclinic structure type would most commonly have C2/m space group symmetry (Hawthorne, 1983). Also, Warren and Modell (1930) would report the crystal structure of anthophyllite to be orthorhombic. All naturally occurring orthorhombic amphiboles so far identified belong to the space group Pnma (Hawthorne, 1983). The polyfilamentous bundles elongate along the c -axis with the fibrils parallel. The unit fibrils are disorientated in the ab -plane; asbestiform monoclinic amphiboles have parallel extinction in polarized light rather than the inclined extinction expected for monoclinic amphiboles (Wylie, 1979; Dorling and Zussman, 1986; Langer et al., 1991).

The essential structural features of the amphibole group are the following:

- Silica tetrahedral groups form a double chain with the repeating single chain unit having the composition $\text{Si}_4\text{O}_{11}^{6-}$ (see Fig. 1). All amphiboles are characterized by double chains of linked silica tetrahedral that repeat every 5.3 Å and lie parallel to the c -axis, almost always the direction of elongation in amphiboles. There are eight silicon atoms in the tetrahedral site per chemical formula unit. Aluminum can substitute for silicon in up to two of eight tetrahedral. Aluminum is not normally found in the commercial asbestos amphiboles but can be found in richterite, edenite, and winchite.
- The silica chain structure is four octahedra wide. These octahedral sites form four crystallographically distinct cation sites referred to as M_1 , M_2 , M_3 , and M_4 . These four types of octahedral sites contain the seven cations per formula unit: two in the M_1 sites, two in the M_2 sites, one in the M_3 site, and two in the M_4 sites. Two

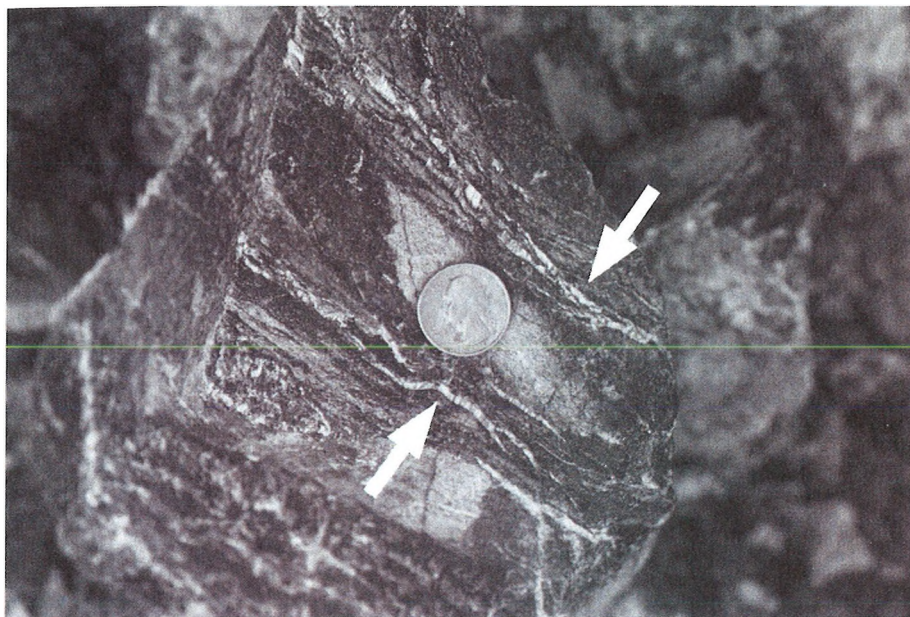


Fig. 3. Chrysotile from the asbestos mine in Belvedere Mountain, Vermont. The seams of chrysotile in the dilated rock are indicated by arrows.

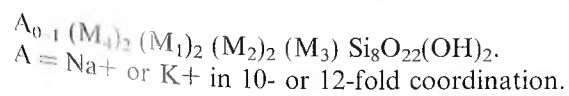
Table 1
Six commercial minerals regulated as asbestos in the United States

Name in Federal Asbestos Standards (Mineralogical Nomenclature)	Crystal Group	Chemical Formula
Actinolite (Actinolite Asbestos)	Amphibole	$\text{Ca}_2 \text{Fe}_5 \text{Si}_8 \text{O}_{22} (\text{OH})_2$
Amosite (Grunerite Asbestos)	Amphibole	$\text{Fe}_7 \text{Si}_8 \text{O}_{22} (\text{OH})_2$
Anthophyllite (Anthophyllite Asbestos)	Amphibole	$\text{Mg}_7 \text{Si}_8 \text{O}_{22} (\text{OH})_2$
Chrysotile (Chrysotile)	Serpentine	$\text{Mg}_3 \text{Si}_2 \text{O}_5 (\text{OH})_4$
Crocidolite (Riebeckite Asbestos)	Amphibole	$\text{Na}_2 (\text{Fe}_3^{2+} \text{Fe}_2^{3+}) \text{Si}_8 \text{O}_{22} (\text{OH})_2$
Tremolite (Tremolite Asbestos)	Amphibole	$\text{Ca}_2 \text{Mg}_5 \text{Si}_8 \text{O}_{22} (\text{OH})_2$

octahedral corners in each chemical formula are not shared with the silica tetrahedral; generally these corners are occupied by hydroxyl groups.

- Between the double chains, within the 6-fold rings of linked silica tetrahedral, there is an additional row of sites referred to as the A sites. These can be occupied by large cations (e.g., sodium or potassium only). These sites are never fully occupied in amphibole minerals, and rarely occupied in the asbestiform amphiboles.

The M_1 , M_2 , and M_3 octahedral sites form a chain consisting of five cations per chemical formula, which are between the opposite facing 6-fold rings of silica tetrahedral. The octahedral chains are linked by the large M_4 cations. Additional large ions can be found in the A structural site. The general formula for all amphibole composition is:



$M_4 = \text{Ca}^{2+}$, Na^+ , Mn^{2+} , Fe^{2+} , and Mg^{2+} in 6- or 8-fold coordination.

M_1 , M_2 , and $M_3 = \text{Mg}^{2+}$, Fe^{2+} , Mn^{2+} , Fe^{3+} in 6-fold coordination. Si^{4+} in the tetrahedral sites forms the double chains.

Complete substitutions can occur between Na⁺ and Ca⁺ and between Mg^{2+} and Fe^{2+} or Mn^{2+} .

These dissimilar octahedral sites can accommodate seven atoms of different sizes and valences allowing the amphibole group to have complex and far ranging element compositions. The amphibole group of minerals is made up of 27 separate mineral types with a large number of varietal species based on 23 chemical species (Whittaker, 1979; Veblen and Wylie, 1993; Leake et al., 1997). Those crystallizing in the asbestiform habit have the designation “asbestos” added after the mineral name.

Chrysotile asbestos is a serpentine mineral, the crystal structure of which is formed by a double layer composed of a tetrahedral and octahedral sheet: the tetrahedral and octahedral sheets having the composition $[n\text{Si}_2\text{O}_5]_{2n}^{2-}$ and the other a nonsilicate sheet of $[\text{Mg}_3\text{O}_2(\text{OH})_4]n^{2n+}$, respectively. The two other common serpentine minerals are lizardite and antigorite. Chrysotile asbestos is the only member of the serpentine group of any importance as a commercial mineral. It is the sixth mineral regulated under the asbestos standards and currently the only asbestos mineral of commercial importance with worldwide production of 2 million metric tons in 2001 (Virta, 2003).

The basic units of the tetrahedral sheets are six-membered rings, having pseudo-hexagonal or trigonal symmetry. These rings are similar to those found in the amphibole double chains. The amphibole chains differ in that the growth is restricted to a single direction to form

chains, whereas in chrysotile asbestos growth extends in two directions to follow an effectively infinite sheet. The octahedral sheet is formed by magnesium octahedrally coordinated with oxygen and hydroxyl groups and is similar to that found in brucite. The dimensions of the two sheets differ. Attention is generally focused on the *b* axis of the octahedral sheet, which is larger than the same axial direction in the tetrahedral sheet (9.45 Å compared with 9.15 Å). The dimensional mismatch of the octahedral and tetrahedral sheets can cause the double sheets to roll up into cylindrical tubes with the layer octahedral portion of the double layer forming to exterior of the curved surface. These fibrils are the ultimate minimum diameter that can be found in chrysotile and generally have a diameter around 25 nm. Usually, polygonal forms of chrysotile also occur rarely. The outer octahedral layer of chrysotile is readily leached of magnesium, even under mildly acid conditions (Hume and Rimstidt, 1992), and indeed chrysotile is now known to have a lower chemical durability than the amphibole asbestos minerals for this reason.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- Alleman, J.E., Mossman, B.T., 1997. Asbestos revisited. *Sci. Am.*, 70–75.
- Browne, K., Murray, R., 1990. Asbestos and the Romans. *Lancet* 336, 445.
- Dorling, M., Zussman, J., 1986. Characteristics of asbestiform and non-asbestiform amphiboles. *Lithos* 20, 469–489.
- Gianfagna, A., Oberti, R., 2001. Fluoro-edenite from Biancavilla (Catanina, Sicily, Italy): crystal chemistry of a new amphibole end-member. *Am. Miner.* 86, 1489–1493.
- Gianfagna, A., Ballirano, P., Bellatreccia, F., Bruni, B., Paoletti, L., Oberti, R., 2003. Characterization of amphibole asbestos linked to mesothelioma in the area of Biancavilla, Eastern Sicily, Italy. *Mineral. Mag.* 67, 1221–1229.
- Hawthorne, F.C., 1983. The crystal chemistry of the amphiboles. *Can. Mineral.* 21, 173–480.
- Hume, L.A., Rimstidt, J.D., 1992. The biodegradability of chrysotile asbestos. *Am. Miner.* 77, 1112–1128.
- Langer, A.M., Rohl, A.N., Wolff, M.S., Selikoff, I.J., 1979. Asbestos, fibrous minerals and acicular cleavage fragments: nomenclature and biological properties. In: Dement, J.M., Lemen, R.A. (Eds.), *Dust and Disease Society for Occupational and Environmental Health*. Pathox Publishers, Illinois, pp. 1–22.
- Langer, A.M., Nolan, R.P., Addison, J., 1991. Distinguishing between amphibole asbestos Fibers and elongate cleavage fragments of their non-asbestos analogues. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms of Fiber Carcinogenesis*. NATO ASI Series. Plenum Press, New York and London, pp. 253–267.
- Leake, B.E. et al., 1997. Nomenclature of Amphiboles: Report of the Subcommittee on Amphiboles of the International Mineralogical Association. Committee on New Minerals and Mineral Names. *Can. Mineral.* 35, 219–246.
- Liebau, F., 1985. *Structural Chemistry of Silicates*. Springer-Verlag, Berlin.
- Mansinghka, B.K., Ranawat, P.S., 1996. Mineral economics and occupational health hazards of the asbestos resources of Rajasthan. *J. Geol. Soc. India* 47, 375–382.
- Nolan, R.P., Langer, A.M., Herson, G.B., 1991. Characterization of paolygarskite specimens from different geological locales for health hazard evaluation. *Br. J. Ind. Med.* 48, 463–475.
- Ross, M., Nolan, R.P., 2003. History of asbestos discovery and use and asbestos-related disease in context with the occurrence of asbestos with ophiolite complexes. In: Dilek, Y., Newcomb, S. (Eds.), *Ophiolite Concept and the Evolution of Geological Thought*. Geological Society of America, Special Paper 373, pp. 447–470.
- Ross, M., Kuntze, R.A., Clifton, R.A., 1984. A Definition for Asbestos. Special Technical Publication 834. American Society for Testing Materials, Philadelphia, pp. 139–147.
- Ross, M., Virta, R.L., 2001. Occurrence, production and uses of asbestos. In: Nolan, R.P., Langer, A.M., Ross, M., Wicks, F.J., Martin, R.F. (Eds.), *The Health Effects of Chrysotile Asbestos*. The Canadian Mineralogist, Special Publication 5, Ottawa, pp. 79–88.
- Veblen, D.R., Wylie, A.G., 1993. Mineralogy of Amphiboles and 1:1 Layer Silicates. In: Guthrie, G.D., Mossman, B.T. (Eds.), *Health Effects of Mineral Dust Reviews*. Mineralogy, 28, Washington DC, pp. 61–137.
- Verkouteren, J.R., Wylie, A.G., 2000. The tremolite-ferro-actinolite series: systematic relationships among cell parameters, composition, optical properties, and habit, and evidence of discontinuities. *Am. Miner.* 85, 1239–1254. (<<http://minerals.usgs.gov/minerals/pubs/commodity/asbestos/>>. Accessed March 23, 2004).
- Virta, R.L., 2003. Worldwide asbestos supply and consumption trends from 1900 through 2003. U.S. Geological Survey Circular 1298, 87 pp., U.S. Department of the Interior, Washington, DC.
- Warren, B.E., 1929. The structure of tremolite $H_2 Ca_2 Mg_5 (SiO_3)_8$. *Z. Kristallogr.* 72, 42–57.
- Warren, B.E., 1930. The crystal structure and chemical composition of the monoclinic amphiboles. *Z. Kristallogr.* 75, 161–178.
- Warren, B.E., Modell, D.I., 1930. The structure of anthophyllite $H_2 Ca_2 Mg_5 (SiO_3)_8$. *Z. Kristallogr.* 75, 161–178.
- Whittaker, E.J.W., 1979. Mineralogy, chemistry and crystallography of amphibole asbestos. In: Ledoux, R.L. (Ed.), *Short Course in Mineralogical Techniques of Asbestos Determination*. Mineralogical Association of Canada, Ottawa, pp. 1–34.
- Wylie, A.G., 1979. Optical properties of fibrous amphibole. In: Selikoff, I.J., Hammond, E.C. (Eds.), *Health Hazards of Asbestos Exposure*. Annals of the NY Academy of Sciences, New York, pp. 611–619.
- Wylie, A.G., Huggins, C.W., 1980. Characteristics of potassium winchite asbestos from the Allamore Talc District, Texas. *Can. Mineral.* 18, 101–107.
- Wylie, A.G., Verkouteren, J.R., 2000. Amphibole asbestos from Libby, Montana: aspects of nomenclature. *Am. Mineral.* 85, 1540–1542.
- Zoltai, T., 1978. History of asbestos-related mineralogical terminology. In: Gravatt, C.C., LaFleur, P.D., Heinrich, K.F.J. (Eds.), *Workshop on Asbestos: Definitions and Measurement Methods*. National Bureau of Standards, Special Publication 506, Maryland, pp. 1–18.
- Zoltai, T., 1981. Amphibole asbestos mineralogy. In: Veblen, D.R. (Ed.), *Amphiboles and Other Hydrous Pyriboles-Mineralogy*. Mineralogical Society of America, Washington, DC, pp. 237–278.



The origins of public concern with taconite and human health: Reserve Mining and the asbestos case

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Abstract

Asbestos first became an issue to Minnesota's iron industry when it was revealed that mineral fibers similar to those in Reserve Mining's tailings were being found in drinking water for several communities that used Lake Superior as their primary water source. This discovery turned what had largely been an environmental court battle into a case concerning public health. The courts listened to much conflicting and uncertain scientific testimony on the size and distribution of the mineral fibers and on the potential health effects imposed by them. In April 1974, the plant was ordered to shut down by a federal judge but the company quickly appealed the decision. The appeals court granted a stay and ultimately ruled that the plant's closure could not be justified based on the unknown health effects of the mineral fibers since the consequences of such an action would have immediate and severe social and economic impacts. The plant was allowed to continue operation, but ordered to abate emissions to air around the plant and to switch to a land-based tailings disposal system. Much of the scientific uncertainty and public concern over mineral fibers in Minnesota's taconite industry remain today.

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1. Introduction

1.1. Legal history of the taconite problem

On April 20, 1974, Federal District Court Judge Miles Lord ordered Reserve Mining to cease its waste taconite tailings discharge into Lake Superior. The shut down order sent shock waves throughout Minnesota and the nation. The immediate question raised was how this extraordinary decision was reached? It directly affected thousands of jobs with a potential negative economic ripple impacting not only Minnesota, but the nation. The cause for the order revolved around micron-sized elongated mineral fragments (hereafter referred to as "mineral fibers") contained in Reserve Mining's waste tailings. Although the order for an immediate shut down did not survive an appeal, and Reserve Mining was given time to convert to an on-land

disposal system, many of the scientific issues debated in the trial hold relevance today.

In the 1950s and 60s, Reserve Mining represented the emergence of a new technology that had revitalized the economy of an iron mining region running out of high-grade ore. To others however, Reserve Mining, with its processing plant located on the lakeshore, was viewed as causing pollution and unacceptable degradation to Lake Superior. Thus, when environmental allegations and asbestos concerns surfaced in state and federal courts, judges were required to strike a balance between protecting public and environmental health and preserving the economic well-being of society. In the Federal district court case, tried before Judge Miles Lord, the balancing struggle was made even more difficult because the scientific and medical evidence presented in the trial was strongly disputed and consequently did not provide a clear answer to the immensity and scale of the health threat provided by the mineral fibers (*United States v. Reserve Mining Company*, 1974). Historically speaking, the case illustrates the difficul-

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ties and uncertainties that are forever part of the mix of environmental, health, and economic issues faced by governmental decision-makers.

Following, we provide a brief background on Reserve Mining and the taconite mining industry and provide details of the trial that threatened the company's existence. Reserve Mining's case files have been preserved in a large restricted compendium at the Minnesota Historical Society. In addition, numerous well-documented summaries exist, as do the court summaries themselves (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974; Huffman, 2000; Schaumburg, 1976; Bartlett, 1980). For a more detailed history of Reserve Mining and the court cases against it, readers are encouraged to consult these sources.

1.2. Minnesota's taconite industry

The iron mining industry in Minnesota began with discovery of iron ore in 1865, initial production in 1885, and rapid expansion through the 1890s. Initially, the targeted ore on the Mesabi Range was high-grade hematite ("natural ore"), which was the oxidized and purified surface weathering product of the much more extensive but lower grade taconite ore beneath. The natural ore could be scooped from deposits and shipped directly through the Great Lakes to steel mills in the eastern United States. As is the case in many ore districts however, the high-grade ore became less abundant with time and through the first half of the 20th century beneficiation of the iron-oxides from the much lighter silicate and carbonate gangue minerals became important. From 1906 to 1940, for example, the percentage of ore beneficiated increased from approximately 0.6% to over 50%. Clearly, the direct shipping ore was running out and survival through the end of the 20th century would require finding a means to utilize the vast reserves of low-grade "taconite" that surrounded or lay beneath the enriched oxidized deposits.

In Minnesota, most of the high-grade ore, and virtually all the taconite that has been mined has come from the Biwabik Iron Formation, a 250–700 foot thick bedded feature that extends approximately 120 miles in a northeastward direction from Grand Rapids to Babbitt, Minnesota (Fig. 1). Deposited originally as a series of soft, iron-rich sediments approximately 2 billion years ago, the formation was subsequently buried and metamorphosed to current form, which includes fine-grained magnetite as the dominant iron-ore mineral. This mineral is interspersed with significant amounts of other non-magnetic phases, including carbonates (ankerite, siderite, etc.) and silicates (quartz, stilpnomelane, minnesotaite, greenalite, etc.), and other minerals that must be removed by ore refining processes. The deposit is extensively metamorphosed on the eastern side of the range to other assemblages including among a variety of minerals, iron-rich amphiboles in the grunerite-cummingtonite series, which in some geologic settings can develop a fibrous or asbestiform habit.

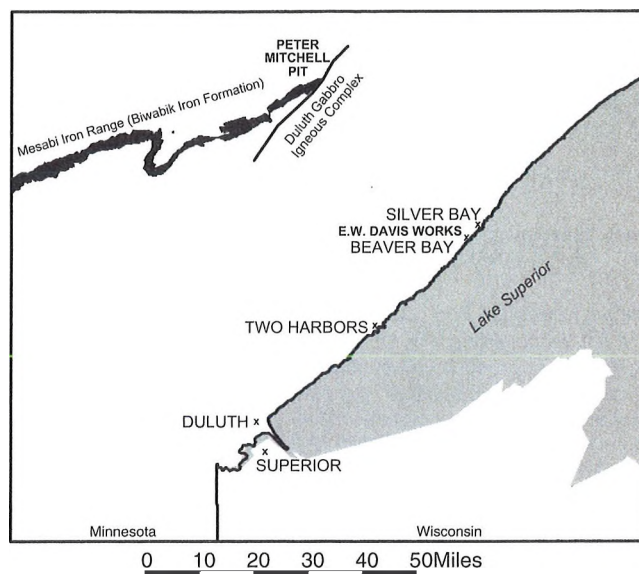


Fig. 1. Map showing locations of Reserve Mining Company's Peter Mitchell Pit and E.W. Davis Works Mineral processing facility. The Peter Mitchell Pit (now Northshore) was located at the eastern extreme of the Biwabik Iron Formation where proximity to the Duluth Gabbro Igneous Complex caused metamorphism of the formation to an assemblage containing the fibrous amphibole cummingtonite-grunerite. Ore was transported to Silver Bay and processed at Reserve's E.W. Davis Works mineral processing facility. Tailings were deposited into Lake Superior. Mineral fibers were found in Silver Bay's air, and in water supplies for Duluth, Two Harbors, and Beaver Bay, MN, as well for Superior, WI.

The difficulties with utilizing taconite as an ore source were many. The fine-grained taconite required extensive grinding to separate the sought-after magnetite (Fe_3O_4) grains from non-ore or "gangue" minerals. Furthermore, the fine-grained magnetite concentrate that resulted after separation was difficult to ship and use in blast furnaces. Finally, 70% of taconite ore winds up as tailings and must be disposed using environmentally sound methods, compared with essentially no tailings for the direct shipping ore.

These issues were all apparently resolved in the 1940s by a small group of mining engineers and investors, led primarily by Dr. E.W. Davis, who was director of the Mines Experiment Station at the University of Minnesota. By their process, much of which has remained nearly the same through today, magnetite grains were sorted from other minerals using large magnetic separators and then combined with other agents (binders and possible fluxing agents) and heated to high temperatures in large furnaces to create taconite pellets. These pellets are easier to ship and to use in the steel making process than simple magnetite concentrate. The unwanted fine-grained gangue minerals, or "tailings", which are composed of a variety of silicate and carbonate minerals, are slurried with water and transported to a disposal site.

Reserve Mining's deposits were first investigated in 1871 by Peter Mitchell who described them as "an iron mountain about twelve miles long and a mile and a half wide". However, composed essentially of taconite that could not be mined as economically as the high-grade deposits in

the western part of the iron range, the deposit laid in wait until a time when mining taconite would become profitable. That time came when Davis and his coworkers perfected their processing techniques. In 1947 and 1948, at a time when environmental laws were less stringent than today, Reserve Mining obtained permits to open the Peter Mitchell pit and to build a taconite processing facility on the shore of Lake Superior. The lake provided a ready source for clean water needed during taconite processing. Production began in 1955. Ore from the Peter Mitchell pit was carried by rail to Silver Bay, where it was processed at the E.W. Davis Works (Fig. 1). Taconite pellets could be loaded directly into ships, while the unused materials, or tailings could be dumped into the lake. Having a bulk density much greater than that of lake water, it was expected that the tailings/water mixture generated during mineral processing would be conveyed along the lake bottom in density currents and the tailings would settle into a nine square mile area within a bathymetric feature known as the Great Trough. According to the permit, discharge into the lake was not to include *material* amounts of wastes other than taconite, nor was it to have *material* effect on fish populations, surface water appearance, or lake navigation outside the nine square mile area. The state reserved the right to revoke the permit should conditions of the permit be violated.

The venture appeared successful and other taconite companies were built. All of the other companies built on-land disposal systems for their taconite tailings. Taconite mining (Fig. 2) as an industry flourished with total production of pellets increasing to over 10 million tons/year by 1960 (Skillings, 2002). Six companies were producing a total of 30 million tons of pellets per year by 1968. Reserve Mining, which had expanded to over 5 million tons of pellet production by 1957 expanded again to over 10 million tons by 1965. When environmental concerns

over Reserve Mining's tailings began to emerge it had already become clear that using magnetic separation to beneficiate taconite had saved Minnesota's mining industry.

By 1979, taconite mining in Minnesota reached its peak, with eight companies producing approximately 55 million tons of pellets (Skillings, 2002). By 2001, a total of 4.3 billion tons of iron shipments had been made from Minnesota since mining began in 1885, with total shipments in the later half of the century eclipsing shipments in the first half (Fig. 3). Through 2001, approximately 1.5 billion tons of taconite pellets had been shipped, all since 1950. This represents only a fraction of the vast taconite ore reserves that, by one estimate, could last at present rates of mining for two centuries or more (Ojakangas and Matsch, 1982). Today, greater than 99% of all iron ore shipments from Minnesota are derived from taconite.

Commensurate with the expansion of taconite mining at Reserve Mining were increased amounts of water used and waste produced. At full capacity after 1963, Reserve Mining was using over 500,000 gallons of Lake Superior water per minute and disposing approximately 67,000 tons of tailings per day. The company accounted for approximately 11% of the total US iron production and approximately 25% of Minnesota's taconite pellet production. Furthermore, the town of Silver Bay had grown up around the E.W. Davis processing facility. In Silver Bay alone, and not including the area around Babbitt (where the ore was mined), the company employed over 1000 workers and supported another 2000 others who provided services for the processing plant or employees that worked there.

1.3. Environmental issues arise

Environmental complaints on Reserve's tailing can be traced back at least to 1963 when Senator Gaylord Nelson

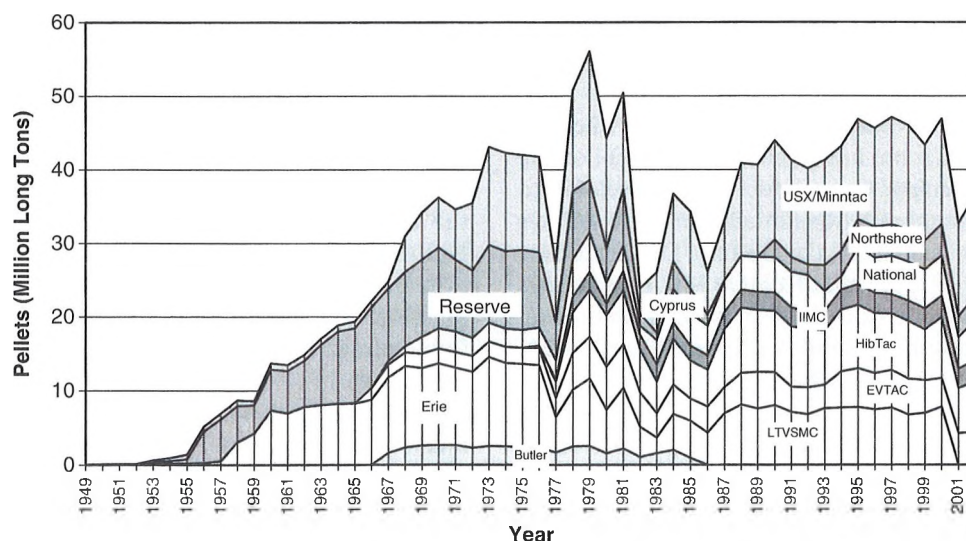


Fig. 2. Pellet production by Minnesota taconite companies. Reserve Mining Company was one of the first large taconite mining companies in Minnesota and the only to dispose tailings into Lake Superior. There are currently six taconite companies that annually produce 30–40 million tons of taconite pellets.

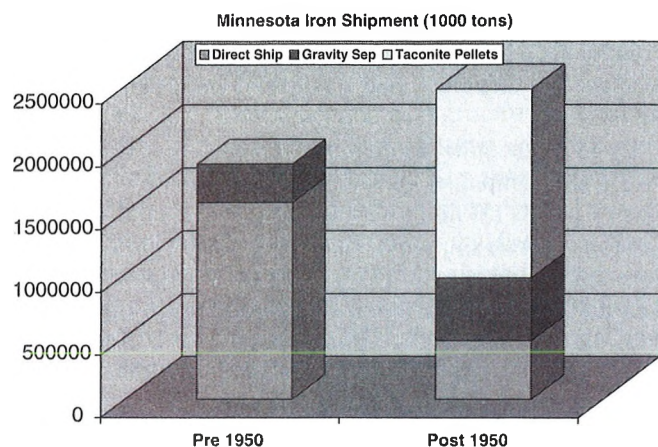


Fig. 3. Iron ore shipments from Minnesota before and after 1950. A total of 4.3 billion tons of direct shipping ore, gravity separated concentrate, and taconite pellets (magnetic separation process) have been shipped. Most of this is in the form of natural ore. Reserve Mining Company ushered in a new era in Minnesota mining as direct shipping and other ore types of ore dwindled. Currently, virtually all of the ore shipped from Minnesota is derived from taconite, but the total of 1.5 billion tons of pellets shipped through 2001 represents only slightly more than 1/3 of the total Minnesota shipments.

of Wisconsin began inquiring federal administrators about possible actions against Reserve Mining concerning pollution control. More specific environmental allegations against Reserve Mining were made in a 1968 U.S. Department of Interior (USDI) study which became known as the Stoddard Report, named after the environmental coordinator for the Lake Superior region. Although never officially released by the USDI or any of its collaborators, it was widely circulated and became the first major technical report to openly attack in-lake disposal of taconite tailings.

Shortly after, in 1969, Reserve Mining found itself in state courts fighting against new water standards and regulations that, if strictly enforced, would cause the shut down of the company. One concern expressed by the MPCA (Minnesota Pollution Control Agency) and others was related to the so called green water phenomena, which was a change in the color of lake water as viewed from the shoreline. The effect had been observed elsewhere in the lake prior to mining, but appeared to increase following Reserve Mining's opening. Other concerns were related to possible declining fish populations in and near the tailings disposal regions. Indeed, the Lake County District Court found on December 15, 1970 that Reserve Mining's tailings were causing an "increase of the 'green water phenomena' both within and without the zone of discharge" and also a "decrease in the presence of Pnotoporeia, commonly known as scud, in the vicinity of the zone of discharge... [with] minimal and immaterial effect on the fish population of the lake." The court chose not to rule, however, on a claim by the MPCA that Reserve Mining was polluting the lake, but it did mandate that the company seek an alternative disposal mechanism to insure that tailings were conveyed to the bottom of the lake in a more efficient fashion.

Although these rulings were significant, more formal and what turned out to be more serious allegations against Reserve Mining were taking root in a series of three Federal Water Pollution Enforcement Conferences held in Minnesota from 1969–1971. Directly following the enforcement conferences, in April, 1971, Reserve Mining was notified by the EPA that they had 180 days to comply with federal and state water quality standards or face a federal law suit. Not satisfied with Reserve Mining's response, the EPA filed suit against the company in the US District Court in Minnesota on February 2, 1972. Although the initial court claims did not even mention the word "asbestos" in connection with Reserve Mining's tailings discharge, they alleged 48 violations of federal and state water quality standards, the Refuse Act of 1899, and federal common-law nuisance standards. Perhaps more significant, is the fact that the complaints and lawsuit fueled extensive research into the nature and extent of tailings distribution in Lake Superior's waters.

1.4. Asbestos becomes an issue

The first appearance of asbestos as an issue for Reserve Mining can be traced to December, 1972, when Arlene Lehto, president of the Save Lake Superior Association, announced in a scheduled hearing before the International Joint Commission that taconite tailings contained a fibrous amphibole that might be a cancer-producing agent and indicated that people drinking water from Lake Superior might be ingesting it. Although the IJC commissioners and the press took no special notice of the announcement, Phillip Cook, Duluth National Water Quality laboratories technical case coordinator for the Reserve Mining case did. In late December, he began filtering Duluth tap water and subsequently discovered that mineral fibers were always present in Duluth's water. John Pegors, director of the PCA regional office in Duluth also heard Arlene Lehto. Subsequently, the PCA hired a geologist, Dr. Stephen Burrell, who documented the occurrence of fibrous minerals in Reserve's ore and also found that fibers were escaping into the air during mineral processing.

The concern was over fibrous minerals found in ore coming from the Peter Mitchell Pit. This pit occurs at the eastern most edge of the Biwabik Iron formation, where the deposit is truncated by igneous intrusions from the Duluth Complex. The high heat that accompanied intrusion of the igneous bodies resulted in intense metamorphism of the formation to an assemblage of minerals not found elsewhere on the Mesabi Iron Range. In some parts of Reserve Mining's ore deposit, as the courts would later hear in testimony, an average of approximately 26% and as much as 60% ore from the Peter Mitchell Pit was composed of cummingtonite-grunerite, a series of amphiboles with the approximate formula $(\text{Fe,Mg})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$ (United States v. Reserve Mining Company, 1974). This series of minerals can occur in a variety of crystal forms, depending on the specific conditions of metamorphism. Amosite is the

term used to describe an economically important and known carcinogenic form of this mineral that is especially iron-rich and exhibits asbestiform habit. Thus, cummingtonite–grunerite and amosite are chemically similar, but may have different crystal forms. Specific concerns over a potential cancer threat peaked when the National Water Quality Laboratory in Duluth performed a literature search and found articles pointing to a possible linkage between ingested asbestos and cancer.

On June 15, 1973, after considerable debate in secret meetings, the public was informed that asbestos-like fibers, believed to be from Reserve Mining Company's tailings, had been found in the water supplies of many lake shore communities, including Duluth and were also being emitted into the air from the plant's exhaust stacks. This was a decided turning point in Reserve's history, as a company that had once been considered a technological marvel and economic savior was not only being accused of polluting Lake Superior water, but also threatened the health of thousands of lakeshore residents.

2. Reserve Mining in federal court

2.1. Tailing toxicity

The central focus of the controversy was related to the toxicity of the tailings. If the tailings were toxic and represented an immediate threat to human health and life then the courts were obligated to stop the discharge as early as possible. A lengthy trial ensued, during which the court heard testimony from many of the world's experts on various issues including asbestos and its possible health effects. The first significant ruling in this regard came from the district court on April 20, 1974, when Miles Lord ordered the closing of Reserve Mining's Silver Bay facility, based on the "substantial" danger that tailings in the water presented to human health (United States v. Reserve Mining Company, 1974). The Reserve Mining Company immediately filed an appeal and received a stay of that order on April 22, 1974. In June, 1974, Reserve Mining was issued a further stay, conditioned upon the company's taking prompt steps to abate air and water discharges. On April 8, 1975, the appeals court granted Reserve "a reasonable time" to stop discharging into Lake Superior and to convert to a land-based system (Reserve Mining Company v. Environmental Protection Agency, 1974). Beneath this brief timeline of court proceedings were hotly contested issues relating to the health risks associated with asbestos. While nobody challenged the fact that asbestos can cause cancer if inhaled, there was much dispute over whether the fibrous mineral mined from Reserve Mining's deposit (cummingtonite–grunerite) was asbestos. Also of concern, was whether it was the source of the mineral fibers found in Lake Superior. In any case, were the minerals in tailings carcinogenic when ingested? The district court and appeals court agreed for the most part on the scientific evidence that there was a concern, but differed on their perceptions

of the degree of action required (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

2.2. Cummingtonite–grunerite distribution

A crucial question of the enforcement conferences, upon which federal authority partly depended, was whether tailings were being transported across state lines. Although the plaintiffs in the federal case did not initially consider cummingtonite–grunerite to be hazardous, its distribution was studied as a potential tool to detect the presence of Reserve Mining's tailings in Lake Superior's water column. Since other potential sources for this mineral did not drain directly into Lake Superior and because significant cummingtonite–grunerite was not found in rivers draining into Lake Superior (except by one discredited witness) or in pre-Reserve Mining lake sediments, and also because this mineral was known to be abundant in Reserve Mining's tailings, cummingtonite–grunerite proved to be an excellent tracer. That cummingtonite–grunerite was detected in the water column, well outside of the originally proposed nine square mile tailings disposal site, was used as evidence that some of the minerals present in Reserve Mining's tailings were not being deposited in the Great Trough, but rather escaping the density current and migrating throughout the lake. Later findings of cummingtonite–grunerite in the drinking water supplies for Duluth and other lakeshore communities provided evidence that people were ingesting small quantities of minerals from Reserve Mining's tailings (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

After extensive testimony from witnesses on both sides of the issue, the district court determined that "where cummingtonite–grunerite is found in the western arm of Lake Superior in detectable quantities, it can be traced to Reserve's discharge." The appeals court agreed (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

2.3. Asbestos or cleavage fragments?

On the issue of whether at least some of the cummingtonite–grunerite in tailings was amosite, the district court struggled to determine if there was a reliable means to distinguish cummingtonite–grunerite from amosite. Reserve witnesses contended that amosite had distinct optical properties and that amosite fibers were more likely to split into longer and thinner fibers than cummingtonite–grunerite. Indeed, government witnesses presented evidence that from 98% to 99.3% of amphibole fibers in Duluth's water supply were under 5 μm in length, and the average length was only about 0.8 μm . Reserve argued that the mineral fibers in tailings were cleavage fragments of cummingtonite–grunerite and not true asbestos fibers. Nevertheless, following testimony from both sides, the court found that "amosite

and cummingtonite–grunerite have in most instances similar morphology, crystallography, and chemistry and are therefore, indistinguishable. . . No one, to the Court's satisfaction, could point out distinguishing characteristics." The appeals court did not argue with this interpretation but noted that the "discharges of fibers dissimilar from amosite adds further uncertainty to equating the likely health consequences from Reserve's discharge with that found in certain other occupational situations" (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

2.4. Are short fibers dangerous?

On the issue of asbestos and harm to human health, there was contention over both air-borne asbestos near the Silver Bay processing plant and water-borne asbestos in Lake Superior. The court recognized published reports of high incidence of cancer and mesotheliomas for asbestos factory workers and their families and also in residents living close to the factories. A Department of Labor occupational safety standard of 2 fibers in excess of 5 microns per cubic centimeter of air existed at the time for prevention of asbestosis. Most fibers in Silver Bay and Lake Superior were much less than 5 μm in length. Doctors with expertise in this area testified, however, that the 5 μm value was set only because smaller fibers could not be easily detected and counted using normal optical microscopic techniques. The district and appeals courts, therefore, both ignored the length standard: short fibers could not be assigned a lower relative risk than long fibers, owing to "the uncertain state of scientific knowledge" (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

2.5. Fiber count difficulty

Both Courts also found that estimating exposure was almost impossible due to the fact that "man's ability to quantify the amount of particles in the air and water is subject to substantial error." Since this problem was faced not only by the court, but also by existing studies on which the standards were based, the district court concluded, "there is no known safe level of exposure. Without knowing what a safe level of exposure is, to permit the present exposure to continue is nothing more than a gamble with hopes that the threshold level, if there is one, has not been or will not be reached." The district court acknowledged problems with obtaining reliable counts but concluded that whatever amount there was, there was "a significant burden of amphibole fibers from Reserve's discharge in the air of Silver Bay." Regarding amphibole fibers in water, the district court concluded that whatever numbers they accepted, that "at all times (of the year) Reserve adds millions of asbestos fibers to every quart of water drunk by every citizen of Duluth, Two Harbors, Beaver Bay, and Superior, Wisconsin." (United States of America et al., vs. Reserve Mining

Company, 1974). The appeals court largely agreed with the assessment that the counts were unreliable and indicated that this added more uncertainty to evaluation of risk associated with Reserve's disposal into Lake Superior (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

2.6. Is ingestion of mineral fibers dangerous?

While little doubt existed that inhaled fibers were dangerous to lungs, considerable more speculation was necessary to evaluate risk associated with mineral fiber ingestion. Three forms of evidence were considered by both the district court, and later, the appeals court. First, asbestos workers were known to have increased incidence of gastrointestinal cancer, presumably because some of the asbestos inhaled is inevitably swallowed. The appeals court noted, however, that many assumptions were needed to compare exposure via this pathway compared to drinking water derived from Lake Superior and that this created more uncertainty. Additional evidence was provided that many small particles, once swallowed by an animal, could pass through the gut wall into the body. The appeals court accepted this, but also noted that animal studies had, so far, not been able to induce tumors by ingestion. Finally, the district court and appeals court varied considerably in their interpretation of results from a court-ordered tissue study of recently deceased Duluth residents who had ingested Duluth water for 15 years. This study, commissioned by the district court in the face of a lack of direct evidence of a health effect concerning ingestion of drinking water, found that the Duluth residents were virtually free of any fibers. Both courts indicated that the negative result did not necessarily exonerate ingestion of fibers in Lake Superior as a hazard. In the district court, it was concluded that "because the specimens examined represented only a small microscopically minute body area, the actual presence of fibers may have been overlooked." The appeals court weighed more heavily on the negative result however, and cited pre-study testimony from Dr. Selikoff, a court appointed specialist, that "if we do not find it [mineral fibers] in the tissues, then I would risk a professional opinion that there is no danger, at least up to this point, to the population no matter what our samples show." They concluded that the results from the tissue study indicated that "no emergency or imminent hazard to health exists" (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974). No evidence of an increase in gastrointestinal cancer rates could be found for Duluth residents for the period 1950–1969 or from another study for residents from 1969–1972. The district court and appeals court determined and both agreed however, that any studies conducted on Duluth residents to evaluate cancer incidence from ingestion of mineral fibers would be premature owing to the long latency period for asbestos related diseases (20 years

or more) (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

2.7. Court actions

Decisions by the district court on the dangers of ingesting asbestos can probably best be summed up by the statement: “The court is asked to permit the present discharge until such a time as it can be established that it has actually resulted in death to a statistically significant number of people. The sanctity of life is of too great value to the court to permit such a thing”. The appeals court concluded, similarly, although in less dramatic terms, that the “the existence of this asbestos contaminant in air and water gives rise to a reasonable medical concern for the public health. The public’s exposure creates some health risk and therefore such a contaminant should be removed” (Reserve Mining Company v. Environmental Protection Agency, 1974).

The difference in terms of required abatement of pollution was considerable. The district court considered the risks of allowing tailings disposal into the lake to be too great to allow it to continue for any length of time and ordered an immediate shut down. The appeals court, as stated above, overturned this decision finding that “an immediate injunction [on Reserve’s operations] cannot be justified in striking a balance between unpredictable health effects and the clearly predictable social and economic consequences that would follow the plant closing”. “A remedy should be fashioned which will serve the ultimate public well by insuring clean air, clean water, and continued jobs in an industry vital to the nation’s welfare” (United States v. Reserve Mining Company, 1974; Reserve Mining Company v. Environmental Protection Agency, 1974).

In terms of abatement, the appeals court considered the air emissions in Silver Bay to be of much more concern than the water discharges. Immediate action was required for the air emissions in the Silver Bay processing plant. “Reserve must use such available technology as will reduce the asbestos fiber count in the ambient air at Silver Bay below a medically significant level.” Since there was no known means to define “medically significant” the court ruled that the “controls may be deemed adequate which will reduce the fiber count to the level ordinarily found in the ambient air of a control city such as St. Paul” (Reserve Mining Company v. Environmental Protection Agency, 1974).

Water discharge abatement was a much more difficult and expensive proposition for the company. Accordingly, Reserve Mining was given “a reasonable time to stop discharging its wastes into Lake Superior. A reasonable time includes the time necessary for Minnesota to act on Reserve’s present application to dispose of its tailings at Milepost 7 (Lax Lake site), or to come to agreement on some other site acceptable to both Reserve and the state” (Reserve Mining Company v. Environmental Protection Agency, 1974).

3. Aftermath

Legal issues stemming from the case were not ended until April, 1982, when in a settlement the company agreed to pay \$2 million to Duluth and surrounding communities for water filtration systems, but not to admit any wrongdoing or causing of harm to public health. Previous to the settlement however, Reserve Mining fought vigorously with the state over the site of a new land-based disposal system for their tailings.

Several sites for tailings disposal were considered and rejected (by either Reserve, the courts, or the state), before the company proposed a facility located several miles inland known as Mile Post 7. The topography was rugged however, and would required construction of five dams totaling 26,700 feet in length. The largest of these would eventually reach 190 feet in height. Minnesota DNR and PCA officials were concerned about the possibility that a dam could rupture and threaten people living downstream and dump many tons of fine tailings into Lake Superior. Furthermore, there was concern over the levels of dust from the tailings that might blow into Silver Bay. Reserve Mining argued that these concerns could be addressed through facility design, technical suppression, and continuous maintenance. Furthermore, the company argued that all other alternative sites proposed by the state were prohibitively expensive and would force the Reserve Mining Company to shut down. Reserve eventually prevailed and was granted a permit for Mile Post 7, but not until April 1978, after a long struggle that brought the case twice before Minnesota’s Supreme Court. Some of the permitting issues the courts helped to settle were the same as those faced in previous court decisions and involved uncertainties and expense associated with the continuous monitoring, measurement, and control of mineral fibers in water discharges and air emissions from the plant. Construction of the new tailings basin began immediately, but was not completed until March, 1980 at a cost of \$375 million. In April, 1980, a full 6 years after Judge Lord’s fateful decision, the last of more than 400 million tons of tailings from Reserve’s processing plant was discharged into Lake Superior.

Economic downturns for the mining industry and the increased cost of mining took a toll on Reserve Mining over the next years. Production never came close to pre-trial levels and in 1986, one of Reserve Mining’s parent companies, LTV Steel, declared bankruptcy and the facility was closed. The company was sold to Cyprus Minerals, Inc., in 1989 and reopened on a much smaller scale. The company was later bought by Cleveland-Cliffs, and currently operates under the name “Northshore Mining Company”. Northshore Mining is testing a new process to produce reduced-iron nuggets (The Mesabi Nugget Project) that, if successful, might expand and change the nature of iron products from Minnesota. The iron-nugget pilot plant will produce pig-iron nuggets for electric furnace steel making and foundries. A time line for major events discussed above is provided in Table 1.

Table 1
Timeline of significant events for Reserve Mining Company

1860s	Iron deposits discovered and mapped in Minnesota
1880s	First shipments of direct shipping ore from Minnesota
1900	Gravity separation becomes necessary for some ores
1940	50% of all ore shipped from Minnesota requires processing
1940s	Taconite processing method developed (magnetic separation and shipping of taconite pellets)
1947–1948	Reserve Mining Taconite company receives permits to open taconite processing plant in Silver Bay, MN, and dispose tailings into Lake Superior
1955	First ore processed by Reserve Mining
1968	Taconite pellet shipment rate exceeds all other iron ore shipments from Minnesota
Dec. 1968	Stoddard Report issued alleging that Reserve Mining is polluting Lake Superior
1969–1970	Reserve in State Court
1969–1971	Enforcement conferences held
Feb. 1972	EPA files suit against Reserve Mining in US District Court
Dec. 1972	Asbestos issue begins to emerge in local meetings and studies of the issue quietly begin
June 1973	Press release: asbestos in Silver Bay air and in drinking water of lakeshore communities
Aug. 1973	Trial begins
Apr. 1974	Judge Lord issues injunction for immediate shut down of Reserve Reserve obtains temporary stay while appeals court hears case
Oct. 1974	Reserve proposes Mile Post 7 site for disposal
Dec. 1974	State rejects Mile Post 7 as site for tailings disposal
March, 1975	Court of appeals: allows Reserve reasonable time to find alternative disposal site
1977–1978	Minnesota Supreme Court orders state to issue permits for Milepost 7 Tailing Disposal facility
March 1980	Mile Post 7 tailings disposal facility completed at cost of \$375 million. Lake Superior discharges end.
April 1982	Legal settlement reached: Reserve pays \$2 million for lakeshore communities' water filtration systems
1986	Reserve Mining closes
1989	Reserve sold to Cyprus Minerals, Inc. and reopens as Cyprus Northshore Mining
1995	Plant and mine begin operation as Northshore Mining, Cleveland-Cliffs

4. Conclusions

The Reserve Mining case set a legal precedent in that it was the first legal opinion to deal with the important concept of balancing scientific uncertainty with economic impact. Despite testimony from essentially all of the world's leading experts in the field, no firm conclusions could be made regarding the health effects of ingested tailings.

The Eighth Circuit Court foresaw the need to monitor future developments when it suggested that the federal district court's appointed medical expert should advise the court regarding "new scientific or medical studies which may require a re-evaluation of the health hazard (either as more or less serious than as comprehended during this lawsuit) attributable to Reserve's discharges." The court also suggested that any party could apply for a modification to the injunctive relief granted by the court "should significant new scientific information justify a reassessment of the hazard to public health" (Reserve Mining Company v. Environmental Protection Agency, 1975).

The Fiber Symposium presents an opportunity to determine whether we are now beyond the "frontiers of medical and scientific knowledge". Significantly, thirty years after the Reserve mining case was in the national spotlight, sufficient time has presumably passed to overcome study problems associated with the long latency period for asbestos related cancers (20–45 years).

Futhermore, there have been technological advances in many fields of analytical chemistry and medical science.

Have these advances made it possible to better distinguish Reserve's mineral fibers from amosite or cleavage fragments from asbestos in general and, if so, what do the differences mean regarding a potential health threat of ingested and/or inhaled minerals? Do we now know whether fiber length makes a difference regarding its pathogenic qualities; what level of exposure is safe?; what pathogenic properties of asbestos fibers cause cancer? And if these studies have not been performed, is there a need to conduct a comprehensive epidemiological study of those persons exposed to the fibers?

Answers to these questions and others are imperative for state agency decision-makers to manage current permits and to make future permitting decisions. Improved scientific understanding of the health concerns associated with taconite tailings can have wide ranging effects on the character, extent and frequency of required monitoring, operation efficiency of tailings disposal facilities, and may open the possibility of alternative uses for tailings.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- Bartlett, R.V., 1980. *The Reserve Mining Controversy: A Case Study of Science, Technology, and Environmental Quality*. Indiana University Press, Indiana.
- Huffman, T.R., 2000. Exploring the legacy of Reserve Mining: what does the longest environmental trial in history tell us about the meaning of American Environmentalism? *Journal of Policy History* 12 (3), 339–368.
- Ojakangas, R.W., Matsch, C.L., 1982. *Minnesota's Geology*. University of Minnesota Press, Minnesota.
- Reserve Mining Company v. Environmental Protection Agency, et al., Reserve Mining Company vs. United States, et al., US Court of Appeals, 8th circuit. Submitted December 9, 1974. Decided March 14, 1975 as modified on rehearing and order on remand, April 8, 1975.
- Schaumburg, F.D., 1976. *Judgement Reserved: A Landmark Environmental Case*. Reston Publishing Co. Inc., Virginia.
- Skilling, 2002. *Minnesota Mining Directory*. Westmorelandflint Publishing, Minnesota.
- United States of America et. al. vs. Reserve Mining Company No. 5-72, Civil 19. US District Court, MN, 5th Division. 380 F. Suppl. 11. April 20, 1974 with supplemental Opinions, May 11, 1974, and August 3, 1974.

Rapporteur's Report Session 1: Origin of the problem: Malcolm Ross

Introduction

The Reserve Mining Co., in the processing of taconite iron ore quarried from the Peter Mitchell Pit, deposited the finely crushed waste rock into Lake Superior near Silver Bay Minnesota. In the early 1970s The U.S. Environmental Protection agency filed a lawsuit against Reserve Mining Co., asking the court to force the company to stop dumping into the lake. On April 20, 1974, after a lengthy court battle, the U.S. District Court concluded that the Reserve Mining discharge into Lake Superior violated federal and state pollution laws and thus ordered Reserve Mining Co., to halt the lake disposal of taconite tailings. At the time many feared that some of the mineral particles contained in the tailings (alleged to be asbestos or asbestos-like) would cause human health problems. This Conference was thus convened to readdress the problem of the mineral content of the Biwabik Iron Formation and to whether any minerals contained in the ore could cause human disease. The four papers given in this session address the nature of the mineral particles in the taconite rock, the definition of the term “asbestos” and the history of the legal controversy over the possible health effects of certain mineral particles contained in the Biwabik iron range ores.

Paper 1—Geology of the Biwabik Iron Formation and Duluth Complex

Mark A. Jirsa, James D. Miller, Jr., G.B. Morey

The Biwabik Iron Formation was a principal source of ore for the American steel industry during the 20th Century. The unaltered iron deposits, called taconite, contain approximately 30% iron and 50% SiO_2 . About 75% of the iron in taconite resides in the mineral magnetite, the remainder is largely in iron carbonate and several iron-silicate minerals.

At the east end of the Mesabi range where the Reserve Mining's Peter Mitchell Pit is located, the Biwabik Iron Formation has been metamorphosed by the intrusion of the Duluth Igneous Complex, the Complex being characterized by various combinations of olivine, pyroxene, and a variety of amphibole minerals. The possible presence of

fibrous minerals in Biwabik rocks of the east Mesabi range, and their potential liberation by iron mining, has raised environmental health concerns and litigation. The amphibole minerals, some suspected to be fibrous, that have particularly come to the attention of the courts.

Biwabik Iron Formation is classified into four zones, each with a distinctive mineralogy:

Zone 1. The unaltered rocks contain quartz, magnetite, hematite, siderite, ankerite, talc, and the iron-silicate minerals chamosite, greenalite, minnesotaite, stilpnomelane, and talc. The minerals quartz, hematite, siderite, chamosite, greenalite, and some magnetites are considered primary minerals.

Zone 2. Transitional taconite contains mineral assemblages that are similar to the unaltered taconite of zone 1, but differs by the extensive replacement of quartz, and ankerite, the reduction of hematite to magnetite and the appearance of clinozoisite.

Zone 3. Moderately metamorphosed taconite is characterized by the development of the iron-rich amphiboles grunerite and cummingtonite, at the expense of original iron carbonates and silicates, and the associated production of calcite.

Zone 4. Highly metamorphosed taconite is completely recrystallized to a metamorphic fabric composed mainly of quartz, iron-bearing amphiboles (the grunerite–cummingtonite series and hornblende), iron-bearing pyroxenes (hedenbergite, ferrohypersthene), magnetite, and rare fayalite and calcite.

Paper 2—Overview of the mineralogy of the Biwabik Iron Formation, Mesabi iron range, northern Minnesota

Peter L. McSwiggen, G.B. Morey

The Biwabik Iron Formation is subdivided into four stratigraphic units (lower cherty, lower slaty, upper cherty, and upper slaty) and into four lateral mineralogical zones (1–4).

Zone 1, the westernmost zone, is characterized by the minerals quartz, magnetite, hematite, carbonates, talc, chamosite, greenalite, minnesotaite and stilpnomelane. Chamosite and greenalite are platy silicates, similar in physical properties to the micas, belonging to the septe-

chlorite mineral group. Minnesotaites is also a platy mineral whose crystal structure is related but not identical to talc and is sometimes intergrown with talc. Stilpnomelane is a typically cryptocrystalline sheaf-like silicate found in a variety of textural settings. Commonly it has a pale brown or reddish brown color, but some varieties have a greenish brown color. Although granules composed entirely of stilpnomelane may occur, this mineral more commonly occurs as individual laths or radiating sheaves. Rarely, stilpnomelane also may be found within the cores of oolites along with fine-grained chamosite and minnesotaites.

Zone 2 contains mineral assemblages similar to those observed in unmetamorphosed iron formation, but exhibits evidence of extensive recrystallization of quartz and magnetite and the widespread replacement of the iron silicates by quartz and ankerite. Such features include granules of very fine-grained acicular minnesotaites and magnetite that are typically fractured. The fractures are in turn filled with tabular grains of minnesotaites.

Zone 3 is a moderately metamorphosed iron formation and occurs about 2.3 miles from the contact with the Duluth Complex. It is marked by the appearance of a variety of amphibole minerals and by the disappearance of original iron carbonates and silicates. The development of grunerite–cummingtonite series amphiboles is pervasive throughout the zone. Grunerite first occurs in Zone 3 as small, tabular crystals surrounded by radiating fibrous sheaves composed of fine needles.

Zone 4 contains minerals that are completely recrystallized. The original silicate minerals have completely reacted and a new suite of minerals forms within the iron formation. These include grunerite, hornblende, hedenbergite, ferrohypersthene (ferrosilite), and fayalite. Grunerite in Zone 4 forms well developed acicular grains which gave way to the east to medium-size prismatic grains. The amphibole hornblende occurs as both prograde and retrograde phases. Prograde hornblende occurs intergrown with hedenbergite in the distal part of Zone 4. More commonly however, very fine acicular to fibrous hornblende is a retrograde phase that replaces hedenbergite, mainly at grain margins.

Since the Reserve controversy of the 1970s, morphological attributes of the cummingtonite–grunerite series have attracted considerable attention, primarily because of their general resemblance to some asbestos-like minerals. However, there appear to be no detailed studies regarding specific stratigraphic, compositional, and structural attributes of these Biwabik Iron Formation minerals. There is a general consensus, however, that these amphiboles formed under both prograde conditions, as metamorphic temperatures increased, and under retrograde conditions as temperatures decreased. To the east and immediately adjacent to the Duluth Complex, paragenetic relationships are complicated by the presence of retrograde cummingtonite. For example, virtually all of the prismatic cummingtonite at the Dunka River locality appears to be paragenetically late, having formed partly from fayalite,

but mainly from ferrosilite and/or pigeonite. At somewhat lower temperatures, prismatic cummingtonite may be replaced by more magnesium-rich phases that have an acicular habit. At still lower temperatures prograde acicular grunerite may be replaced by acicular or fibrous cummingtonite.

Paper 3—The mineral nature of asbestos

Malcolm Ross, Arthur M. Langer, Gordon L. Nord, R.P. Nolan, R.J. Lee, D. Van Orden, John Addison

The various words used to denote the asbestos minerals, including asbestos, asbestus, asbestinon, asbest, asbeste, asbeston, abeston, amiantos, amiantus, amianthus, amiant, and amiante, can be traced back to the writings of the ancient Greek philosophers and their use of two words—*αμιαντος* and *ασβεστος*. The Greek word *αμιαντος* (transliterated as “amiantos”), when used as a noun, is synonymous with the English word asbestos, when used as an adjective it can mean pure or undefiled. The ancient Greek writers used the noun *ασβεστος* (“asvestos”) to mean quicklime; a meaning retained in modern Greek. However, Pliny the Elder, apparently misunderstanding the use of this word by the early Greek philosophers, replaced the Greek noun for quicklime (*ασβεστος*) with the dubious Greek word *ασβεστινον* which he interpreted to mean a non-combustible material. Pliny then transliterated *ασβεστινον* into the Latin noun “asbestinon”, alluding to an incombustible linen, cleansed by fire, and used as shrouds for royalty during cremation.

The term asbestos is now used to describe a group of six commercially important minerals having many desirable industrial properties. Asbestos grows within shear planes, faults and folds of deformed rock, either perpendicular (cross-fiber) or parallel (slip-fiber) to the opening in the rock, however, the formation of fibrous minerals in nature is rare. The unique mineralogical characteristic common to all of the asbestos minerals is that their morphologic form or habit of crystallization is in the form of polyfilamentous fiber bundles. Commercial asbestos includes one serpentine mineral (chrysotile asbestos) and five amphibole minerals (anthophyllite, tremolite, actinolite, crocidolite, and amosite asbestos). However, these five amphiboles usually crystallize in non-asbestiform habits. These non-asbestos habits, on a population basis, lack the morphological appearance of asbestos and do not possess the desirable industrial properties.

The amphibole mineral group accounts for approximately 5% by volume of earth's crust. However, due to the rarity of the asbestiform growth in rocks, commercially viable deposits of asbestos are exceedingly rare. Limited amounts of asbestos were used in ancient times, but with the needs of modern industrial development in the last decades of the 19th Century, asbestos mining became commercially important. Historically, more than 95% of the commercially mined asbestos is chrysotile asbestos. The remaining 5% is amphibole asbestos, predominately

crocidolite and amosite, although anthophyllite asbestos and tremolite asbestos have been mined to a very minor extent.

Knowledge concerning the elemental compositions and crystal structure of the amphibole and serpentine minerals developed in the 19th and 20th Century, respectively. It was known to 19th Century mineralogists that minerals crystallizing in the asbestiform habit had higher tensile strength and flexibility than those crystallizing in the more common acicular or prismatic form. By the time of World War I the elemental composition of many amphiboles had been determined and analysis of the morphology of large single crystals clearly delineated the amphibole mineral class. By 1916, the chemical formula of tremolite amphibole was described and in 1929 B.E. Warren first described the crystal structure of a tremolite. By 1930 he reported on five more amphiboles crystal structures—kupferite, actinolite, hornblende, grunerite, and anthophyllite. The amphibole group is made up of 27 separate mineral types with a large number of varietal species based on 23 chemical species. Amphiboles crystallizing in the asbestiform habit has the designation asbestos added after the mineral name.

The essential structural features of the amphibole group are: linked silica tetrahedral forming a double silica chain. Further, a double chain of octahedra is linked to this double silica chain. There are four dissimilar octahedral sites which accommodate several kinds atoms, including Mg, Fe, Al, Mn, Ti, Na, and Ca. Varying amounts potassium and sodium may also appear in the amphibole A-sites located between the linked double tetrahedral–octahedral chains.

Chrysotile asbestos is a serpentine mineral and is one of the six minerals regulated under the asbestos standard and currently is only asbestos mineral of commercial importance. The crystal structure of chrysotile is composed of linked double sheets, one sheet of linked SiO_4 tetrahedra and the other of linked $\text{MgO}_2(\text{OH})_4$ octahedral. The octahedral portion of the double layer is similar to that of brucite. The two sheets differ, particularly in their *b*-axis dimensions, causing an internal distortion. To compensate for the larger size of the octahedral sheet, the double sheets roll up into long cylindrical tubes, the octahedral sheet forming the exterior of the curved surface.

Paper 4—The origins of public concern with taconite and human health: Reserve Mining and the asbestos case

Michael E. Berndt, William C. Brice

A review is given of the history of the Reserve Mining taconite mining operations at the Peter Mitchell Pit and of the lengthy court case that examined the possible human health effects of certain mineral particles contained within the taconite waste rock that was deposited into Lake Superior. Mineral particles belonging to the amphibole group were alluded by some to be asbestos or asbestos-like, and when ingested by drinking Lake Superior water thought to cause cancer.

Iron ore deposits were first discovered in Minnesota in the 1860s and until the 1940s most of the ore was unmetamorphosed “soft ore” containing much hematite (Fe_2O_3). In the 1940s techniques for processing taconite rock (“hard ore”) was developed, removing the iron-bearing magnetite by magnetic separation from the crushed rock that also contained various silicate minerals including amphiboles. Reserve Mining shipped its first taconite ore pellets in 1955. Alleged polluting of Lake Superior by ore tailings was reported in 1968 and State Court proceedings were initiated soon afterward. In 1972 the U.S. EPA filed suit against Reserve Mining in U.S. District Court and the trial began in August of 1973. Phillip Cook reported in a June 1973 press release that the Lake Superior water contained asbestos. In April 1974 Judge Miles Lord issued an injunction for the immediate closing of the Reserve Mine, but a temporary stay was obtained by Reserve so the Company could develop a landfill for waste rock disposal. The landfill was finally approved by the Minnesota Supreme Court and permits were sued for a Milepost 7 Tailing Disposal Facility. This facility was completed in March of 1980 and discharge of waste rock into Lake Superior ended. By 1986 Legal settlement with Reserve was reached, but without a clear mineralogical description of asbestos or asbestos-like minerals in the waste rock or on the health effects that might ensue from drinking the Lake Superior waters. One of the Reserve Mining parent companies, LTV Steel, declared bankruptcy in 1989 and the mining facility was closed. The company was sold to Cyprus Minerals, Inc. in 1989 and was later sold to Cleveland-Cliffs; the mine currently operating as Northshore Mining. The true nature of the minerals contained in the taconite rock remains unresolved.



The search for asbestos within the Peter Mitchell Taconite iron ore mine, near Babbitt, Minnesota

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Abstract

Asbestos crystallizes within rock formations undergoing intense deformation characterized by folding, faulting, shearing, and dilation. Some of these conditions have prevailed during formation of the taconite iron ore deposits in the eastern Mesabi Iron Range of Minnesota. This range includes the Peter Mitchell Taconite Mine at Babbitt, Minnesota. The mine pit is over 8 miles long, up to 1 mile wide. Fifty three samples were collected from 30 sites within areas of the pit where faulting, shearing and folding occur and where fibrous minerals might occur. Eight samples from seven collecting sites contain significant amounts of ferroactinolite amphibole that is partially to completely altered to fibrous ferroactinolite. Two samples from two other sites contain ferroactinolite degraded to ropy masses of fibers consisting mostly of ferrian sepiolite as defined by X-ray diffraction and TEM and SEM X-ray spectral analysis. Samples from five other sites contain unaltered amphiboles, however some of these samples also contain a very small number of fiber bundles composed of mixtures of grunerite, ferroactinolite, and ferrian sepiolite. It is proposed that the alteration of the amphiboles was caused by reaction with water-rich acidic fluids that moved through the mine faults and shear zones. The fibrous amphiboles and ferrian sepiolite collected at the Peter Mitchell Mine composes a tiny fraction of one percent of the total rock mass of this taconite deposit; an even a smaller amount of these mineral fragments enter the ambient air during mining and milling. These fibrous minerals thus do not present a significant health hazard to the miners nor to those non-occupationally exposed. No asbestos of any type was found in the mine pit.

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Keywords: Taconite; Asbestos; Amphibole; Reserve mining; Tailings; Mesabi iron range; Mineral fibers

1. Introduction

1.1. Origin of the asbestos

Asbestos crystallizes under very special conditions that occur within rock formations that are undergoing intense deformation characterized by folding, faulting, shearing, and dilation. Such deformations are often accompanied by the intrusion of magmatic fluids that solidify to form dikes and sills. The fibers crystallize in high strain environments, such as within folds, shear planes, faults, dilation cavities, and at intrusion-host rock boundaries. Fibers

can crystallize from solutions moving within the fault and shear zones; the fibers being oriented parallel to the two rock faces that compose the shear or *slip* plane—thus the term *slip fiber*. Slip fiber growth can also occur during folding of layered rocks for the folding process causes a shearing between adjacent layers. Fibers can also crystallize from a fluid phase within cracks formed when the rock undergoes dilation due to tectonic stress, a process in which parallel cracks and fissures form open spaces within the rock. The process of folding in layered rocks can also produce openings or dilation cavities between adjacent layers. Such fibers nucleate on a wall of the crack or cavity and grow across to the opposite wall—thus the term *crosses fibers* (Ross and Nolan, 2003).

Cross and slip fiber growth of crocidolite and amosite asbestos occurs in the intensely folded Precambrian banded

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ironstones of the Transvaal and Cape Provinces of South Africa. The asbestos deposits in the Cape Province are generally found within monoclinical folds. The crocidolite asbestos deposits of Western Australia are also found. Precambrian banded ironstones, the deposits generally confined to the northern limb of a broad syncline of the Hamersley Range. Here, crocidolite asbestos grew within dilation cavities between folded iron formation bands. Asbestos-bearing serpentinites, such as those found in Quebec, Canada, commonly contain cross-fiber chrysotile asbestos that crystallized within dilation cavities. Slip fiber chrysotile asbestos is less common but is ubiquitous in the serpentinite located in Eden Mills, Vermont (Ross, 1981; Ross and Nolan, 2003).

In our examination of numerous mines and construction sites within igneous and metamorphic terrain located in the eastern United States, Arkansas, Michigan, California, Cyprus, and Ontario and Quebec, Canada, we observe that asbestos occurs within faults and shear zones, in folds, or at contacts between igneous intrusions and the host rock. In any of these geologic features it is possible that other fibrous minerals can form as describe above. However, in most rock formations, other than those exploited for asbestos production, such non-asbestos fibers are restricted to a very small volume of rock.

1.2. Survey of the Peter Mitchell Mine for fibrous minerals

With the above mentioned criteria in mind we made a detailed survey of the rocks within the Peter Mitchell Mine to see if any rocks contained asbestos or asbestos-like minerals; our results are reported below. The history of the asbestos controversy over exposure to mineral particulates, including those suspected to be asbestos, released during

the mining and milling of taconite iron ore is given by Berndt and Brice (2008) and Wilson et al. (2008). This asbestos controversy is particularly related to litigation involving the Reserve Mining Company which previously operated the Peter Mitchell Mine (Reserve Mining Company v USEPA, 514 F.2d 492, 8th Cir. 1975).

2. The Peter Mitchell Taconite Mine

2.1. Mine survey

The Peter Mitchell Taconite Mine is owned by the Northshore Mining Corporation and is located approximately 3 miles south of Babbitt, Minnesota. The mine pit is over 8 miles long, up to 1 mile wide, and one to two hundred feet deep (Fig. 1). The mine is located within the Biwabik iron formation. In Table 1 are listed the minerals commonly found in this formation, especially important are the amphibole minerals which can sometimes occur in fibrous form. For detailed descriptions of the Minnesota iron formations see Jirsa et al. (2008) and McSwiggen and Morey (2008). Mark J. Severson (Technical Report NRRI/TR-93/24) states the at least 17 faults, five basaltic dikes, and several large-scale folds occur in the Peter Mitchell Mine pit. Over a five day period we surveyed and then collected samples from the areas within the pit where fibrous minerals might occur. Geological maps and structural analysis of the mine pit made by Mark J. Severson, augmented by a detailed map of the current working area, was used as a base to select and mark the sampling sites. The absence of any fibrous mineral growth in undeformed rock permitted us to sample only in those zones showing some form of rock deformation. As far as we know, ours is the only publication to make a detailed min-



Fig. 1. View of a portion of the Peter Mitchell Taconite Mine, Babbitt, Minnesota.

Table 1
Names and composition of the major minerals and selected minor found in the Biwabik iron formation

Mineral name	Chemical composition
Amphiboles	
Cummingtonite	$(\text{Mg}, \text{Fe}^{2+})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$
Grunerite	$(\text{Fe}^{2+}, \text{Mg})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$
Actinolite	$\text{Ca}_2(\text{Mg}, \text{Fe}^{2+})_5\text{Si}_8\text{O}_{22}(\text{OH})_2$
Hornblende	$\text{Ca}_2(\text{Na}, \text{K})(\text{Mg}, \text{Fe}^{2+}, \text{Fe}^{3+}, \text{Al})_5(\text{Si}, \text{Al})_8\text{O}_{22}(\text{OH})_2$
Pyroxenes	
Diopside	$\text{CaMgSi}_2\text{O}_6$
Pigeonite	$(\text{Mg}, \text{Fe}^{2+}, \text{Ca})_2\text{Si}_2\text{O}_6$
Hedenbergite	$\text{CaFe}^{2+}\text{Si}_2\text{O}_6$
Ferrohypersthene	$(\text{Fe}^{2+}, \text{Mg})_2\text{Si}_2\text{O}_6$
Other silicates	
Quartz	SiO_2
Wollastonite	CaSiO_3
Vesuvianite	$\text{Ca}_{10}(\text{Mg}, \text{Fe})_2\text{Al}_4[\text{Si}_2\text{O}_7]_2[\text{SiO}_4]_5(\text{OH}, \text{F})_4$
Andradite	$\text{Ca}_3(\text{Fe}^{3+}, \text{Ti})_2\text{Si}_3\text{O}_{12}$
Almandine	$(\text{Fe}^{2+})_3\text{Al}_2\text{Si}_3\text{O}_{12}$
Fayalite	$(\text{Fe}^{2+}, \text{Mg})_2[\text{SiO}_4]$
Olivine	$\text{Mg}_2[\text{SiO}_4]$
Biotite	$\text{K}_2(\text{Fe}, \text{Mg}, \text{Al})_6[\text{Si}, \text{Al}]_8\text{O}_{20}(\text{OH}, \text{F})_4$
Plagioclase	$(\text{Na}, \text{Ca})\text{Al}(\text{Al}, \text{Si})\text{Si}_2\text{O}_8$
Greenalite	$(\text{Fe}^{2+}, \text{Fe}^{3+})_{2-3}\text{Si}_2\text{O}_5(\text{OH})_4$
Chamosite	$(\text{Fe}^{2+}, \text{Mg}, \text{Fe}^{3+})_5\text{Al}(\text{Si}_3\text{Al})\text{O}_{10}(\text{OH}, \text{O})_8$
Minnesotaite	$(\text{Fe}^{2+}, \text{Mg})_3\text{Si}_4\text{O}_{10}(\text{OH})_2$
Talc	$\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$
Stilpnomelane	$\text{K}(\text{Fe}^{2+}, \text{Mg}, \text{Fe}^{3+})_8(\text{Si}, \text{Al})_{12}(\text{O}, \text{OH})_{27}$
Ferrian sepiolite	$(\text{Fe}^{3+}, \text{Fe}^{2+}, \text{Mg})_8(\text{Si}, \text{Fe}^{3+})_{12}(\text{OH})_4(\text{H}_2\text{O})_n$
Non-silicates	
Calcite	CaCO_3
Siderite	FeCO_3
Ankerite	$\text{Ca}(\text{Mg}, \text{Fe}^{2+}, \text{Mn})(\text{CO}_3)_2$
Magnetite	$\text{Fe}^{2+}(\text{Fe}^{3+})_2\text{O}_4$
Hematite	Fe_2O_3
Pyrite	FeS_2

erological survey of the mine and to discover the source of the mineral particulates released from the Peter Mitchell Mine ore that are suspected to be asbestos.

2.2. Sample descriptions

Fifty-three samples were collected at thirty sites from the Peter Mitchell Mine. Sampling was made particularly in fault and shear zones and within folds. In these areas the amphibole minerals within the rock were particularly susceptible to low temperature alteration due to infusion of rain water acidified by oxidation of sulfide minerals, these chemical processes being contemporaneous with rock shearing. We separated the 53 samples into four categories or types:

- (1) *Type 1 samples.* Type 1 samples are represented by 10B, 10C, 20A, 20B, 21A, 24A, and 24B (from sites 10, 20, 21 and 24) and the U.S. EPA's ferroactinolite sample which was collected by IIT Research Institute (for the EPA) from the eastern end of the mine in 1975

in the area of site 10 (personal communication, 1998, Dennis Wagner Northshore's environmental engineer who was present at the time of collection). We were able to obtain a portion of the original EPA sample from Dr. P. Cook for our present study. Site 10 is a particularly distinctive shear zone with much soft rock gouge lying at the base of the cliff face (Fig. 2).

- *Type 1 samples* contain three distinct stages of crystal alteration. (1) Little altered composite ferroactinolite-grunerite crystals (Fig. 3) contain (100) and (10–1) exsolution lamellae of grunerite within the ferroactinolite portion of the crystal and (100) and (10–1) lamellae of ferroactinolite within the grunerite portion. (2) Unmixing and alteration can produce crystals in which the grunerite areas are relatively unaltered whereas the ferroactinolite areas are very fibrous in appearance (Figs. 4 and 5). (3) Ferroactinolite that is almost completely altered to a fibrous habit is shown in Fig. 6.
- (2) *Type 2 samples.* Type 2 samples, represented by 5C and 13E, were collected from sites 5 and 13. In sample 5C the original amphibole, ferroactinolite, is degraded to a ropy mass (Fig. 7), only small amounts of the original amphibole are left. This ropy material is a magnesium, iron and silica-rich mineral belonging to the clay mineral group. The X-ray powder pattern (Fig. 8) and transmission electron microscope X-ray spectra showing major Mg, Fe and Si identify

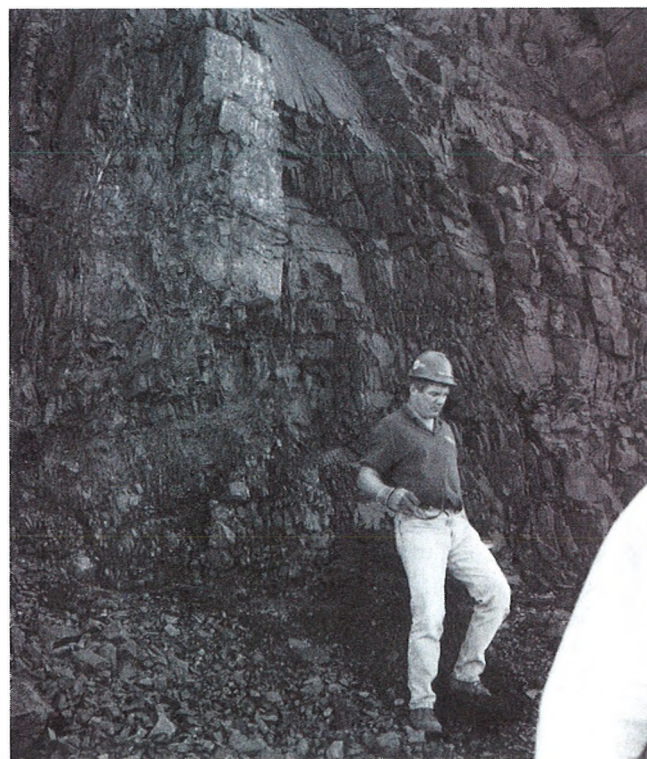


Fig. 2. Site 10 shear zone within rock face of the Peter Mitchell pit. Soft rock gouge from this shear zone lies at the base of the cliff face (dark area upon which the mining geologist is standing). The gouge contains fibrous ferroactinolite and ferrian sepiolite.

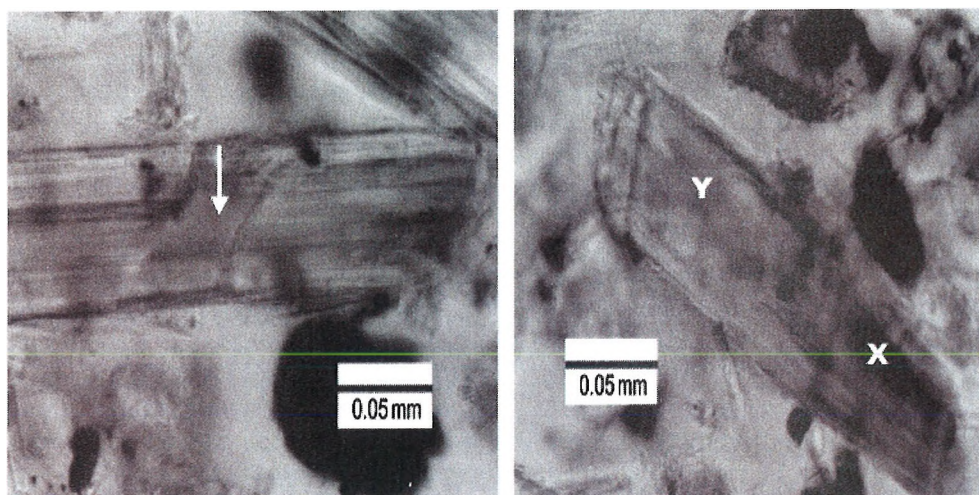


Fig. 3. Sample 10B-left: thick pristine grunerite lamella (arrow) oriented on the (10–1) plane of a relatively non-fibrous ferroactinolite crystal host. Nearly horizontal striations within the host ferroactinolite are due to (100) exsolution of grunerite. Sample 10B-right: Composite crystal of grunerite with (10–1) ferroactinolite exsolution lamellae trending N–S (area Y) and ferroactinolite (area X).

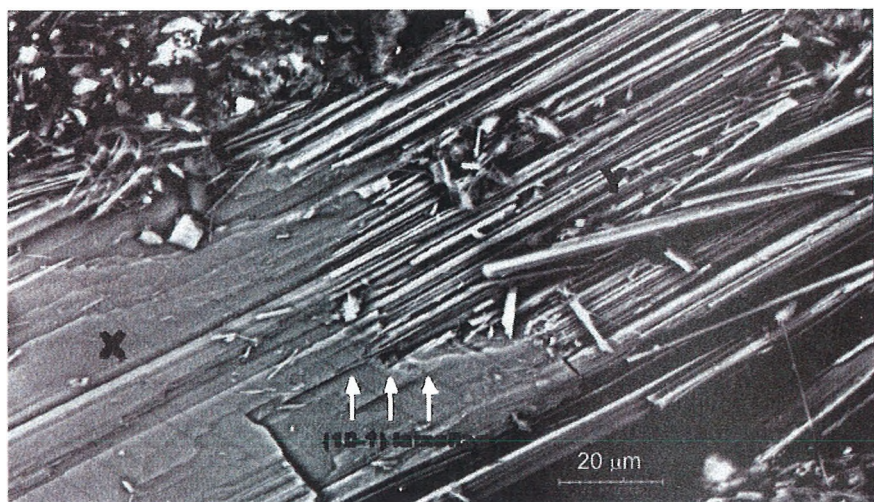
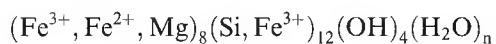


Fig. 4. Sample 10B. Scanning electron microscope photomicrograph of a composite crystal of grunerite (area X at lower left) and fibrous ferroactinolite (area Y at upper right). Note (10–1) exsolution lamellae of ferroactinolite within the grunerite area (arrows pointing to thin gray lines trending NW–SE). SEM X-ray spectra from areas X and Y are shown in Fig. 5.

this mineral as ferrian sepiolite (Fig. 11). The ropy masses, when subjected to lengthy ultrasonic treatment, are seen to be composed of a myriad of very thin ferrian sepiolite fibers as demonstrated by the TEM photomicrograph presented in Fig. 9. The chemical composition and crystal structure of ferrian sepiolite are not well understood, but an approximate chemical formula is:



- (3) *Type 3 sample.* The type 3 sample 30B from site 30 contains well crystallized ferroactinolite and grunerite and but also contains small amounts of brownish fibrous actinolite and brown mats of completely decomposed amphibole.

- (4) *Type 4 samples.* Type 4 samples include 13C, 13F, 21B, and 29 and were collected from sites 13, 21, and 29. The amphiboles in these samples appear as blocky prismatic crystals with no fibrous structure. No fibers were detected in these samples. Table 2 gives a summary of these four sample types.

2.3. Geologic processes within the Peter Mitchell Mine

We propose that water-rich fluids, acidified by oxidation of sulfide minerals, moved through the active mine faults and shear zones. Here chemical reactions, including oxidation of ferrous to ferric iron, occurred between the fluids and some of the constituent minerals, particularly with the grunerite and ferroactinolite amphiboles. In rocks con-

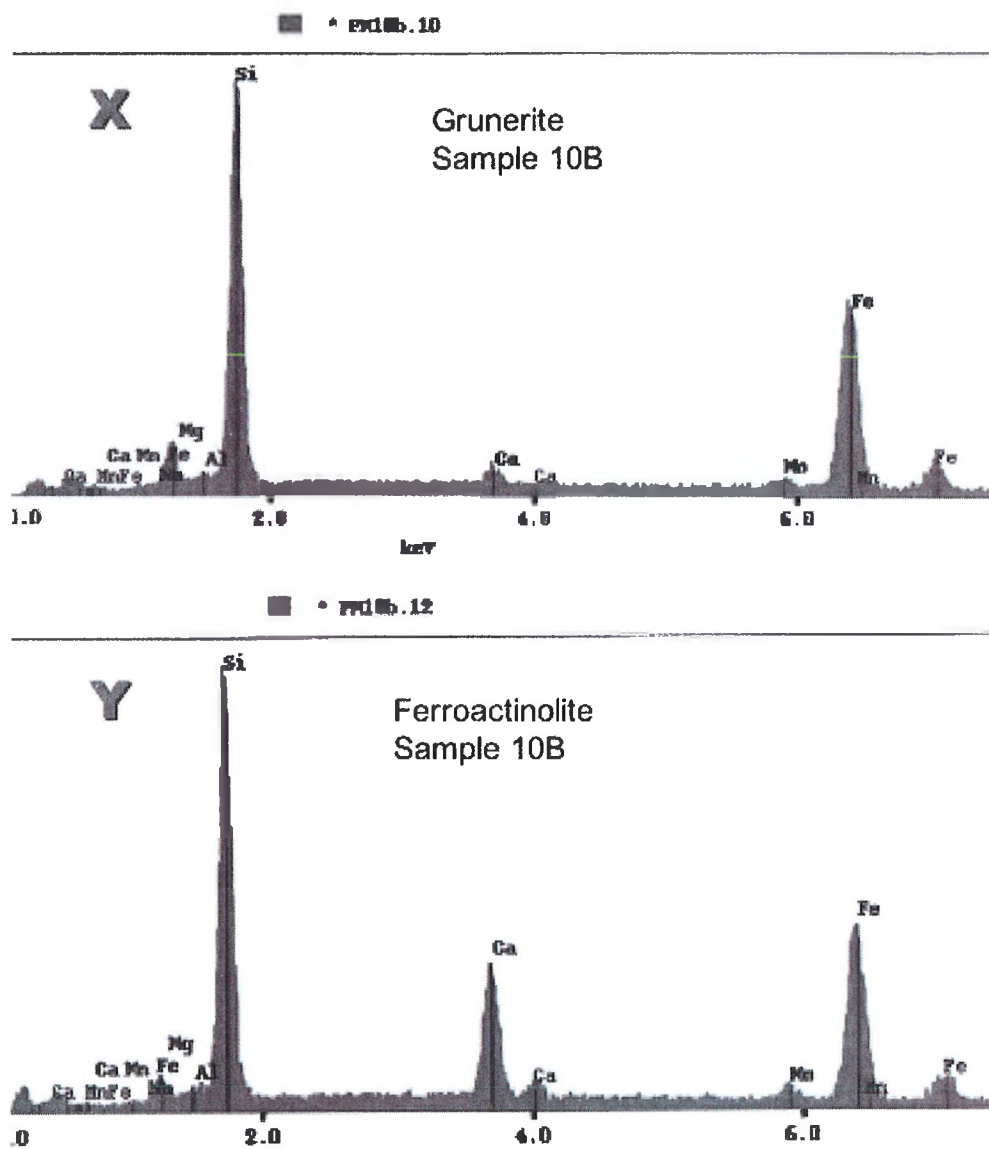


Fig. 5. SEM X-ray spectra analysis of grunerite taken in area X of Fig. 4 and of ferroactinolite taken in area Y of Fig. 4.

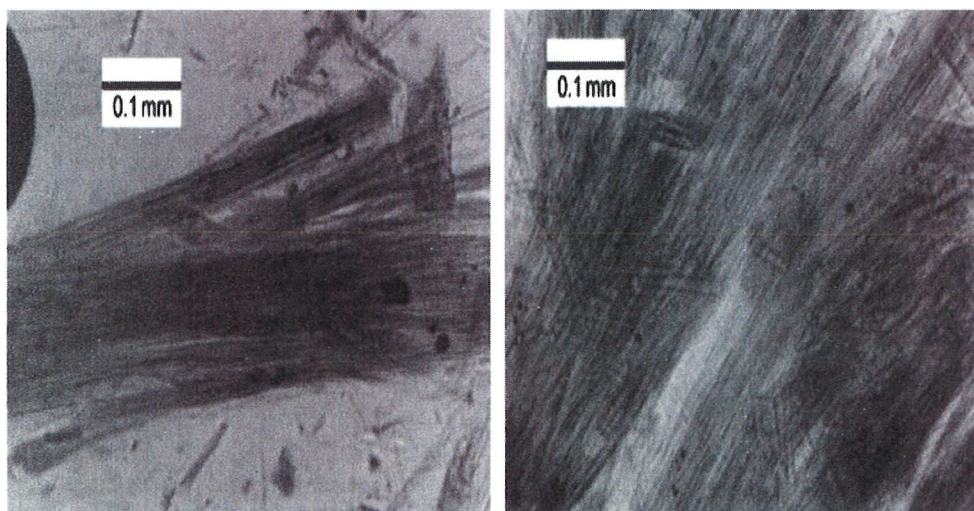


Fig. 6. Two photomicrographs showing mats of fibrous ferroactinolite (sample 24A). Small amounts of ferrian sepiolite and grunerite may also be present in these mats.

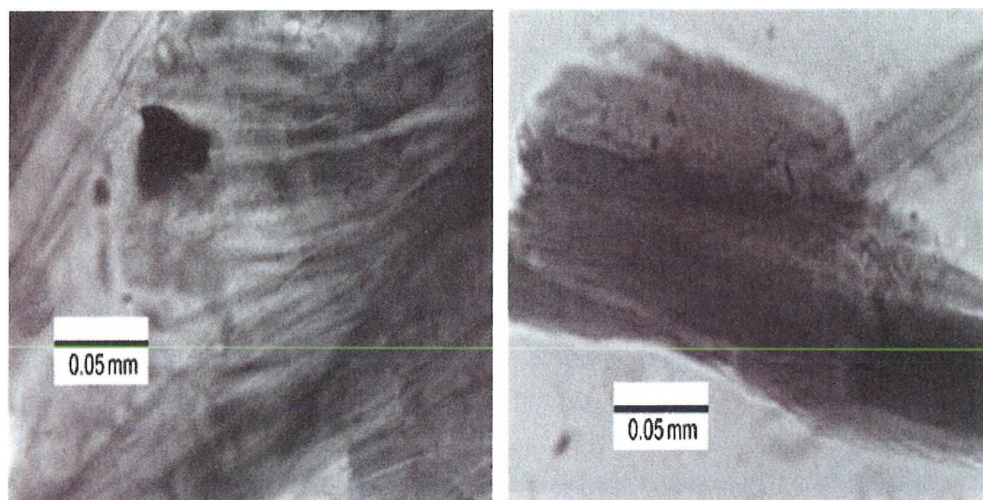


Fig. 7. Two photomicrographs of sample 5C showing ropy masses resulting from the nearly complete alteration of primary grunerite and ferroactinolite amphiboles to ferrian sepiolite. The X-ray powder diffraction pattern of this sample is shown in Fig. 8.

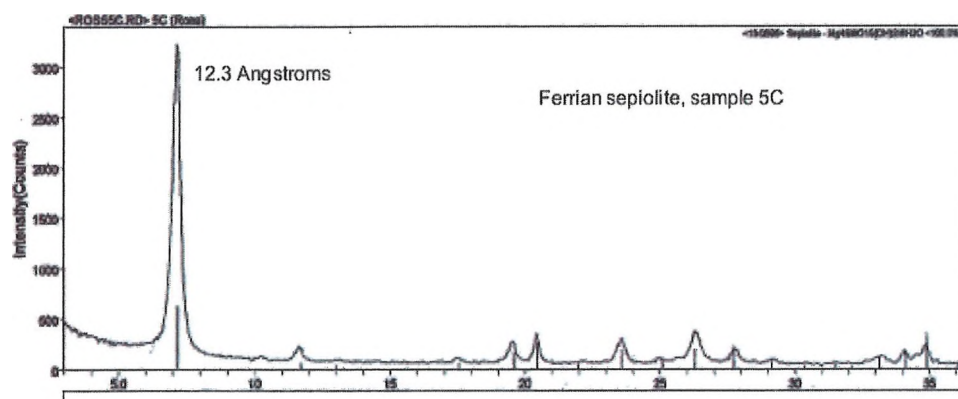


Fig. 8. X-ray diffraction powder pattern of sample 5C (Fig. 7) identifying the sample as ferrian sepiolite. Copper α radiation. Note the characteristic 12.3 ($2\theta = 7.2$ degrees) and 7.5 ($2\theta = 11.8$ degrees) Angstrom lines of sepiolite. This X-ray pattern is a good match to that given by Brindley (1959, p. 498) for sepiolite from four localities.

taining the two amphibole assemblage ferroactinolite-grunerite, exsolution of grunerite on (10–1) and (100) planes of host ferroactinolite and of ferroactinolite on (10–1) and (100) planes of host grunerite are commonly observed. The very thick (10–1) lamellae of grunerite within the host ferroactinolite crystals of sample 10B (Fig. 3) indicates that this amphibole crystallized under high temperature conditions near the top of the ferroactinolite–grunerite solvus and thus contained a large grunerite component within the crystal structure (Ross et al., 1969, p. 291; Fig. 6). On slow cooling the ferroactinolite and grunerite components may segregate to form a crystal, such as shown in Figs. 3 and 4, where one end of the crystal is mostly grunerite, the other, mostly ferroactinolite. If the amphiboles had originally crystallized as true asbestos, textures such as seen in Figs. 3 and 4 would not have developed. For a review of exsolution processes occurring in amphiboles (see Ross et al., 1968, 1969).

The transmission electron microscope photomicrograph presented in Fig. 10 reveals that (100) grunerite exsolution lamellae (now partly to completely altered to ferrian sepiolite)

are present within a single fiber of the host ferroactinolite, the fiber being derived from a composite ferroactinolite–grunerite crystal such as that shown in area Y of Fig. 4. The TEM X-ray spectra of the interleaved ferroactinolite host and (100) grunerite /ferrian sepiolite lamellae (Fig. 10) are shown in Fig. 11. We suggest that the interfaces between the ferroactinolite host and the (100) exsolution lamellae of grunerite are places where reaction with fluids within the fault or shear zone fluids can readily occur. Decomposition of the grunerite lamellae within the ferroactinolite host (area Y, Fig. 4) to ferrian sepiolite could promote the formation of the fibrous textures seen in (Figs. 4 and 6). Where alteration is incomplete, some of the pristine amphibole remains. It also appears that some iron was removed from the amphibole grains during this weathering process to recrystallize as iron oxide, probably in the form of goethite [$\text{FeO}(\text{OH})$] and appearing as brown masses within the ropy mats of ferrian sepiolite. A complete alteration of both grunerite and ferroactinolite could produce ferrian sepiolite and iron oxides such as found in the Type 2 samples.

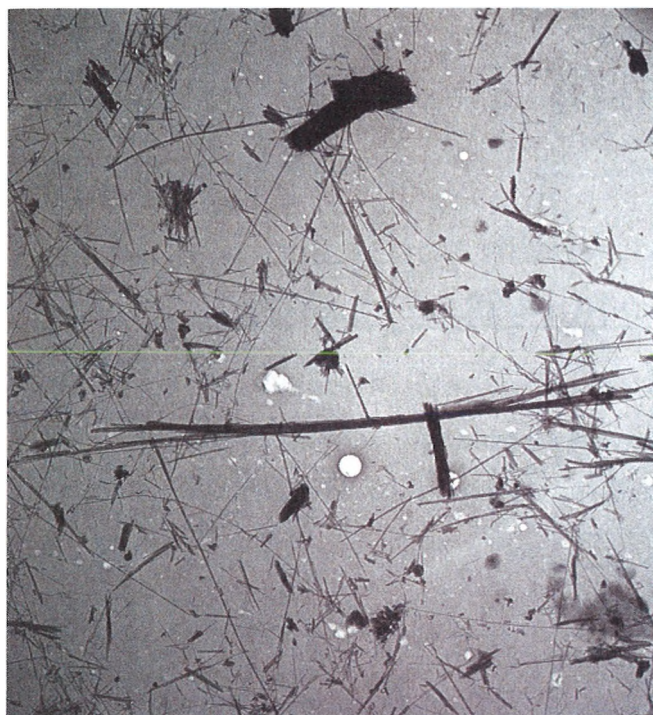


Fig. 9. Transmission electron micrograph of sample 5C showing ferrian sepiolite fibers that have formed from the alteration of primary amphiboles (width of field is 0.04 mm). The thinnest fibers are less than 0.1 μm in width.

Table 2

Summary description of the samples collected from various sites within the Peter Mitchell Taconite Mine

- (1) *Type 1 samples.* Type 1 samples are represented 10B, 10C, 20A, 20B, 21A, 24A, 24B and the EPA ferroactinolite. These samples contained ferroactinolite amphibole and composite grunerite-ferroactinolite amphibole that have partially or completely altered to very fibrous crystallites
- (2) *Type 2 samples.* Type 2 samples represented by 5C and 13E. In sample 5C the original amphibole, ferroactinolite, is degraded to a ropy mass composed mostly of the clay mineral ferrian sepiolite. TEM examination of sample 5C shows to be composed of a myriad of very thin fibers
- (3) *Type 3 sample.* The type 3 sample 30B from site 30 contains well crystallized ferroactinolite and grunerite and but also contain small amounts of brownish fibrous actinolite and brown mats of completely decomposed amphibole
- (4) *Type 4 samples.* Type 4 samples include 13C, 13F, 21B, and 29. The amphiboles in these samples appear as blocky prismatic crystals with no fibrous structure

3. Conclusions

The fibrous amphiboles and ferrian sepiolite collected in the Peter Mitchell pit composes a tiny fraction of one percent of the total rock mass within the mine. This fibrous ferroactinolite is a low temperature alteration product of non-fibrous amphibole; it does not occur in the manner of true asbestos which crystallizes as a primary mineral from hydrothermal solutions into open

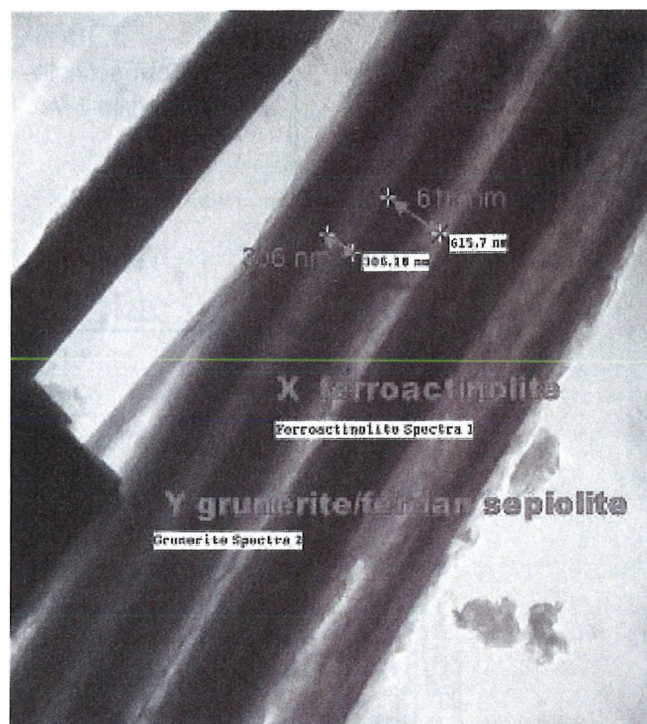


Fig. 10. Transmission electron microscope photomicrograph of a single fiber from a composite crystal of ferroactinolite and grunerite (sample 21A). This fiber is composed of alternating lamellae of ferroactinolite (lamella at X) and grunerite/ferrian sepiolite (lamella at Y) as identified by the respective TEM X-ray spectra. Lamellae within the fiber vary from 300 to 700 nm in thickness. Total thickness of the fiber is about 3000 nm. Width of field is about 6500 nm. TEM X-ray spectra collected from areas X and Y are shown in Fig. 11.

veins within deformed rock. The ropy mats of ferrian sepiolite are composed of inter-woven sub-micrometer sepiolite fibers. Due to inter-weaving of the fibers within the mats, individual fibers will be released only with great difficulty. Ultrasound was used to disperse the fibers for TEM analysis. Ferrian sepiolite has not appeared in the air samples collected in the taconite mill area and in the nearby town of Silver Bay (Wilson et al., 2008).

The fibers collected during ambient air sampling at the taconite mill where the Northshore iron ore is processed and at the town of Silver Bay are not asbestos, but rather are non-asbestiform ferroactinolite and grunerite. The mean air concentration in Silver Bay is less than 0.00036 fibers per milliliter, a value within the expected background for airborne asbestos reported by the World Health Organization and the U.S. Environmental Protection Agency. The risk-related cancer to such an exposure is less than 0.77 excess cancer cases in 1,000,000 lifetimes (Wilson et al., 2008).

Conflict of Interest

The authors declare that they have no conflicts of interest.

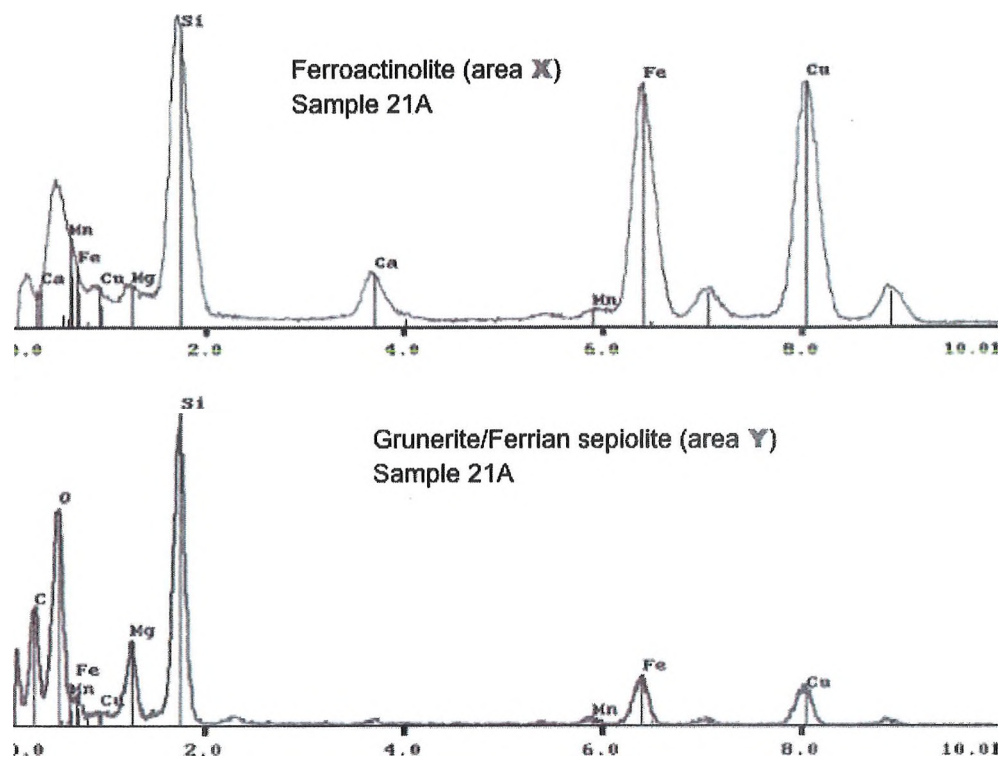


Fig. 11. SEM X-ray spectra analysis of ferroactinolite taken in area X of Fig. 10 and of grunerite/ferrian sepiolite taken in area Y of Fig. 10.

Acknowledgments

We thank Dr. Ronald G. Graber, Dennis M. Wagner and Dennis Wagner for their help with the geological survey. We acknowledge support from a Higher Education Advance Technology grant from New York State and the International Environmental Research Foundation (www.ierfinc.org) of New York, New York and assistance from Cleveland-Cliffs, Cleveland, Ohio.

References

- Berndt, M.E., Brice, W.C., 2008. The origins of public concern with taconite and human health: Reserve mining and the asbestos case. *Reg. Tox. Pharm.* 52, S31–S39.
- Brindley, G.W., 1959. X-ray and electron diffraction data for sepiolite. *Am. Mineral.* 44, 495–500.
- Jirsa, M.A., Miller, J.B., Morey, G.B., 2008. Geology of the Biwabik Iron Formation and Duluth Complex. *Reg. Tox. Pharm.* 52, S5–S10.
- McSwiggen, P.L., Morey, G.B., 2008. Overview of the Mineralogy of the Biwabik Iron Formation, Mesabi Iron Range, Northern Minnesota. *Reg. Tox. Pharm.* 52, S11–S25.
- Ross, M., 1981. The geological occurrences and health hazards of amphibole and serpentine asbestos. In: Veblen, D.R. (Ed.), *Amphiboles and Other Hydrous Pyroboles—Mineralogy. Reviews in Mineralogy*, vol. 9A. Mineralogical Society of America, Washington, DC, pp. 279–323.
- Ross, M., Papike, J.J., Weiblen, P.W., 1968. Exsolution in clin amphiboles. *Science* 159, 1099–1102.
- Ross, M., Papike, J.J., Shaw, K.W., 1969. Exsolution textures in amphiboles as indicators of subsolidus thermal histories. *Mineralogical Society of America Special Paper* #2, 275–299.
- Ross, M., Nolan, R.P., 2003. History of asbestos discovery and use and asbestos-related disease in context with the occurrence of asbestos within ophiolite complexes. In: Dilek, Y., Newcomb, S. (Eds.), *Ophiolite Concept and Evolution of Geologic Thought*, 373. Geological Society of America Special Publication, pp. 447–470.
- Wilson, R., McConnell, E.E., Nolan, R.P., Axten, C.W., Ross, M., 2008. Risk assessment due to environmental exposures to fibrous particulates associates with taconite ore. *Reg. Tox. Pharm.* 52, S232–S245.

Mineralogical and microscopic evaluation of coarse taconite tailings from Minnesota taconite operations [☆]

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Abstract

Eighteen coarse taconite tailings samples were collected in 2000–2001 from five western Mesabi Range taconite (iron ore) operations located in northern Minnesota, i.e., EVTAC, Hibbing Taconite (Hibtac), USX Minntac, Ispat Inland (Minorca), and National Steel Pellet Company (NSPC), to test their physical, geological, chemical, and mineralogical properties [Zanko, L.M., Niles, H.B., Oreskovich, J.A., 2003. Properties and aggregate potential of coarse taconite tailings from five Minnesota taconite operations, Minnesota Department of Transportation, Local Road Research Board, St. Paul, MN, Report No. 2004-06 (also as Natural Resources Research Institute technical report, NRRI/TR-2003/44)]. The goal was to assemble a body of technical data that could be used to better assess the potential of using a crushed taconite mining byproduct like coarse tailings for more widespread construction aggregate purposes, primarily in roads and highways. An important part of the mineralogical assessment included X-ray diffraction (XRD) analyses and microscopic (polarized light microscopy, scanning electron microscopy, and transmission electron microscopy, i.e., PLM, SEM, and TEM, respectively) evaluation of the size and shape (morphological) characteristics of potentially respirable microscopic mineral particles and fragments.

Quantitative mineralogy, based on XRD analyses, showed that the dominant mineral in all samples was quartz (55–60%), followed by much smaller amounts of iron oxides, carbonates, and silicates. Specialized microscopic analyses and testing performed by the RJ Lee Group, Monroeville, PA, on both pulverized (–200 mesh, or 0.075 mm) and as-is sample composites showed that no regulated asbestos minerals or amphibole minerals were detected in the western Mesabi Range samples. A small number (26) of non-asbestos and non-amphibole mineral cleavage fragments/mineral fibers were detected by SEM out of 1000 fields analyzed, but most were identified as minnesotaite and talc, silicate minerals common to the Biwabik Iron Formation. Amphibole minerals, absent in coarse tailings samples from the five western Mesabi Range taconite operations, were present in a single eastern Biwabik Iron Formation sample collected in 2003 for Lake County from the Cliffs Northshore operation in Silver Bay, MN.

Importantly, the *Superfund Method for the Determination of Releasable Asbestos in Soils and Bulk Materials* [United States Environmental Protection Agency (USEPA), 1997. Superfund method for the determination of releasable asbestos in soils and bulk materials, EPA 540-R-97-028, U.S. Environmental Protection Agency, Washington], as modified by Berman and Kolk [Berman, D.W., Kolk, A.J., 2000. Modified elutriator method for the determination of asbestos in soils and bulk materials, Revision 1: Submitted to the U.S. Environmental Protection Agency, Region 8, May 23, 2000] failed to generate any protocol fibers, i.e., fibers longer than 5 µm and thinner than 0.5 µm, from either the western coarse tailings samples or the single eastern Biwabik Iron Formation sample. The combined findings suggest coarse tailings and other taconite mining byproducts should be treated with the same common sense safety and industrial hygiene approach practiced for all mineral-based materials that have the potential to generate respirable dust.

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[☆] Changes of ownership have occurred at three of the taconite operations. First, National Steel was purchased by U.S. Steel, and National Steel Pellet Company (NSPC) has been re-named; it is now called U.S. Steel Keewatin Taconite (Keetac). Second, EVTAC Mining Co. was purchased by Cleveland-Cliffs, Inc. and China's Laiwu Steel Group, and is now called United Taconite LLC (UTAC). Third, Ispat Inland (Minorca) Mining is now called ArcelorMittal Steel Minorca Mine Inc. (Minorca). However, this paper uses the company names in effect when the original sampling and analytical work was performed, unless otherwise noted.

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Keywords: Taconite; Amphibole; Biwabik Iron Formation; Mesabi iron range

1. Aggregate potential of taconite mining byproducts

Over 50 million short tons of aggregate are used annually in Minnesota, with 75% coming from sand and gravel sources, and the remaining 25% from crushed stone sources. Recent studies by Southwick et al. (2000) and the Aggregate Resources Task Force (1998, 2000), have addressed the growing pressure on aggregate resources in the State of Minnesota, particularly in the seven-county Twin Cities (Minneapolis and Saint Paul) Metro Area. There, aggregate shortages have been predicted within the next 10–15 years, as currently permitted reserves near exhaustion, and as residential and commercial developments expand and encroach on remaining aggregate resources. Other areas of the state, like the Highway 61 corridor along the north shore of Lake Superior, have also had difficulty supplying new sources of high quality crushed aggregate for local construction jobs. Southeastern Minnesota carbonate (limestone and dolomite) quarries have experienced similar pressures for providing quality construction aggregates that meet Superpave (Superior Performing asphalt Pavement) specifications. Compounding these resource pressures, the permitting of pit and quarry expansions and new aggregate mines has become more complex and difficult, environmentally and socially, given the growing “not in my back yard” (NIMBY) reaction to such projects.

Millions of tons of taconite mining byproducts are generated annually by Minnesota’s taconite mining operations, and coarse tailings are one of the largest components. Because these byproducts represent a potentially huge alternative to conventional crushed stone aggregates, a project was funded by the Minnesota Local Road Research Board (LRRB) to conduct a more detailed evaluation of coarse taconite tailings (Zanko et al., 2003). Despite being used extensively for road and other construction applications at the mines, coarse tailings usage beyond the confines of the mining properties has generally been limited to local projects. This is unfortunate, because byproducts like coarse tailings are the end result of tremendous expenditures of energy and capital used in mining and processing taconite. If one or more taconite mining byproduct like coarse tailings are found to be suitable for uses in large-scale road and construction aggregate applications, and are demonstrably superior to other types of aggregate, then the economic and environmental benefit to the taconite companies and the State of Minnesota could be significant, given their potential to offset some of the impending aggregate shortages just discussed.

The project’s main goal, therefore, was to generate and document, following a 1-year sampling program, the technical data needed for making such determinations, i.e., relating geological, mineralogical, and chemical properties

to potential aggregate performance, and to address some of the important economic issues like transportation. It was also believed that the lack of well-documented technical information on several fronts, such as the potential health risk posed by inhalation of taconite dust, may have been contributing to perceptions about taconite mining byproducts like coarse tailings that were needlessly limiting their use potential. With respect to this latter point, a more detailed mineralogical evaluation of the samples was conducted during the project. The evaluation consisted of qualitative and quantitative mineralogy, plus specialized microscopic analyses and testing. The findings are summarized and discussed in this paper.

2. Taconite mine locations

Fig. 1 shows the relative location of each taconite operation on Minnesota’s Mesabi Range. The Biwabik Iron Formation (BIF), which runs diagonally from southwest to northeast on the map, is the source of ore for the mines. Coarse tailings generated at the five westernmost operations, i.e., Ispat Inland (Minorca), EVTAC (now United Taconite), Minntac, Hibbing Taconite (Hibtac), and National Steel Pellet Company (NSPC; now Keewatin Taconite), were the focus of the study. The two easternmost taconite facilities, i.e., Northshore Mining Company in Babbitt and Silver Bay, and the now closed Cliffs Erie (LTV Steel) operation in Hoyt Lakes, were not part of the study.

3. Taconite tailings

Davis (1964) describes taconite as a hard, dense rock, composed largely of an intimate mixture of silicates and very fine magnetite (Fe_3O_4) crystals. Because magnetite constitutes less than one-third of the weight of crude taconite ore, large amounts of tailings are generated during the taconite process. Taconite tailings range in size from clay (less than 2 microns) to coarse sand ($3/8$ in., or about 10 mm), and are produced during various stages of crude taconite ore beneficiation. They are highly siliceous and contain a low percentage (3–5%) of iron in the magnetic form, i.e., magnetite.

Tailings are typically described as being fine or coarse. *Fine tailings* are composed of extremely fine rock particles, more than 90% of which are smaller than 0.003 in. (0.075 mm, or –200 mesh); they have little practical use at the mines, and end up in tailings basins. *Coarse tailings*, conversely, contain less than 10% fines, i.e., particles smaller than 0.003 in. (0.075 mm, or –200 mesh), and their top size is about $3/8$ in. (10 mm, or –4 mesh). Coarse tailings are used for mine-site projects like tailings basin contain-

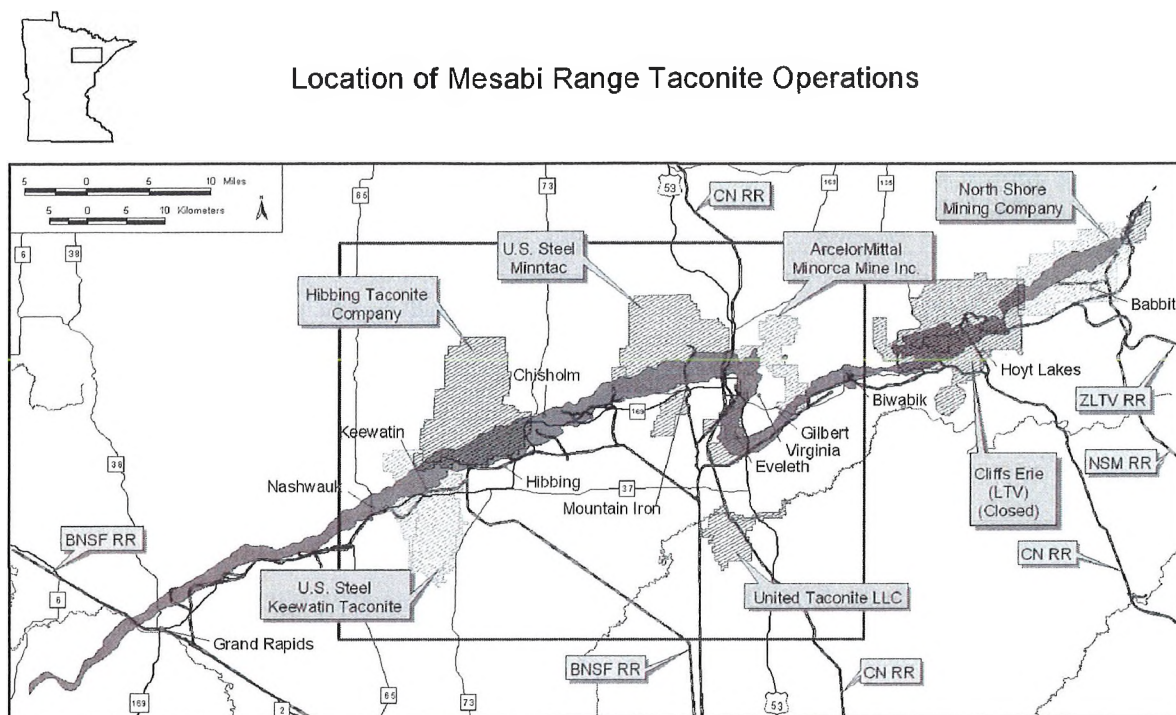


Fig. 1. Taconite mine location map and coarse tailings sources in boxed area, with names updated to reflect ownership as of 2007 (modified from Zanko et al., 2003).

ment cells, dikes, dams, as construction fill material, and for building and maintaining haul roads and shovel pads.

Coarse tailings generally meet the construction industry's definition of *fine aggregate*, i.e., aggregate particles less than 3/8 in. As a byproduct of crushing and grinding, they are angular (100% fractured faces) and comparable to manufactured fine aggregates used widely in construction (N. Whiting, Pers. Comm., 2002). Consequently, the physical properties that make coarse taconite tailings suitable for heavy-duty applications at the mines suggest expanded use in local, state, and federal highway construction projects. That is why coarse tailings from taconite mining operations were the focus of the research project.

EVTAC, Ispat Inland, and Minntac have separate coarse and fine tailings circuits in their plants, whereas no separation of coarse and fine tailings occurs at the Hibtac and NSPC plants. At EVTAC, Ispat Inland, and Minntac, coarse tailings are produced from cobber tailings (non-magnetics) and are separated from the fine fraction with spiral classifiers.

Coarse tailings are *not* separated from fine tailings in the Hibtac and NSPC concentrators. Combined fine and coarse tailings flow as slurry to the tailings basin in two flumes at Hibtac, and through a pipe at NSPC. However, some size separation is achieved as the larger particles settle out of the slurries near the points of entry to the basins. Over time, the tailings build up, much like sediments in a river delta, and periodically this buildup of coarser tailings is excavated and placed in piles. At Hibtac, a dragline removes and stockpiles these coarse tailings when they tend to dam the entry to the basin; at NSPC, a bulldozer pushes

the built-up of coarse tailings out of the channel that leads into the basin.

4. Sample collection

Coarse tailing samples from the five western taconite operations were acquired on a quarterly basis over a 1-year period, beginning in the Fall of 2000. Following their acquisition, samples were prepared by the NRRI's Cole-raine Minerals Research Laboratory (CMRL) for all subsequent project testing. Tailings from EVTAC, Ispat Inland, and Hibtac were sampled by CMRL research technicians; at Minntac and NSPC, the samples were collected by plant personnel. Sufficient sample was collected at each operation to fill one plastic-lined 55-gallon drum. Each drum contained about 450 lbs (200 kg) of sample.

Samples were typically collected during an 8-h shift; at Minntac, samples were collected over several days and shifts. The goal was to collect samples that were reasonably representative not only of the tailings, but of portions of the iron-formation from which the ore originated, i.e., multiple shovel positions located throughout each mine. Admittedly, characterizing coarse tailings from all five taconite operations was a compromise in sampling practicality, given that about 30 million long tons of coarse tailings would be generated during the sample collection year, which translates into over 80,000 long tons *per day*. However, it is believed that the project's sampling strategy not only provided materials that reflected the typical range of taconite ore blends processed by each company during a production year, it provided

Table 1
Sampling dates and sample numbers

Event	EVTAC		Hibtac		Minntac		Ispat Inland (Minorca)		NSPC	
	Date	Sample No.	Date	Sample No.	Date	Sample No.	Date	Sample No.	Date	Sample No.
Sampling 1	12/13/2000	NRRI-40-00	11/16/2000	NRRI-36-00	11/22/2000	NRRI-37-00	12/8/2000	NRRI-39-00		
Sampling 2	3/6/2001	NRRI-10-01	3/9/2001	NRRI-11-01	2/15/2001	NRRI-08-01	3/1/2001	NRRI-09-01		
Sampling 3	6/13/2001	NRRI-31-01	7/24/2001	NRRI-42-01	5/7/2001	NRRI-17-01	6/11/2001	NRRI-30-01	7/9/2001	NRRI-37-01
Sampling 4	9/11/2001	NRRI-49-01	9/12/2001	NRRI-50-01	8/8/2001	NRRI-46-01	9/18/2001	NRRI-52-01	10/1/2001	NRRI-62-01

materials that could be used by potential aggregate consumers. Table 1 shows the sample collection dates, and the corresponding sample numbers used throughout the project.

The 18 samples were collected at the following mine locations:

- EVTAC: at the conveyor discharge above the truck pocket.
- Hibtac: from the tailings basin at recently deposited dragline stockpiles.
- Minntac: directly from spiral classifier discharge points.
- Ispat Inland (Minorca): at a conveyor discharge point inside the concentrator building.
- NSPC: from piles excavated from of the channel that leads into the tailings basin.

5. Sample preparation

At CMRL each sample was dumped into a rotating hopper that fed an eight-way rotary splitter. The eight splits were dumped back into the drum twice to blend each sample before representative portions were removed for testing and analyses.

After another pass through the rotary splitter, the one-eighth portions were adjusted using a Jones riffle. This step provided two 50-pound samples for testing by Mn/DOT, one 50-pound and six 25-pound samples for aggregate testing by Braun Intertec Engineering, Inc., and a 25-pound head sample for processing at CMRL. All sample pails were tagged with sample identification and all drums and pails were tightly closed with lids to retain the moisture that was present when sampled at each taconite facility. Mn/DOT samples were delivered to the District 1 facility in Duluth. Braun Intertec, having a facility relatively nearby in Hibbing, picked up their samples at CMRL.

CMRL head samples were weighed, dried at 110 °C, and weighed to determine moisture percentages. After the dried samples were mixed, approximately 1000 g were split out (riffled) for size analyses, and approximately 2000 g were split out for chemical analyses and X-ray diffraction (XRD). The latter were further prepared by standard CMRL procedures, i.e., they were stage crushed in a roll crusher to pass 20 mesh, and 150–200 g portions were split out and stage pulverized in a Braun pulverizer to pass a 200 mesh screen. About 20 g were split and bagged for XRD, and the balance of pulverized samples were submitted for

chemical analyses. Samples were similarly prepared and composited for specialized microscopy.

6. Size analyses

CMRL conducted particle size (sieve) analyses on each coarse tails sample. The data, composited for each mine, are presented in Fig. 2. The analyses show that a minimal amount of fines (–200 mesh material) is present in most of the coarse tailings samples. This is especially true for EVTAC, Minntac, and Ispat Inland, where coarse and fine tailings are separated. In fact, their size distribution plots are very similar. Overall, samples from Hibtac and NSPC contain a larger percentage of particles finer than 0.5 mm, while EVTAC and Minntac samples contain a smaller percentage.

Note how similarly the gradations plot for EVTAC, Minntac, and Ispat Inland (Minorca), and the minimal amount (about 2.5%) of –200 mesh material that is present in their samples. The Hibtac and NSPC plots reflect the more variable composition of their coarse tails, and the higher percentage of –200 mesh material. The difference between the size distribution of samples collected at Hibtac and NSPC and those collected from the other three operations (at which coarse and fine tailings are separated) simply reflects the basic differences in each company's process flow-sheet. The plots also show that EVTAC and Minntac coarse tailings contain a smaller percentage of particles finer than 1 mm than do coarse tailings from the other companies.

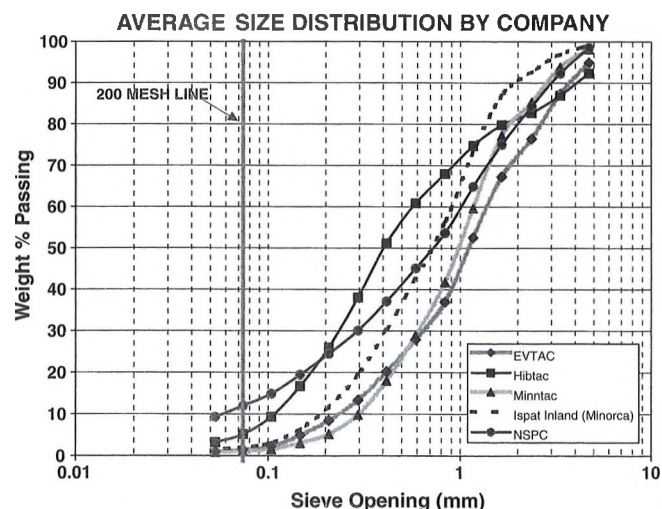


Fig. 2. Average coarse tailings size distribution, by company.

7. Mineralogy

Taconite ore from the Biwabik Iron Formation is composed primarily of quartz and magnetite, plus varying amounts of iron oxides, carbonates, and silicates. To determine the mineralogy of the coarse taconite tailings samples, X-ray diffraction and geochemistry were used.

X-ray diffraction (XRD) is an analytical method that can be used for identifying specific minerals in a rock or soil sample. Minerals will refract X-rays in diagnostic ways, depending on their crystal/molecular structure, and generate X-ray peaks that enable both qualitative and quantitative mineral identification to be performed. In qualitative XRD, the resultant peaks are used to identify the major,

minor, and trace minerals present in a sample. Quantitative XRD combines peak intensity interpretation with whole rock chemistry or comparison to pure minerals (Chung, 1975) to determine the relative percentages (quantities) of the minerals present within a sample.

X-ray diffraction patterns for the first nine tailing samples were generated by NRRI Economic Geology Group (EGG) personnel on the Philips XRD machine in the University of Minnesota, Duluth (UMD), Department of Geosciences. The last nine samples were run at the University of Minnesota Characterization Facility at the Shepherd Laboratories in Minneapolis. Fig. 3a and b are examples of the XRD patterns produced at UMD and Shepherd Laboratories, respectively. The peaks in the patterns showed the

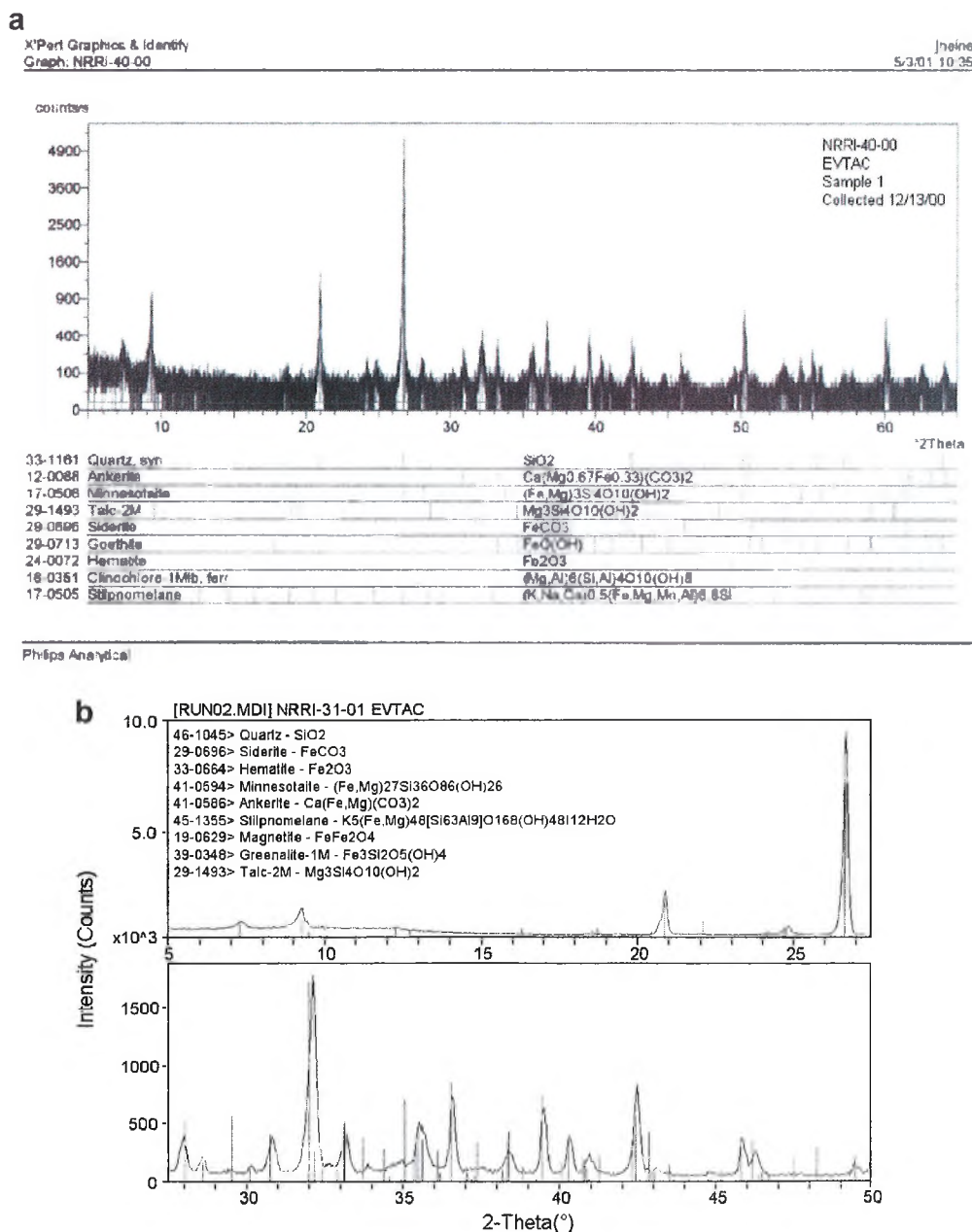


Fig. 3. (a) Typical XRD pattern: NRRI/University of Minnesota, Duluth, analysis; (b) typical XRD pattern, University of Minnesota Shepherd Laboratories analysis.

presence of various combinations of minerals. Again, this is the *qualitative* aspect of the technique. However, when the patterns were used with reference to major oxide chemical analyses performed by CMRL (Table 2), and total oxides were normalized to 100%, the percentage of each mineral in the sample could be calculated. This is the *quantitative* aspect of the technique. Total iron, or TFe_2O_3 as reported in Table 2, is based on the CMRL Fe% assay, multiplied by 1.42972. Percent sulfur (S%) is also reported, but it is not included in the major oxide total. The sulfur assay is used for determining the sulfide mineral content of the tailings. Finally, the H_2O and CO_2 values, when combined, give the equivalent of loss on ignition (LOI).

A spreadsheet routine developed by one of the authors was used to calculate mineral percentages, based on the XRD patterns and chemical analyses. As each mineral was calculated, its chemical constituents were subtracted from the original analysis or from the residual percentage, so that: (1) the latter was as near zero as possible; and (2) the total of the mineral percentages was at least within 0.5% of the total chemical percent, i.e., total oxides. Minerals were calculated as follows:

- Magnetite was determined by the Satmagan magnetic iron measurement.
- Stilpnomelane was calculated assuming all K_2O was present in this mineral.
- Apatite was assumed to be the only P_2O_5 -bearing mineral.
- Ankerite and/or other Ca-bearing carbonates used all CaO.
- Siderite (and/or Rhodochrosite) used the remaining CO_2 and MnO.
- Minnesotaite, Talc, and Greenalite used the remaining MgO and FeO.
- Chamosite was calculated if Al_2O_3 residual was greater than 0.05%.
- Hematite (and Goethite) used remaining Fe_2O_3 .
- Quartz was equal to the remaining SiO_2 .
- Rutile equivalent equaled TiO_2 percent.
- Pyrite was calculated using all S.
- Carbon was total C minus carbon as CO_2 .

The chemical compositions of the various minerals (Table 3) were determined from the following reference sources: Deer et al. (1962), Blake (1965), Klein (1974) and Floran and Papike (1975, 1978). The composite quantitative mineralogy for all 18 samples is illustrated in Fig. 4, showing that quartz is by far the dominant mineral, followed by lesser amounts of iron oxides, carbonates, and silicates.

8. Specialized microscopy

Specialized microscopic work was subcontracted to a National Institute of Standards and Technology (NIST) accredited laboratory, the RJ Lee Group of Monroeville, PA. This work was done, in part, to address concerns

Table 2
CMRL major oxide chemical analyses used for quantitative mineralogy calculations

Material	Sample	Rec'd. No.	Property	Fe%	Fe++%	Satmagan MagFe%	$\text{TF}_2\text{O}_3\%$	$\text{SiO}_2\%$	$\text{Al}_2\text{O}_3\%$	CaO%	MgO%	MnO%	$\text{Na}_2\text{O}\%$	$\text{K}_2\text{O}\%$	$\text{TiO}_2\%$	$\text{P}_2\text{O}_5\%$	$\text{CO}_2\%$	$\text{H}_2\text{O}\%$	Total Oxides%
Coarse tails	NRR1-40-00		EVTAC	18.4	7.46	2.92	26.31	63.07	0.25	1.25	2.63	0.517	0.017	0.072	0.020	0.044	5.22	1.65	101.05
Coarse tails	NRR1-10-01		EVTAC	19.4	5.15	5.23	27.74	63.68	0.34	1.06	2.69	0.455	0.017	0.063	0.026	0.041	3.19	1.42	100.72
Coarse tails	NRR1-31-01		EVTAC	19.7	11.86	1.92	28.17	58.27	0.50	0.97	3.28	0.797	0.059	0.125	0.039	0.060	7.70	1.70	101.66
Coarse tails	NRR1-49-01		EVTAC	15.3	7.27	1.86	21.87	64.95	0.33	1.66	3.44	0.553	0.080	0.114	0.011	0.034	6.42	1.55	101.02
Coarse tails	NRR1-36-00		Hibbtac	16.5	8.41	1.79	23.59	63.53	0.37	1.55	3.22	0.637	0.018	0.082	0.011	0.044	6.57	1.57	101.19
Coarse tails	NRR1-11-01		Hibbtac	17.5	8.28	1.54	25.02	61.79	0.36	1.60	2.78	0.710	0.011	0.073	0.009	0.044	7.10	1.68	101.18
Coarse tails	NRR1-42-01		Hibbtac	14.6	8.59	1.29	20.87	65.70	0.30	1.63	3.31	0.596	0.053	0.093	0.010	0.039	6.96	1.65	101.22
Coarse tails	NRR1-50-01		Hibbtac	17.3	7.49	2.84	24.73	63.82	0.22	1.65	2.63	0.634	0.052	0.044	0.019	0.030	5.60	1.60	101.03
Coarse tails	NRR1-37-00		Mintnac	16.4	7.52	2.63	23.45	66.15	0.45	1.12	2.68	0.533	0.025	0.103	0.033	0.041	4.37	1.89	100.84
Coarse tails	NRR1-08-01		Mintnac	15.8	8.67	2.72	22.59	65.46	0.90	1.45	2.77	0.689	0.031	0.126	0.070	0.060	5.24	1.69	101.07
Coarse tails	NRR1-17-01		Mintnac	18.2	5.73	2.52	26.02	65.20	0.33	0.87	2.26	0.617	0.013	0.069	0.020	0.037	3.83	1.42	100.68
Coarse tails	NRR1-46-01		Mintnac	20.3	4.77	2.94	29.02	61.62	0.39	1.61	1.96	0.733	0.019	0.110	0.025	0.046	3.54	1.42	100.53
Coarse tails	NRR1-39-00		Minorca	16.7	4.40	2.55	23.88	67.28	0.29	1.62	2.04	0.662	0.041	0.078	0.022	0.037	3.45	1.23	100.62
Coarse tails	NRR1-09-01		Minorca	13.3	4.95	1.80	19.02	70.72	0.27	1.11	3.27	0.646	0.022	0.081	0.013	0.030	4.04	1.48	100.70
Coarse tails	NRR1-30-01		Minorca	13.5	7.94	3.02	19.30	71.95	0.12	0.97	1.67	0.787	0.052	0.042	0.007	0.025	4.52	1.67	101.12
Coarse tails	NRR1-52-01		Minorca	17.0	8.89	2.35	24.31	65.53	0.20	1.33	2.57	0.733	0.043	0.036	0.016	0.032	4.77	1.68	101.24
Coarse tails	NRR1-37-01		NSPC	19.4	5.90	3.10	27.74	61.71	0.30	1.29	3.08	0.656	0.012	0.081	0.016	0.032	4.51	1.40	100.83
Coarse tails	NRR1-62-01		NSPC	20.6	5.36	2.57	29.45	59.11	0.32	1.59	3.31	0.660	0.014	0.074	0.015	0.032	4.49	1.67	100.74

Table 3
Mineral chemistries used for qualitative mineralogy calculations (see note below)

Mineral	Assumed chemical compositions of minerals Chemistry (%)														
	Tot. Fe	FeO	Fe ₂ O ₃	SiO ₂	Al ₂ O ₃	CaO	MgO	MnO	Na ₂ O	K ₂ O	CO ₂	Comb. H ₂ O	P ₂ O ₅	S	F
Ankerite	13.99	18.00				29.00	8.50	1.50			43.00				
Apatite, Carb-fluor						52.50		2.50			2.20	0.51	38.00		4.30
Calcite						56.03					43.97				
Chamosite	32.00	36.35	5.37	24.21	19.87		2.44					11.76			
Dolomite						30.41	21.86				47.73				
Fe-Dolomite	9.41	12.11				29.34	12.90	0.77			44.88				
Goethite	62.85		89.86									10.14			
Greenalite	39.48	46.31	5.00	35.59	1.00		2.31					9.79			
Greenalite	39.07	41.00	10.31	35.59	1.00		2.31					9.79			
Greenalite ^a	38.13	29.00	22.31	33.59	1.00		4.31					9.79			
Hematite	69.94		100.00												
Magnetite	72.36	31.03	68.97												
Minnesotaite	27.05	34.81	1.45	51.29	0.55		6.26					5.64			
Minnesotaite	27.05	34.81	2.00	51.29			6.26					5.64			
Pyrite	46.55													53.45	
Quartz				100.00											
Rhodochrosite (MGS)	1.04	1.34				3.06	0.80	53.08			41.72				
Siderite	40.59	52.24					3.05	4.06			40.65				
Siderite ^a	36.08	46.44					8.85	4.06			40.65				
Siderite, SIDMN	38.75	48.70					2.60	8.50			40.20				
Siderite, SIDMN ^a	34.73	44.70					6.60	8.50			40.20				
Siderite, Hi-Mn (MGS)	34.15	43.95					2.72	13.59			39.74				
Siderite, VHi-Mn (MGS)	26.36	33.92					2.45	24.00			39.64				
Stilpnomelane	25.00	27.67	5.00	46.98	5.07		4.22	1.20	0.30	1.74		7.82			
Stilpnomelane	24.66	23.27	9.40	46.98	5.07		4.99	0.59	0.14	1.74		7.82			
Talc				62.35	1.00		31.35					5.30			

Notes: Siderite, SIDMN = manganese bearing siderite; (MGS) = Minnesota Geological Survey determination.

^a Mineral form having higher MgO content.

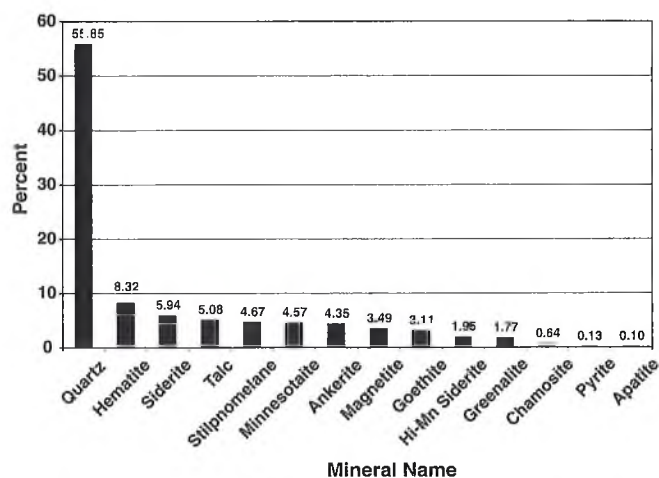


Fig. 4. Composite quantitative mineralogy of coarse tailings samples, all mines: $n = 18$ samples.

and questions about whether coarse tailings contained asbestos or had the potential to generate mineral particles of a size and shape that could be termed fibrous. These concerns and questions have direct lineage to the Reserve Mining Co. trial of the 1970s, and to the mineralogy of the Biwabik Iron Formation at its eastern end. Bartlett (1980) provides useful detail and background on the issues surrounding the Reserve Mining case.

The iron-formation's eastern end was metamorphosed 1.1 billion years ago during the emplacement of a series of mafic igneous intrusions, collectively known as the Duluth Complex, and amphibole minerals were formed. The amphiboles are principally of the cummingtonite-grunerite series, and include some actinolite and hornblende (French, 1968; Ross et al., 1993). These minerals first appear in the iron-formation midway through the former LTV Steel (now Cliffs Erie) property near Hoyt Lakes, Minnesota, as depicted by the diagonal lines in Figs. 5 and 6, and their cleavage fragments can take on a morphology and an aspect ratio (length to width) of $>3:1$ (and greater than 5 microns in length). The presence of amphibole minerals having these morphological characteristics was at the heart of the Reserve Mining Co. trial.

All of the coarse tailings samples studied by Zanko et al. (2003) came from taconite operations well to the west of the amphibole mineral area (Figs. 5 and 6). Nevertheless, it was believed important to subject the samples to state-of-the-art analytical techniques and methods for detecting asbestos minerals and mineral cleavage fragments because: (1) associations between "taconite tailings" and "asbestos" were still being made, regardless of where in the iron-formation the taconite ore and tailings originated; and (2) the potential use of coarse tailings and other taconite mining byproducts on a more widespread and significant basis inside and outside Minnesota

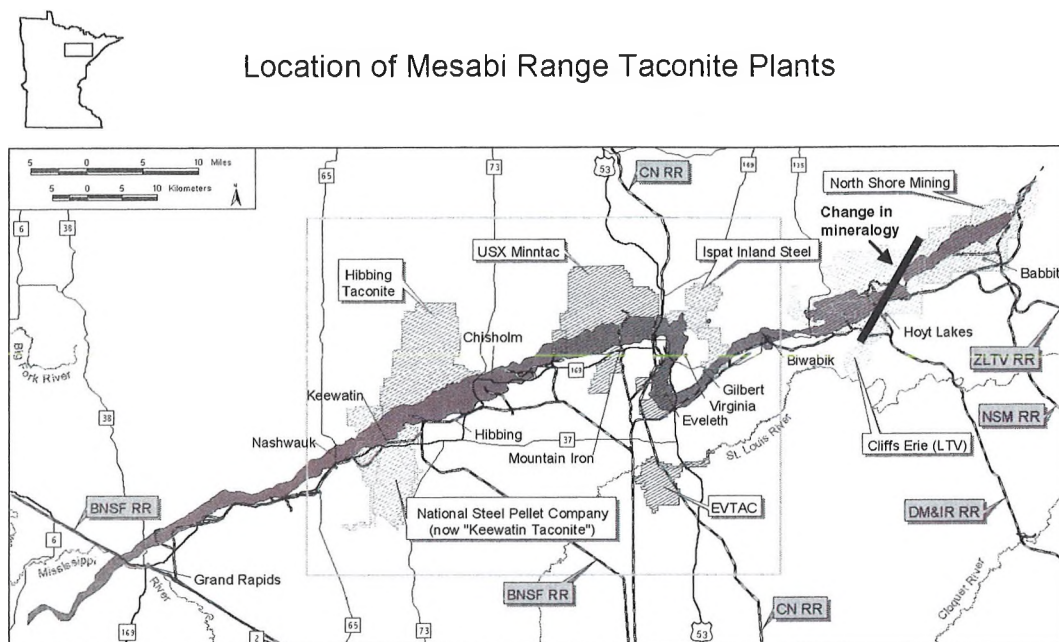


Fig. 5. Change in mineralogy relative to location of taconite mines, indicated by diagonal black line at Hoyt Lakes.

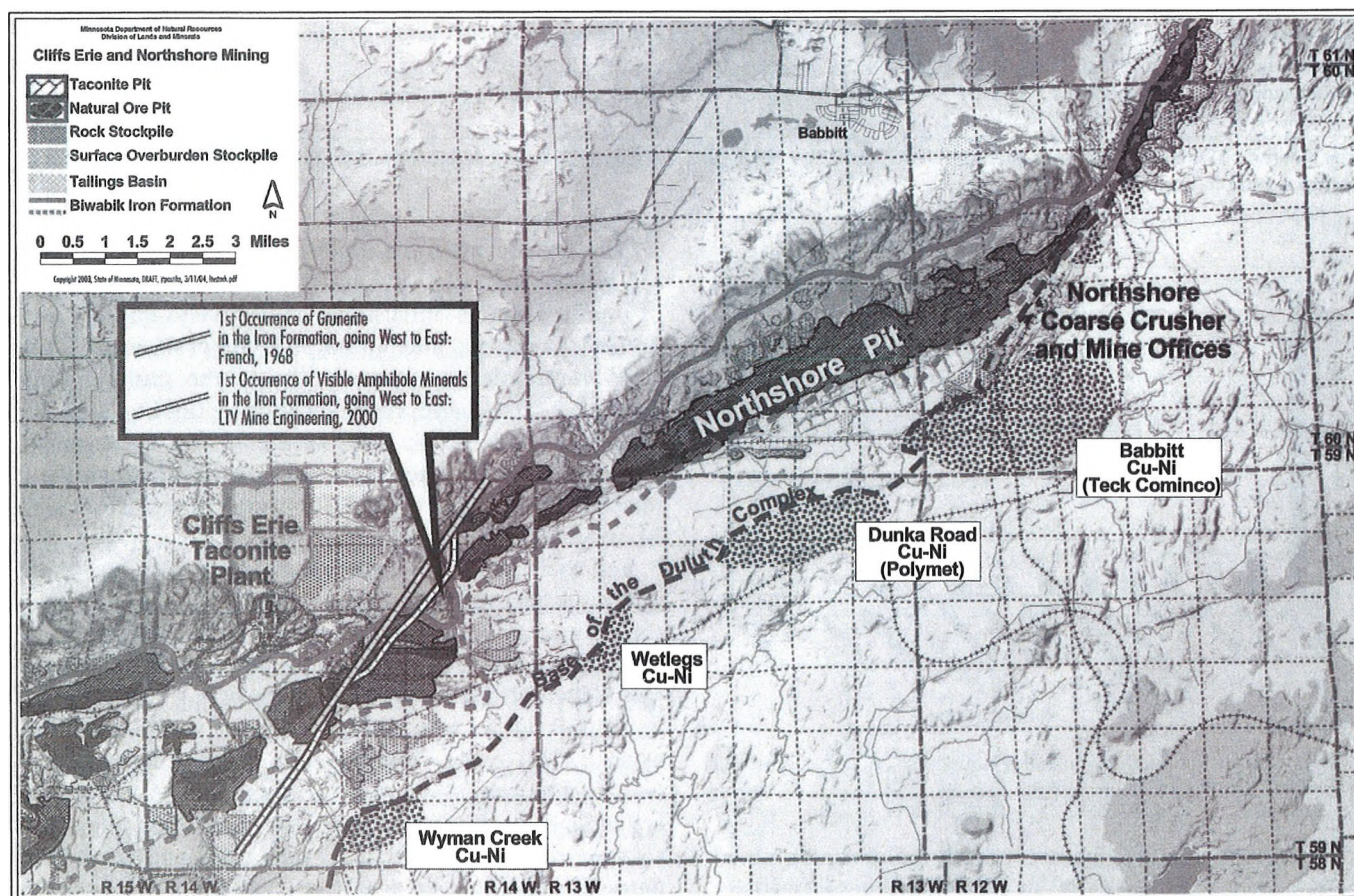


Fig. 6. Detailed map of Cliffs Erie (formerly LTV) and Northshore Mining Company properties showing line where grunerite and other amphibole minerals first appear at the eastern end of the BIF (map courtesy of Minnesota Department of Natural Resources, Division of Lands and Minerals, 2003).

would only generate more questions about those perceived associations. Therefore, the specialized microscopy work was performed to provide a factual and science-

based evaluation and documentation of the mineralogical and physical nature of potentially respirable microscopic coarse tailings particles.

9. Specialized microscopy summary for coarse tailings samples from five western Biwabik Iron Formation taconite operations

A combination of X-ray diffraction (XRD), polarized light microscopy (PLM), scanning electron microscopy (SEM), and transmission electron microscopy (TEM) was used by the RJ Lee Group to determine the mineralogy and size and shape characteristics of the mineral particles in the coarse tailings samples, and to determine if any asbestos minerals were present.

Two sample types were submitted from each taconite operation:

- (1) composited, as-is, samples; and
- (2) composited samples pulverized to pass a 200 mesh screen (–200 mesh: nominal opening of 75 μm).

These composited samples were believed to be reasonably representative of the coarse tailings generated over a single production year at each mine. Excerpts and summaries from the RJ Lee Group's report of analytical methods and testing results follow.

9.1. X-ray powder diffraction

A portion of each pulverized sample was ground in a mortar and pestle, mixed with fluorite (used as an internal standard), and backloaded into a standard XRD holder for analysis. The samples were processed using standard run parameters on a Philips XRD unit equipped with graphite monochromatized copper radiation. The XRD method had a detection limit of 0.5%.

As established in the previous XRD analyses performed by NRRI and the University of Minnesota, the RJ Lee Group's XRD analyses determined that the primary component of all samples was quartz (SiO_2 ; range of 55.7–64.9 weight percent). Hematite (Fe_2O_3), magnetite (Fe_3O_4), siderite (FeCO_3), ankerite ($\text{CaFe}(\text{CO}_3)_2$), and kaolinite ($\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4$) were the next most common minerals identified, in individual concentrations ranging from 1.6 to 13.8 weight percent. Minnesotaitite ($\text{Fe}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$) and stilpnomelane ($\sim\text{K}_{0.6}(\text{Mg}, \text{Fe}^{2+}, \text{Fe}^{3+})_6\text{Si}_8\text{Al}(\text{O}, \text{OH})_{27} \cdot 2\text{--}4\text{H}_2\text{O}$) were typically present in minor concentrations in all samples, followed by trace amounts of talc ($\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$), kaolinite, and goethite ($\alpha\text{FeO} \cdot \text{OH}$). Minnesotaitite was the primary silicate mineral identified by XRD. No amphibole minerals were observed during these analyses. Note: XRD cannot differentiate between fibrous and cleavage fragment varieties of minerals.

9.2. Polarized light microscopy

Both the pulverized samples and the <200 mesh fraction of the tailings were analyzed for asbestos content using polarized light microscopy (PLM) following the analytical procedures outlined in EPA/600/R-93/116, *Method for the*

Determination of Asbestos in Bulk Building Materials (Perkins and Harvey, 1993). Any non-asbestos materials, including cleavage fragments, were also identified and quantified during the PLM analysis. Quantitation of the sample was performed using a 1000-point count procedure. This procedure had an effective detection limit of 0.1%.

Trace levels of non-amphibole cleavage fragments were observed in the Ispat Inland (Minorca) and Minntac samples by PLM. With the point count procedure, fragments were considered to be at trace levels if they were seen within the field of view but not in the crosshair. The cleavage fragments (four fragments, total, in the *entire* PLM analyses of all samples) had moderate aspect ratios (greater than 3:1, length/width), but showed no evidence of fibril structure. Based on the PLM analyses, no regulated asbestos minerals were detected.

9.3. Scanning electron microscopy

The pulverized samples and the <200 mesh fraction of the as-received samples were analyzed using scanning electron microscopy (SEM) in general accordance with the methods outlined in ISO/DIS 14966 (2002). The SEM method had a detection limit of 0.0001 (1×10^{-4}) weight percent. A portion of each sample was weighed and placed in a beaker containing acetone. The suspension was shaken and an aliquot removed and deposited on a polycarbonate filter. A portion of the filter was placed on a carbon planchette and carbon coated (to reduce electrical charging on the particles). One hundred (100) separate fields were analyzed per sample, representing 12.64514 mm^2 of filter area.

The samples were analyzed in a SEM at an accelerating voltage of 20 keV at a working distance of 15–17 mm. During the analyses, back-scattered electron images and energy dispersive spectroscopy (EDS) were used to evaluate the particles. Typical images and EDS spectra were acquired for major particle types, e.g., quartz, minnesotaitite, talc, iron oxides, and carbonates. Back-scattered electron images and EDS spectra were also obtained for particles that had a greater than 3:1 aspect ratio and were greater than 0.25 μm in diameter. Fig. 7a–f are examples of images and spectra produced for the samples.

No asbestos minerals or amphibole minerals were observed during the SEM analyses. SEM identified 26 (total) mineral particles that had aspect ratios >3:1 and diameters greater than 0.25 μm , out of 1000 fields analyzed; i.e., 10 samples at 100 fields per sample. Several cleavage fragments were observed in the <200 mesh fraction that was sieved from the “as-received” Minorca tailings; no cleavage fragments were observed in the pulverized Minorca sample. The chemistries for the cleavage fragments observed in the Minorca sample were consistent with minnesotaitite and talc.

As summarized in a report to EPA by Berman and Crump (2003), there is general agreement that long and thin fibers pose the greatest health risk, although some have suggested that not enough is known about the relative potency of shorter fibers to assign them no risk. Page 1.4 of

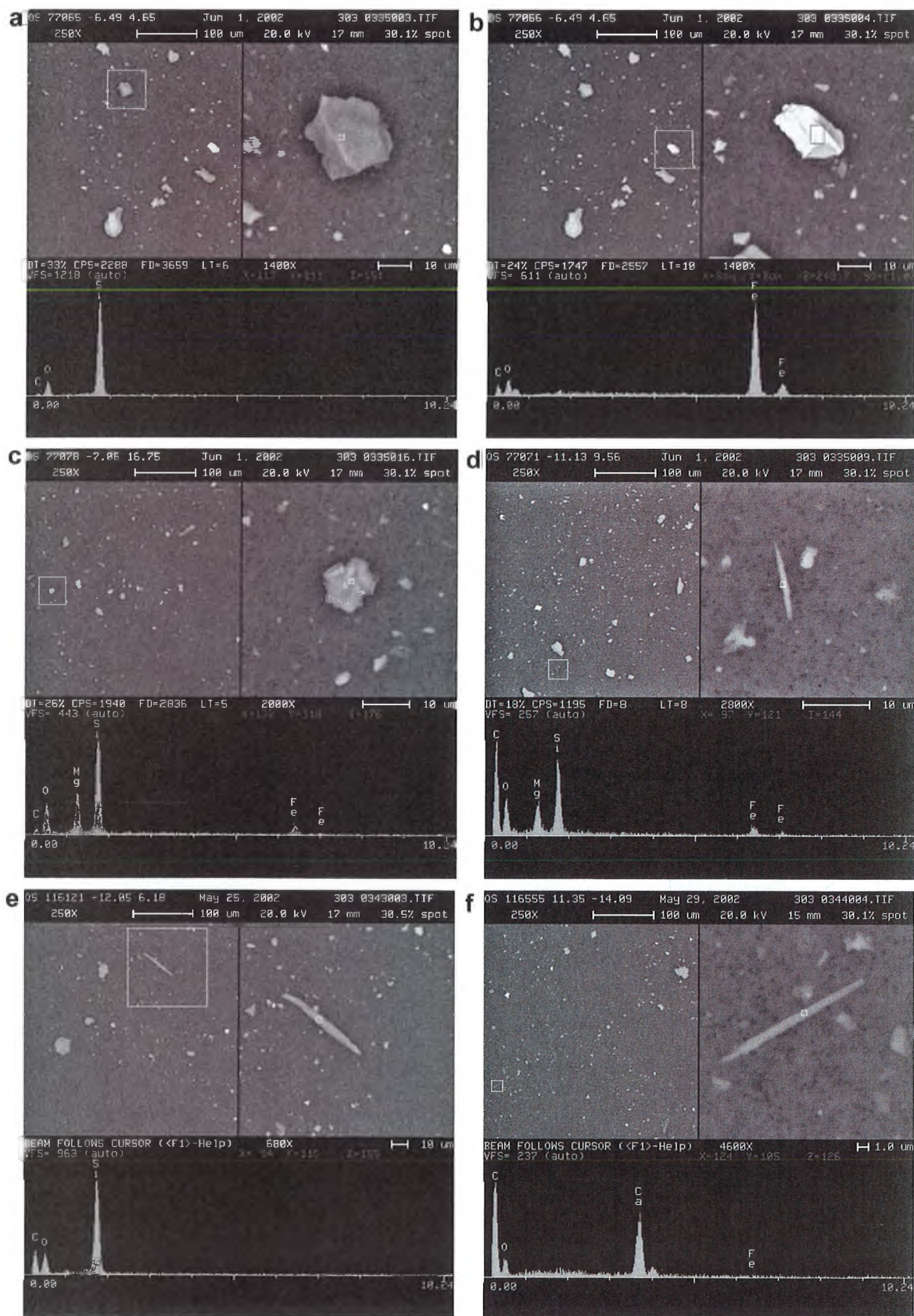


Fig. 7. (a) SEM image of quartz fragment: Ispat Inland (Minorca); (b) SEM image of iron-oxide fragment: Ispat Inland (Minorca); (c) SEM image of talc fragment: Ispat Inland (Minorca); (d) SEM image of talc cleavage fragment: Ispat Inland (Minorca); (e) SEM image of silica-rich (quartz) cleavage fragment: EVTAC; (f) SEM image of calcium-rich (calcite?) cleavage fragment: EVTAC.

their report, titled, “*Final Draft: Technical Support Document for a Protocol to Assess Asbestos-Related Risk*”, states the following:

“(5) The optimal exposure index that best reconciles the published literature assigns equal potency to fibers longer than 10 μm and thinner than 0.4 μm and assigns no potency to fibers of other dimensions.”

The SEM results showed that particles having these length and width characteristics were all but absent in the coarse tailings samples. Of the 26 particles identified by SEM as having aspect ratios $>3:1$ and diameters greater than 0.25 μm , only one particle (identified as talc) was longer than 10 μm and thinner than 0.4 μm .

9.4. Transmission electron microscopy/EPA Superfund Method

The tailings samples that were pulverized to <200 mesh were analyzed by transmission electron microscopy (TEM) to determine the weight percent of asbestos and cleavage fragments. The analytical procedure used for the TEM analysis was in general accordance with the analytical portion of ASTM D 5756 (2002). The TEM method had a sensitivity (detection limit) of 0.00002 (2×10^{-5}) weight percent. A portion of each sample was weighed and placed in a beaker, which was then filled to 100 ml with distilled water. The suspension was sonicated for 3 min, then allowed to settle for 2 min before an aliquot of the supernatant was removed and redeposited onto a 25 mm mixed cellulose ester (MCE) filter. The filter was then prepared for analysis using direct preparation procedures.

No asbestos minerals or amphibole cleavage fragments were observed during the TEM weight percent analysis.

9.5. EPA Superfund Method

The “as-received” samples were analyzed using the *Superfund Method for the Determination of Releasable Asbestos in Soils and Bulk Materials*, EPA 540-R-97-028 (1997), as modified by Berman and Kolk (2000). The samples were sieved through a 1 mm screen (#18) and the two size fractions weighed. Seventy grams of the <1 mm fraction were placed in the holder and tumbled as described in the method. Several filters of the elutriated sample were collected over varying times until one filter contained approximately 100 μg of samples. This filter from each sample was evaluated in the TEM for protocol fibers (fibers longer than 5 μm and thinner than 0.5 μm).

No asbestos fibers or cleavage mineral fragments longer than 5 μm and thinner than 0.5 μm were observed during the TEM analyses of the elutriated samples.

9.6. Significance of specialized microscopy results

Based on the combined results of the various tests, the RJ Lee Group concluded that no asbestos minerals were

detected in the coarse tailings samples collected from the five western Mesabi Range taconite facilities. The PLM and SEM analyses showed that some mineral cleavage fragments with an aspect ratio of $>3:1$ were present, but none belonged to the amphibole mineral group. Most of the cleavage fragments were consistent with minnesotaite or talc. As previous mineralogical work has shown, e.g., French (1968), minnesotaite and talc are silicate minerals typically found on the western Mesabi Range. Interestingly, one of the cleavage fragments was silica-rich (quartz/chert?) (Fig. 7e), and another was calcium-rich (calcite?) (Fig. 7f). These results suggest that mineral particles with an aspect ratio of $>3:1$ can be produced by crushing and grinding rocks that contain neither amphibole minerals nor asbestos.

10. Specialized microscopy results for an eastern Biwabik Iron Formation sample

As a point of comparison, Lake County, Minnesota, submitted an eastern Biwabik Iron Formation sample to the RJ Lee Group. The same specialized microscopic analyses and testing methods performed on the western Mesabi Range coarse tailings samples, i.e., PLM, SEM, TEM, and EPA Superfund Method, were done on the eastern sample. Refer to the previous section for specific analytical method descriptions.

The sample, submitted as-is and pulverized to -200 mesh, was a composite of dry cobber lean ore collected in January, 2003, from several locations within the Milepost 7 basin at the Cliffs Northshore taconite operation in Silver Bay, Minnesota. Dry cobber lean ore is a byproduct of the ore processed from Northshore’s taconite mine near Babbitt, Minnesota (refer to Figs. 1, 5 and 6). This byproduct is much coarser (more than 50% of the particles are coarser than 3/8 in.) than the coarse tailings produced at the five western taconite plants, yet it contains a low percentage of fines (less than 3% finer than 200 mesh). PLM, SEM, and TEM were performed on the sample split pulverized to -200 mesh; the EPA Superfund Method was performed on the as-is sample split.

10.1. Polarized light microscopy

PLM analysis of the pulverized -200 mesh sample showed it contained approximately 10–15% cleavage amphibole fragments identified as “tremolite/actinolite”. The cleavage fragments were reported to have moderate aspect ratios ($>3:1$, length/width), but showed no evidence of fibril structure. The presence of amphiboles is consistent with the mineralogy of the metamorphosed eastern end of the Biwabik Iron Formation. The relatively large number of cleavage fragments detected by PLM in the pulverized Northshore sample contrasts with the trace amounts found in samples from the five western operations. The difference suggests that amphibole-bearing taconite from the eastern Biwabik Iron Formation generates cleavage fragments more readily than does taconite from the western BIF.

10.2. Scanning electron microscopy

Amphibole cleavage fragments were observed in the pulverized –200 mesh sample during the SEM analyses that were consistent with tremolite/actinolite. SEM identified 51 particles that had aspect ratios >5:1 and diameters between 0.25 and 2 μm in 35 of the 50 fields analyzed. Fig. 8a–d are SEM images and spectra produced for some of the Northshore amphibole cleavage fragments. Note the calcium peaks that are indicative of tremolite and actinolite. Fig. 8a and b depict blocky cleavage fragments; Fig. 8c and d depict narrower cleavage fragments.

10.3. Transmission electron microscopy

TEM was used to determine the weight percent of asbestos and cleavage fragments in the pulverized –200 mesh sample. No asbestos was observed, but tremolite/actinolite

cleavage fragments were observed at the 0.02 weight percent concentration. According to the RJ Lee Group, the TEM cleavage fragment concentration is said to differ from the PLM concentration due to the size of the cleavage fragments. Because the TEM suspension was allowed to settle for 2 min, particles larger than about 20 μm settle out, and are not analyzed in the TEM. Therefore, the low (0.02 weight percent) indicates that cleavage fragments are primarily larger than this dimension.

10.4. EPA Superfund Method

The “as-is” Northshore sample was analyzed using the *Superfund Method for the Determination of Releasable Asbestos in Soils and Bulk Materials*, EPA 540-R-97-028 (1997), as modified by Berman and Kolk (2000). The procedure failed to generate any protocol fibers (fibers longer than 5 μm and thinner than 0.5 μm). No asbestiform fibers

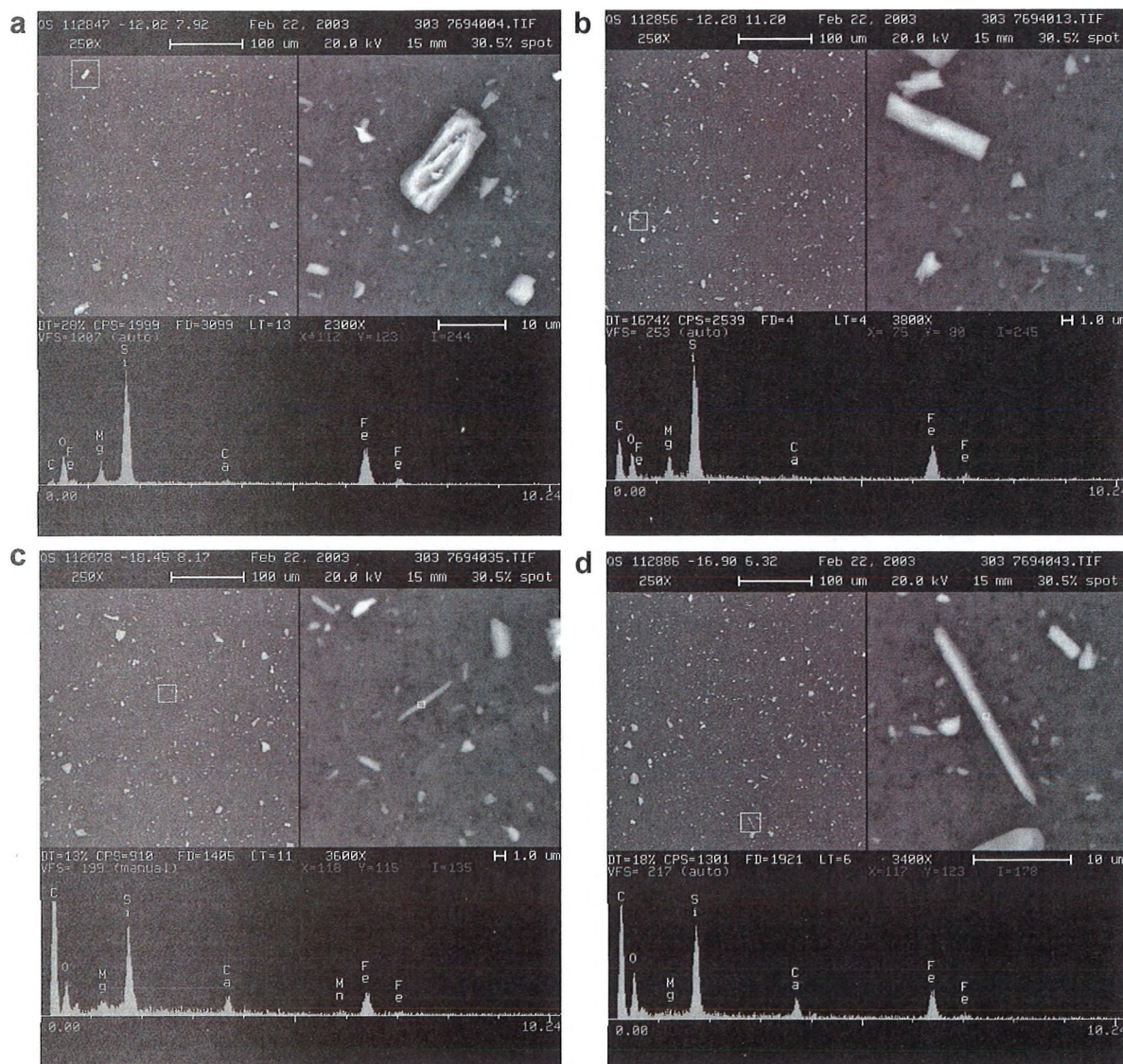


Fig. 8. (a and b) SEM image of blocky amphibole cleavage fragment; (c and d) SEM image of narrow amphibole cleavage fragment.

or mineral cleavage fragments longer than 5 μm and thinner than 0.5 μm were observed during the TEM analyses of the elutriated sample.

10.5. Significance of specialized microscopy results for an eastern Biwabik Iron Formation sample

Based on the combined results of the various tests, the RJ Lee Group concluded that amphibole cleavage fragments but not asbestos were detected in the sample collected from the Cliffs Northshore property. Amphibole cleavage fragments were detected by both PLM and SEM in the sample split pulverized to -200 mesh. The TEM analyses, in general accordance with the analytical portion of ASTM D 5756 (2002), indicated that nearly all of the cleavage fragments were larger than 20 μm . Lastly, the EPA Superfund Method failed to generate protocol fibers from the “as-is” sample split, i.e., the size and type of material that would most likely be used as construction aggregate.

These results appear to show that amphibole-bearing eastern Biwabik Iron Formation taconite mining byproducts, when pulverized to -200 mesh, will generate a larger number of cleavage fragments than comparably pulverized western Biwabik Iron Formation taconite mining byproducts. In his Ph.D. thesis, Stevenson (1983) determined that the number of amphibole “fibers” generated by the processing of copper–nickel ore from the adjacent Duluth Complex was proportional to the amount of amphibole present in the ore and to the fineness of grind during processing. However, it is important to remember that typical dry cobber lean ore production generates less than 3% -200 mesh-sized particles in the final product. This latter point, when viewed with the EPA Superfund Method test results on the “as-is” sample split, indicates a low potential for problematic dust generation if the material is used as construction aggregate. But because only one sample was subjected to the microscopy testing, supplemental testing of additional eastern Biwabik Iron Formation taconite mining byproducts would be desirable.

11. MSHA sampling data and Minnesota Department of Health mesothelioma findings

Mineral “fibers” can be present in a variety of geological settings, as revealed in an analysis of air sampling conducted by the Mine Safety and Health Administration (MSHA). Following news reports in 1999 that described serious health problems associated with amphibole asbestos-contaminated vermiculite mined at Libby, Montana (Schneider, 1999), MSHA collected air samples from several mines and quarries in the United States between January 10, 2000, and March 25, 2002. The air sample data summarized herein can be found at MSHA’s web site:

www.msha.gov/asbestos/asbestos.htm.

MSHA’s intent was to assess the air quality at mining and quarrying operations where respirable mineral fibers

could be generated, but especially at other U.S. vermiculite mines.

The MSHA tests make no distinction as to mineral type, only to the total number of particles that are >5 μm in length and have a minimum aspect ratio (length:width) of 3:1 as determined by Phase Contrast Microscopy (PCM), in accordance to the National Institute for Occupational Safety and Health (NIOSH), Method 7400, Issue 2 (NIOSH, 1994). The current MSHA personal exposure limit (PEL) is 2.0 fibers/cc for an 8 h, shift weighted average. The OSHA PEL is much more stringent at 0.1 fibers/cc for an 8 h, shift weighted average. However, fibers <0.25 μm in diameter cannot be detected by the PCM method.

Fig. 9 summarizes the MSHA air sampling findings by mine/quarry type for which at least six samples were available for averaging. These data are for fiber counts as determined by PCM only. The 0.1 fibers/cc OSHA PEL standard is represented on the graph by the horizontal dashed line. The average PEL is graphed for samples that exceed the detection limit at each mine/quarry type. The number of samples used for determining the average PEL for each mine/quarry type is also reported. The data are taken in their entirety; no distinction is made between the various job categories for which air samples were collected. The data (and graph) show Minnesota iron mines having an average PEL of 0.026 fibers/cc for an 8 h, shift weighted average for the 2000–2002 data. This value is well below OSHA’s 0.1 fibers/cc standard, is comparable to the granite average, and is lower than the limestone average. For comparative purposes, samples taken in the 1970s at the Libby, Montana, vermiculite mine measured fiber levels at 18 fibers/cc.

Iron ore mines in Minnesota and Michigan were also sampled more thoroughly, in response not only to the Libby situation, but to two Minnesota Department of Health (MDH) Minnesota Cancer Surveillance System (MCSS) reports published in 1997 (MCSS Epidemiology Report 97-1) and 1999 (MCSS Epidemiology Report 99-2). The MDH reports showed a higher rate (70% higher than expected) of the asbestos-related cancer, mesothelioma, occurring in males in a seven-county region of north-eastern Minnesota.

Because some people ascribed the higher cancer rate to taconite dust exposure, the MDH conducted a follow-up study (MCSS Epidemiology Report 03:1, published in 2003) to look specifically at the incidence of mesothelioma in iron miners and possible sources of commercial asbestos exposure in the mining industry. In a full report released in November, 2003 (Brunner et al., 2003) stated the following:

“It was found that: (a) 14 of the 15 iron miners (for whom a sufficient occupational history was available to make a judgment) had jobs with potential exposures to commercial asbestos, (b) these jobs were held at least 20 years or more prior to diagnosis, and (c) only one miner could be identified as having potentially held any of the highest silica-dust exposure job titles. The explanation most consistent with these findings is that commercial

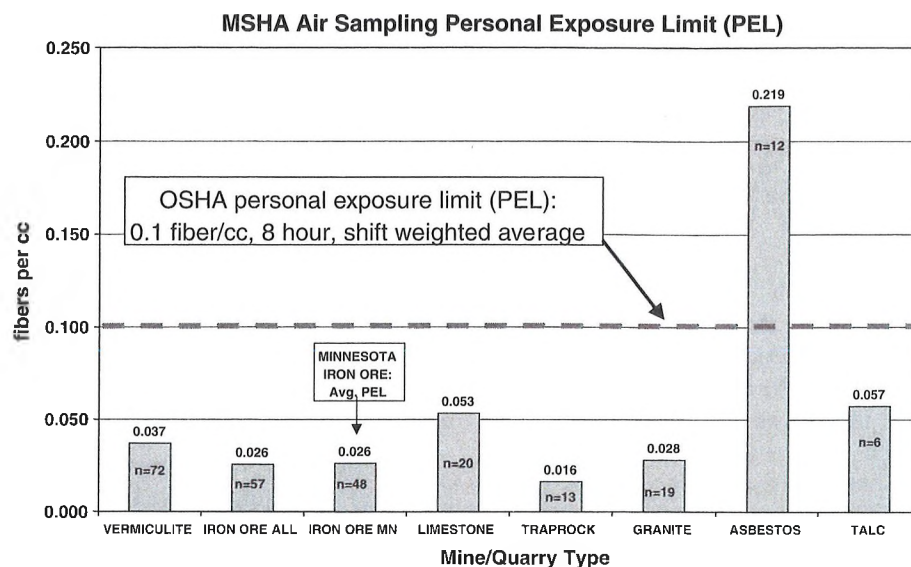


Fig. 9. MSHA air sampling Phase Contrast Microscopy (PCM) data: January 10, 2000 to March 25, 2002 (data source: www.msha.gov/asbestos/asbestos.htm).

asbestos exposure, rather than taconite dust, is the most likely cause for the occurrence of mesothelioma in men employed in the mining industry. However, at least one miner had no obvious source of exposure to commercial asbestos and other causes cannot be ruled out"

These findings suggest that exposure to commercial asbestos products may have been a significant factor in the development of mesothelioma in the miners.

12. Conclusions

Mineralogical and specialized microscopic analyses of coarse taconite tailings sample composites from five western Mesabi Range taconite mines indicated neither the presence of the six regulated asbestos minerals nor amphibole minerals. A very small number of cleavage fragments/mineral fibers were detected by SEM (primarily minnesotaite and talc). Amphibole minerals, absent in coarse tailings samples from the five western Mesabi Range taconite operations, were present in the single eastern Biwabik Iron Formation sample submitted by Lake County.

Mineral cleavage fragments can also be generated from many rock types, not just taconite, as demonstrated by the Mine Safety and Health Administration's (MSHA) 2000–2002 air sampling data. Importantly, the *Superfund Method for the Determination of Releasable Asbestos in Soils and Bulk Materials*, EPA 540-R-97-028 (1997), as modified by Berman and Kolk (2000) and performed by the RJ Lee Group, failed to generate any protocol fibers (fibers longer than 5 μm and thinner than 0.5 μm) from either the western coarse tailings samples or the eastern Biwabik Iron Formation sample.

The specialized microscopy analyses, coupled with the MSHA data and recent Minnesota Department of Health

findings, should provide useful information to regulators and potential end-users about the nature of the dust that would be encountered when handling and using taconite mining byproducts like coarse tailings for construction aggregate purposes. The combined results show how geology, mineralogy, chemistry, physical properties, particle size, shape, and morphology, and intended end-uses must all be taken into account when working with any potential dust-generating aggregate, and should be viewed with proper context and perspective.

With respect to coarse taconite tailings, context and perspective includes the following points:

- most of the potentially respirable dust generated during the production of coarse tailings occurs at the mine sites;
- coarse tailings are a byproduct of typically wet mineral processing techniques, and are often transported as a slurry; they are, to varying degrees, a "washed" product;
- coarse tailings contain a small percentage of fines (–200 mesh), especially at operations that make a fine and coarse separation, where the percentage of fines is typically less than 2.5%;
- coarse tailings are hard and resist abrasion;
- coarse tailings are composed primarily of quartz; and
- coarse tailings would most likely be used in buried applications, such as granular fill, or encapsulated in bituminous asphalt or concrete mixes, thereby reducing the potential for post-construction dust exposure to negligible levels.

Therefore, coarse tailings and other taconite mining byproducts should be treated with the same common sense safety and industrial hygiene approach practiced for all mineral-based materials that have the potential to generate respirable dust, silica or otherwise.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- Ad Hoc Aggregate Committee, 1998. Minnesota's aggregate resources: road to the 21st century, Aggregate Resources Task Force, 34 p.
- Aggregate Resources Task Force, 2000. Aggregate resources task force—final report to the Minnesota legislature: Representative Tom Rukavina, Chair, 38 p.
- ASTM D 5756, 2002. Standard test method for microvacuum sampling and indirect analysis of dust by transmission electron microscopy for asbestos mass concentration, ASTM International.
- Bartlett, R.V., 1980. The Reserve Mining Controversy—Science, Technology, and Environmental Quality. Indiana University Press, Bloomington and London, 293 p.
- Blake, R.L., 1965. Iron phyllosilicates of the Cuyuna District in Minnesota. *The American Mineralogist* 50, 148.
- Berman, D.W., Crump, K.S., 2003. Final Draft: Technical Support Document for a Protocol to Assess Asbestos-related Risk: Prepared for Office of Solid Waste and Emergency Response, U.S. Environmental Protection Agency, Washington, DC, EPA # 9345.4-06, October, 2003.
- Berman, D.W., Kolk, A.J., 2000. Modified Elutriator Method for the Determination of Asbestos in Soils and Bulk Materials, Revision 1: Submitted to the U.S. Environmental Protection Agency, Region 8, May 23, 2000.
- Brunner, W., Williams, A.N., Bender, A.P., 2003. Exposures to commercial asbestos in northeastern Minnesota iron miners who developed mesothelioma, Minnesota Department of Health Chronic Disease and Environmental Epidemiology, Minneapolis, Minnesota, 42 p., November 25, 2003.
- Chung, F.H., 1975. Quantitative interpretation of X-ray diffraction patterns of mixtures. III. Simultaneous determination of a set of reference intensities. *Journal of Applied Crystallography* 8, 17–19.
- Davis, E.W., 1964. Pioneering with taconite, Minnesota Historical Society, 246 p.
- Deer, W.A., Howie, R.A., Zussman, J., 1962. In: *Rock-forming Minerals*, vols. 3 and 5. Longmans, Green and Co., Ltd., London.
- Floran, R.J., Papike, J.J., 1975. Petrology of the low-grade rocks of the Gunflint Iron-Formation, Ontario-Minnesota. *Geological Society of America Bulletin* 6, 1169.
- Floran, R.J., Papike, J.J., 1978. Mineralogy and petrology of the gunflint iron formation, Minnesota-Ontario: correlation of compositional and assemblage variations at low to moderate grade. *Journal of Petrology* 19, 15, Part 2.
- French, B.M., 1968. Progressive contact metamorphism of the Biwabik Iron-formation, Mesabi Range, Minnesota, University of Minnesota, Minnesota Geological Survey Bulletin 45, 103 p.
- Klein Jr., C., 1974. Greenalite, stilpnomelane, minnesotaite, crocidolite, and carbonates in a very low-grade metamorphic Precambrian iron formation. *Canadian Mineralogist* 12, 475.
- ISO/DIS 14966, 2002. Ambient air—determination of numerical concentration of inorganic fibrous particles—scanning electron microscopy method, International Organization for Standardization.
- Minnesota Department of Health, 1997. Cancer rates and trends in Northeastern Minnesota, Minnesota Cancer Surveillance System (MCSS) Epidemiology Report 97-1, Minnesota Department of Health, Minneapolis, Minnesota, 15 p.
- Minnesota Department of Health, 1999. Cancer incidence rates in Northeastern Minnesota, Minnesota Cancer Surveillance System (MCSS) Epidemiology Report 99-2, Minnesota Department of Health, Minneapolis, Minnesota, 11 p.
- Minnesota Department of Health, 2003. Cancer incidence rates in Northeastern Minnesota with an emphasis on mesothelioma, Minnesota Cancer Surveillance System (MCSS) Epidemiology Report 03-1, Minnesota Department of Health, Minneapolis, Minnesota, 6 p.
- National Institute of Occupational Safety and Health (NIOSH), 1994. Method: 7400, Issue 2, Asbestos and other fibers by PCM. In: Schlecht, P.C., O'Connor, P.F. (Eds.), *Manual of Analytical Methods (NMAM[®])*, fourth ed., DHHS (NIOSH) Publication 94-113 (August, 1994).
- Perkins, R.L., Harvey, B.W., 1993. Method for the determination of asbestos in bulk building materials, EPA/600/R-93/116, U.S. Environmental Protection Agency.
- Ross, M., Nolan, R.P., Langer, A.M., Cooper, W.C., 1993. Health effects of mineral dusts other than asbestos. In: Guthrie, G.D., Jr., Mossman, B.T. (Eds.), *Health Effects of Mineral Dusts, Reviews in Mineralogy*, vol. 28. Mineralogical Society of America, pp. 361–407.
- Schneider, A., 1999. A town left to die, *Seattle Post-Intelligencer*, Thursday, November 18, 1999.
- Southwick, D.L., Jousseau, M., Meyer, G.N., Mossler, J.H., Wahl, T.E., 2000. Aggregate resources inventory of the seven-county metropolitan area, Minnesota. Minnesota Geological Survey Information Circular 46, 1.
- Stevenson, R.J., 1983. Amphiboles at the base of the Duluth Complex, Minnesota: Unpubl. Ph.D. Thesis, University of Minnesota, 162 p.
- United States Environmental Protection Agency (USEPA), 1997. Superfund method for the determination of releasable asbestos in soils and bulk materials, EPA 540-R-97-028, U.S. Environmental Protection Agency, Washington.
- Zanko, L.M., Niles, H.B., Oreskovich, J.A., 2003. Properties and aggregate potential of coarse taconite tailings from five Minnesota taconite operations, Minnesota Department of Transportation, Local Road Research Board, St. Paul, MN, Report No. 2004-06 (also as Natural Resources Research Institute Technical Report, NRRI/TR-2003/44).



Analysis of airborne and waterborne particles around a taconite ore processing facility

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Abstract

Since the mid-1970s, samples of airborne and waterborne fibrous particulates have been collected in the area of the Northshore Taconite Ore Processing Facility by the Minnesota Department of Health (MDH), the Minnesota Pollution Control Agency (PCA), and the University of Minnesota. Indirect sample preparation has consistently been used although other aspects of the sampling methods and sites have varied and analytical procedures were altered over time as more accurate and precise microscopy methods were developed (i.e., phase contrast optical microscopy, transmission electron microscopy, transmission electron microscopy with energy dispersive spectroscopy). In the mid-1970s, levels of airborne fibrous particulate in the Silver Bay area averaged from 0.00030 to 0.03 f/ml. This level was significantly greater than levels of similar particulates in the St. Paul, MN area, although two of the Silver Bay sampling sites, considered individually, did not indicate levels of fibrous particulate markedly different than that seen in St. Paul. More recent sampling data (i.e., 1990–2001) indicate mean concentration of airborne fibrous particulates (amphibole-like fibrous particulates) of 0.0020 f/ml with a range of values from 0.0001 to 0.0140 f/ml. Such levels are not significantly different from those seen in other non-urban environments in the US and Europe. Concentrations of fibrous particulates in water samples were higher in the mid-1970 when iron ore tailings were being deposited in Lake Superior, but since the tailings have been deposited on land waterborne levels of fibrous particulate in the Beaver River have remained relatively constant averaging in the range of 7.5 MFL. This level is only slightly in excess of the current EPA drinking water standard for fibrous particulates. Review and consideration of this data is important in determining the potential health risks associated with airborne and waterborne fibrous particulates in the areas of the Northshore Taconite Ore Processing Facility.
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Keywords: Taconite; Asbestos; Asbestiform fibers; Fibrous particulates; Cleavage fragments; Phase contrast optical microscopy; Transmission electron microscopy

1. Introduction

Public health concerns relative to fibrous particulates, specifically asbestos in its various forms, resulted in an extensive air and waterborne sampling program by individuals at the Northshore Taconite Ore Processing Facility and representatives of the Minnesota Department of Health (MDH), the Minnesota Pollution Control Agency (PCA), and the University of Minnesota in the early to

mid-1970. Unfortunately, the lack of a standardized definition of what constituted a fiber as opposed to a particulate and/or cleavage fragment (i.e., chemical/geological composition, fiber length, diameter and relevant aspect ratio, requirement for parallel sides, etc.), varying methods of sample collection and preparation (i.e., direct and indirect methods), and the use of multiple microscopy techniques (i.e., polarized light microscopy, phase contrast optical microscopy, scanning and electron transmission) produced airborne and waterborne sample results which were extremely variable and often times contradictory.

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Nevertheless, in an attempt to utilize this data to some extent the time of the Reserve Mining Case (Berndt and Brice, 2008), complex mathematical models were developed to estimate both the number of fibers that would be emitted from the Northshore Taconite Ore Processing Facility and the expected concentrations at population centers. Values for numerous variables were entered into multiple formulas to arrive at projections for both total suspended particulates and fiber levels in both air and water. Despite this laudable effort, after reviewing arguments presented by both plaintiff's and the defendant in the case, the US Court of Appeals for the eighth Circuit

rules in 1975 that "It is not known what the level of fiber exposure is, other than it is relatively low, and it is not known what level of exposure is safe or unsafe" (Bartlett, 1980).

However, based on the data available, the Court of Appeals did consider the air emissions in the area of Silver Bay to be of much greater concern than the concentrations of fibrous particulates documented in the various bodies of water in the area surrounding the Northshore Taconite Ore Processing Facility. Thus, the Court declared that "Reserve must use such available technology as will reduce the asbestos fiber count in the ambient air at Silver Bay below a

Air Monitoring Sites (Fibers) And Selected Geological Features

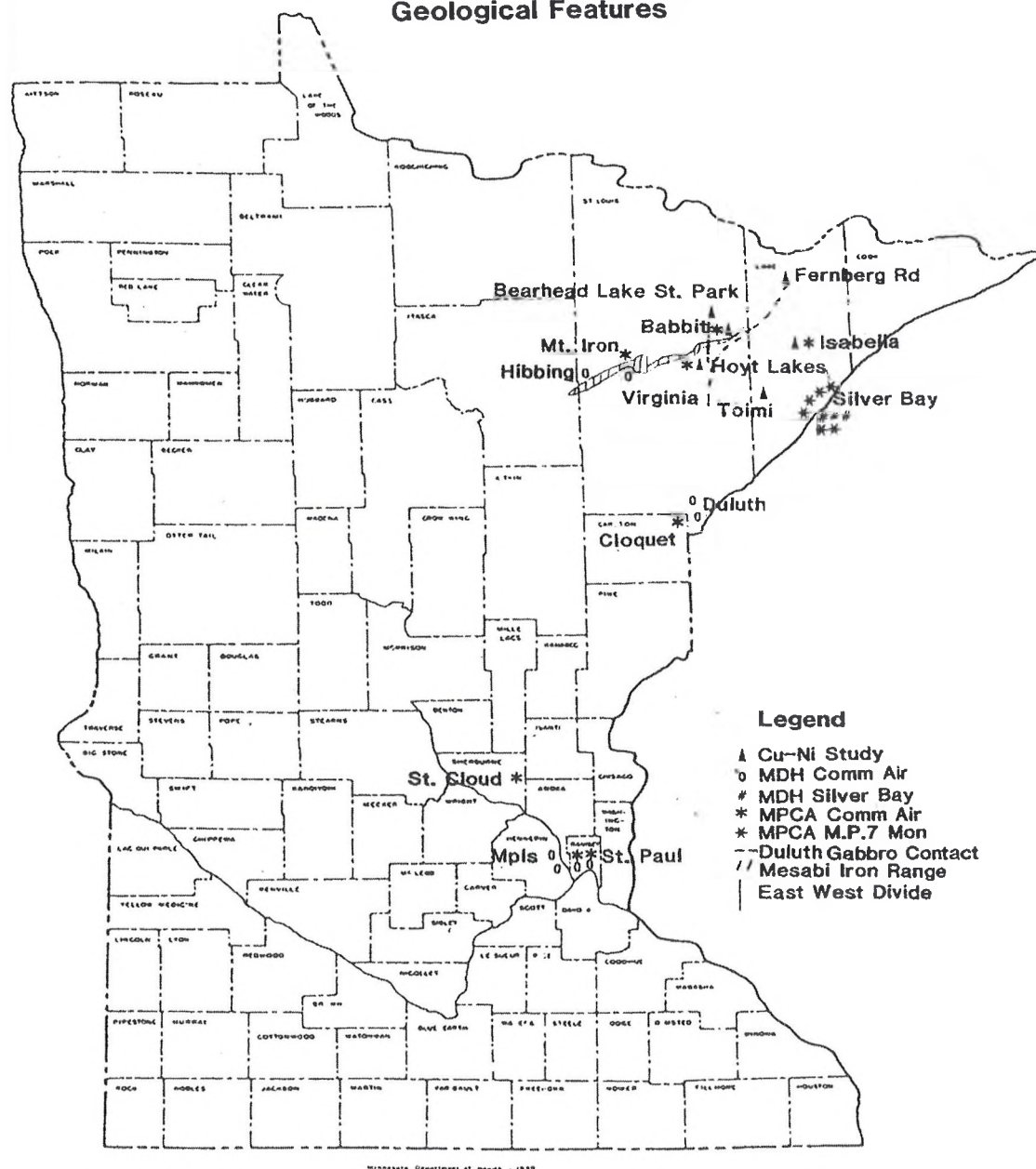


Fig. 1. Air monitoring sites (fibers) and selected geological features.

medically significant level.” Since there were no established criteria to define “medically significant,” the Court ruled that the “controls may be deemed adequate which reduce the fiber count to a level ordinarily found in the ambient air of a control city such as St. Paul” (Reserve Mining Company vs. the US Environmental Protection Agency et al., 1975).

2. Materials and methods

2.1. Ambient air monitoring

In response to the Court’s Ruling, the Minnesota Department of Health (MDH) established specific airborne fiber monitoring sites in and around the town of Silver Bay, MN and in the communities of Babbitt, Hoyt Lake, Virginia, Duluth, Hibbing, St. Paul, and Minneapolis, MN. (See Figs. 1 and 2). To standardize collection and analytical protocols from site to site, MDH initially adopted the use of standardized airborne fiber monitoring techniques (EPA, 1973). MDH soon developed its own method for analyzing fibers (Minnesota Department of Health, 1976). During the 1970s, samples were taken on membrane filters using high volume monitoring devices. Samples were collected for a period of 18 days at a time with the monitor operating 1 h on and 5 h off. Sampling sites were reduced to the Silver Bay/Beaver Bay area in the late 1970s, and the sam-

ples were collected on 105 mm diameter membrane filters, and later on 47 mm diameter filters. Samples were collected for 96 h continuously every 18 days.

After such protracted sampling periods, the filters on which the fibrous particulates were deposited became too heavily loaded for direct examination. Thus, the filters were dissolved using chemicals and/or low-temperature ashing and redispersed in water. An aliquot was then filtered onto a new membrane filter at a lower particle density for counting purposes. By selecting aliquots of various volumes the loading was adjusted for optimum counting of the fibrous particulates present. This “indirect” method of sample preparation facilitated fiber counting, but was also found over time to alter both the particle number and size distribution of the particles present.

Analysis was performed by transmission electron microscopy (TEM). Fibrous particulates were defined as any structures which exhibited a 3:1 aspect (length to width) ratio, had reasonably straight sides and were determined to have a crystalline structure by the use of electron diffraction. No attempt was made to distinguish between particulates, cleavage fragments and asbestiform “fibers” because the structures were known to exist on a continuum (Ross et al., 2008) and an arbitrary decision would have been necessary based on morphology of each structure alone. However, most of the fibrous particulates analyzed by electron microscopy were cleavage fragments. Generally, only about 10% of the airborne fibrous particulates were greater than 5 μm in length, and very few (i.e., <1%) were considered truly asbestiform in nature.

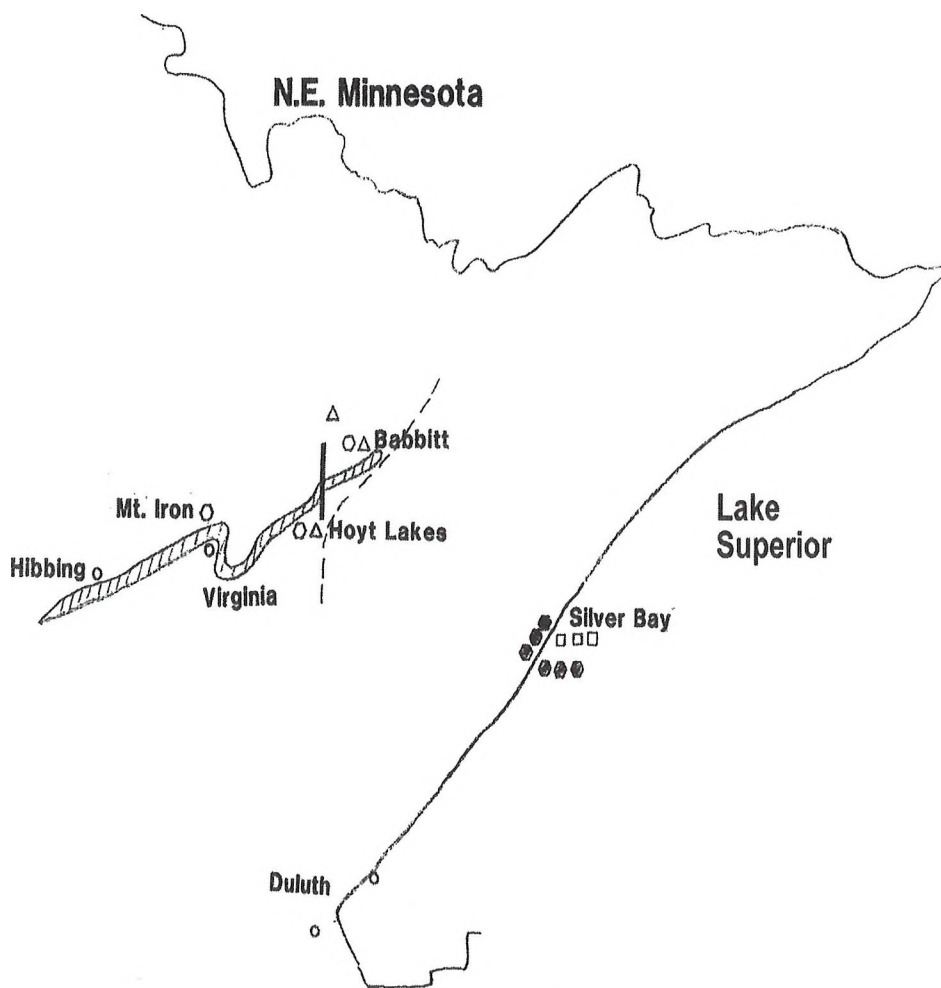


Fig. 2. N.E. Minnesota.

Analytical sensitivity depended on the loading of the original filter and on preparing a sample suitable for counting, but a typical value was in the range of 0.0005–0.001 structures of air sampled. The use of energy dispersive X-ray analysis (EDX) and selected area electron diffraction (SAED) allowed for specific characterization of fibrous particulates which included differentiating the various amphibole types present, especially hornblende, cummingtonite-grunerite, and tremolite-actinolite.

2.2. Water quality monitoring

To address concentrations of fibrous particulates extant in ground and sub-surface water courses adjacent to the Northshore Taconite Ore Processing Facility, the MDH established a number of monitoring wells in and around the property, at the inflow and discharge points of the Facility's Tailings Basin treatment plant, and at several mining pit discharge sites. As representative of surface water courses in the area, the Beaver River was selected for evaluation. Four specific long term monitoring sites were established (i.e., Site 101—upstream from the MP7 Tailings Basin; Site 102—downstream from the MP7 Tailings Basin; Site 105—at the main branch of the river, upstream from the MP7 Tailings Basin; and, Site 106—at the main branch of the river, downstream from the MP7 Tailings Basin).

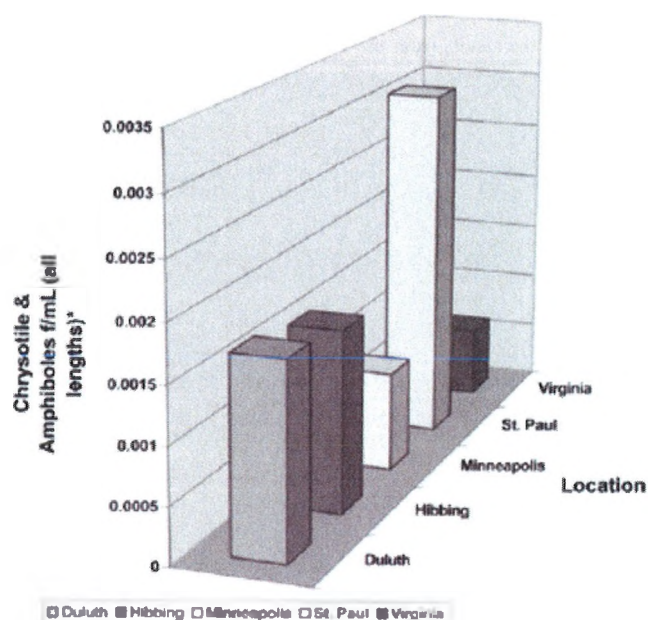
Beaver River samples were collected three times a year in April, July, and November, and other surface water samples were sampled at various schedules. The samples were analyzed by TEM in accordance with MDH Method 851; Minnesota Department of Health, 1975. Within 48 h of collection, the samples were deposited on 0.1 μ m polycarbonate filters. Three or four volumes were usually filtered to insure proper loading. All fibrous particulates were counted which exhibited a 3:1 aspect ratio, and no minimum length requirement was established. The analytical sensitivity varied greatly, depending on the amount filtered, which, for the Beaver River, was on some occasions as low as 5 ml; giving an analytical sensitivity of 1.5 MFL. Each fibrous particulate was examined by SAED in order to classify it as an amphibole, chrysotile, or other mineral, and then it was examined by EDX to determine the chemical composition. The concentration of fibrous particulates was reported as million fibers per liter (MFL).

3. Results

3.1. Air monitoring results

Air monitoring results collected in the 1974–1975 time frame from three schools in the Silver Bay, MN area demonstrated mean concentrations of fibrous particulates in the 0.0030–0.03 f/cc range. Concentrations of fibrous particulates measured in the ambient air of comparison cities in and around the state collected during approximately the same time period (i.e., 1978–1979) ranged from a low of 0.001 f/cc in Virginia, MN to a high of 0.003 f/cc in St. Paul, MN (See Fig. 3). Additional sampling in Silver Bay, MN area in the mid to late 1970s resulted in an average fibrous particulate concentration of 0.0626 f/cc (95% CI 0.035–0.9 f/cc) significantly in excess of the level of fibrous particulates detected in the ambient air of the “control city,” St. Paul, MN, although two of the Silver Bay sampling sites, considered individually, did not indicate levels of fibrous particulate significantly different than that seen in St. Paul.

Monitoring of the ambient air in the Silver Bay, MN area continued throughout the 1980s and into the 1990s to evaluate changes in concentrations of fibrous particulates effected by modifications in the production processes



* No breakdown for individual types of amphiboles and assume all lengths.

Fig. 3. Comparison of asbestos fibers in the ambient air by collecting and analyzing air samples from five different cities in Minnesota in 1978–1979.

and implementation of updated air filtration equipment at various locations throughout the Northshore Taconite Ore Processing Facility. In addition, with the utilization of TEM and EDX analytical techniques, it became possible to further characterize the fibrous particulate concentrations detected in the air samples collected as to their physical and chemical nature.

As indicated in Table 1 and Fig. 4, grunerite fibrous particulate concentrations in the ambient air at various sampling sites in and around the Northshore Taconite Ore Processing Facility declined from an average 0.048 f/cc in 1990 to an average of 0.0088 f/cc in 1998. The same was evident for tremolite-actinolite fibrous particulate which declined from an average 0.0186 f/cc in 1990 to an average of 0.0029 f/cc in 1998.

3.2. Water quality results

Historically, when iron ore tailings were being deposited in Lake Superior, concentrations of fibrous amphiboles in aquifers and surface water courses in and around the Northshore Taconite Ore Processing Facility were uncertain, but estimated to be in excess of 12 MFL. However, fibrous particulate data collected from the mid-1960s through 2002 from the monitoring wells adjacent to the plant, at the inflow and discharge points of the facility's Tailings Basin treatment plant, at several mining pit discharge sites (data not shown), and especially the Beaver River monitoring sites demonstrated that fibrous amphibole concentrations declined significantly over time, and currently average on the order of 7.5 MFL (See Table 2 and Fig. 5).

Table 1

Summary of the results from the Minnesota Department of Health Air Monitoring (1990–1996) by analytical transmission electron microscopy

Summary of the Results from the Minnesota Department of Health Air Monitoring (1990–1996) by Analytical Transmission Electron Microscopy.

a) Station N°1

	1990	1991	1992	1993	1994	1995	1996	1997	1998
Grunerite	0.0073	0.011	0.00023	0.0020	0.0018	0.014	0.0048	0.0023	0.0066
Range	0.00048–0.012	ND–0.14	ND–0.00055	0.00030–0.0038	0.000097–0.0068	0.00013–0.056	ND–0.028		
Tremolite-Actinolite	0.0048	0.0075	0.00017	0.00087	0.00082	0.0062	0.002	0.0011	0.0032
Range	0.000075–0.048	ND–0.094	ND–0.00065	ND–0.003	ND–0.0025	0.00013–0.024	ND–0.010		

b) Station N°5

Grunerite 0.035
Range 0.0077–0.099

Actinolite-
Tremolite 0.0234
Range 0.0050–0.065

c) Station N°7

Grunerite	0.048	0.030	0.0021	0.0033	0.011	0.0069	0.011	0.0089	0.0088
Range	0.00066–0.54	ND–0.39	0.0011–0.0055	0.0002–0.011	0.00024–0.070	0.0001–0.003	0.0017–0.045		
Tremolite-Actinolite	0.0186	0.0045	0.0012	0.0018	0.0040	0.0038	0.0057	0.0055	0.0029
Range	ND–0.16	ND–0.024	ND–0.0067	ND–0.005	ND–0.013	ND–0.019	ND–0.024		

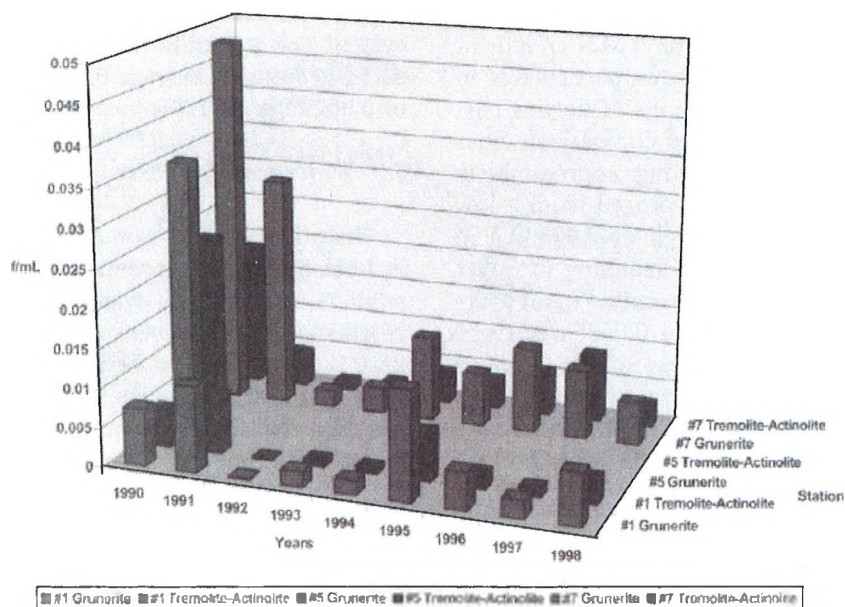


Fig. 4. Summary of the results from the Minnesota Department of Health Air Monitoring (1990–1998) by analytical transmission electron microscopy.

Table 2

Beaver river fibrous particulate data 1966–2002 (million fibers/l)

Beaver River Data Fibrous Particulate Data 1966–2002 (Million Fibers/Liter)			
Sampling Site	Minumum	Maximum	Average
Site 101	<0.2	4.0	0.9
Site 102	<0.3	24.0	5.6
Site 105	<0.3	32.0	7.0
Site 106 (Downstream From MP 7 Discharge)	<0.5	32.0	16.7

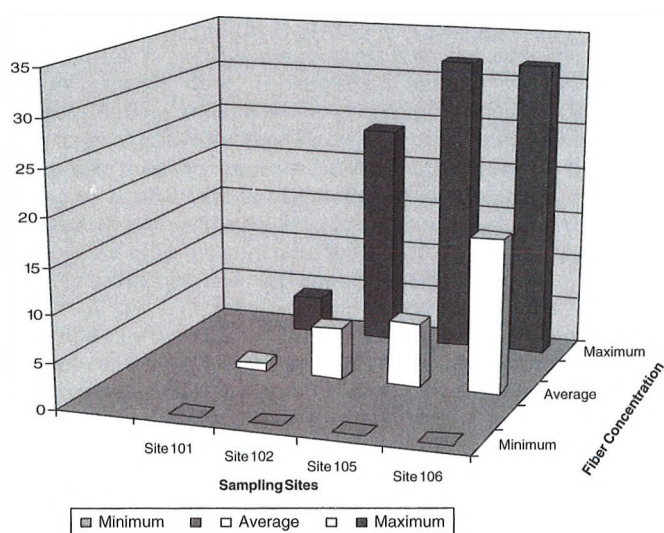


Fig. 5. Beaver River fibrous particulate data 1966–2002 (million fibers/l).

4. Conclusions

As indicated by this data, concentrations of fibrous particulates both in ambient air in the Silver Bay, MN area as

well as in water courses in and around the Northshore Taconite Ore Processing Facility have declined considerably since the mid-1970 when the Reserve Mining case was litigated. Airborne fibrous particulate concentrations, historically averaging 0.0626 f/cc (95% CI 0.035–0.9 f/cc) now average 0.0022 f/cc (95% CI 0.0001–0.0014 f/cc). Such levels are not significantly different from those seen in other non-urban environments in the US and Europe (Schneider et al., 1996).

Concentrations of fibrous particulates in water samples were higher in the mid-1970 when iron ore tailings were being deposited in Lake Superior, but since the tailings have been deposited on land waterborne levels of fibrous particulate in the Beaver River have remained relatively constant averaging in the range of 7.5 MFL. Since all fiber lengths were measured, and almost all of the fibers were less than ten micrometers in length, this level falls well within the current EPA drinking water standard (7.0 MFL longer than 10.0 μm) for asbestos (EPA, Safe Drinking Water Act, 1974). Review and consideration of this data is critical factor in determining the potential health risks associated with airborne and waterborne fibrous particulates in the areas of the Northshore Taconite Ore Processing Facility (See Wilson et al., 2008).

Conflict of Interest

The authors declare that they have no conflicts of interest

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References

- Bartlett, R.V., 1980. *The Reserve Mining Controversy: a Case Study of Science, Technology, and Environmental Quality*. Indiana University Press, Indiana.
- Berndt, M.E., Brice, W.C., 2008. The origins of public concern with taconite and human health: reserve Mining and the asbestos case. *Regul. Toxicol. Pharmacol.* 52, S31–S39.
- Environmental Protection Agency, 1973. National Emissions Standards for Hazardous Air Pollutants (NESHAP)—Asbestos, 40 CFR Part 61, under Section 112 of the Clean Air Act (CAA).
- Environmental Protection Agency, 1974. Safe Drinking Water Act (SDWA).
- Minnesota Department of Health, 1975. Method 851: Transmission Electron Microscopy Analysis for Mineral Fibers in Water.
- Minnesota Department of Health, 1976. Method 852: Transmission Electron Microscopy Analysis for Mineral Fibers in Air.
- Reserve Mining vs. the US Environmental Protection Agency et al., Reserve Mining Company vs. United States, et al., US Court of Appeals, 8th Circuit. Submitted December 9, 1974, Decided March 14, 1975 as modified on rehearing and order on remand, April 8, 1975.
- Ross, Malcom, Langer, Arthur M., Nord, Gordon L., Nolan, Robert P., Lee, R.J., Van Orden D., Addison, John, 2008. The Mineral Nature of Asbestos. *Regul. Toxicol. Pharmacol.*, 52, S26–S30.
- Schneider, T., Burdett, G., Martinon, L., Brochard, P., Guillemin, M., Teichert, U., Drager, U., 1996. Ubiquitous fiber exposure in selected sampling sites in Europe. *Scand. J. Work Environ. Health* 22, 274–284.
- Wilson, Richard, McConnell, E.E., Ross, Malcom, Axten, Charles W., Nolan, R.P., 2008. Risk assessment from human exposure to fibrous particulates in taconites ore due to environmental exposure and those associated with the use of aggregate waste rock. *Regul. Toxicol. Pharmacol.* 52, S232–S245.



Rapporteur's Report Session 2: Characterization of fibrous minerals: Arthur M. Langer

The central question concerning the health risks associated with mining and processing of taconite ores in the Eastern Mesabi Range is "does asbestos, of any variety, occur within the gangue mineral population?" Free silica in the form of quartz does exist in the taconite, but silicosis has been relegated to a secondary issue. The focus has shifted to the asbestos minerals and the malignancies that might occur following low-level exposure to dust. Although mineral fibers do exist in the Mesabi taconite ores, Ross, Nolan and Nord conclude "no asbestos", as explained in their contribution *"The Search for Asbestos within the Peter Mitchell Taconite Iron Ore Mine, near Babbitt, Minnesota"*.

Their area of study is located in the eastern Mesabi Range. It is here that the tectonic and metamorphic effects associated with the intrusion of the Duluth Gabbro have been profound. A variety of amphibole minerals have developed as a result of these geological events, some with names recognized within the US Asbestos Standard. The issue tackled by the authors is whether or not these amphiboles are present in the mine and if so whether or not they are asbestiform in habit.

Ross and colleagues point out that asbestos is found in locales where folding, faulting, shearing and dilation cracks have formed, and if the chemistry of the host rock is "right" asbestos may form in dilated cracks and fissures as "cross fiber," or along the limbs of tight folds as "slip fiber." The process of formation requires hydrothermal solutions and the proper geochemical conditions that promote crystal growth. The Peter Mitchell pit, located in the "amphibole area" of the Eastern Mesabi, is almost 8 miles long and up to 1 mile wide in places. Ross and colleagues recognized 30 locations within the mine as areas that might give rise to the formation of asbestos minerals. These were sampled and analyzed by X-ray diffraction and electron beam techniques.

Most of the sampled sites, five of seven, contained unaltered amphiboles in the main, but several also contained mineral fiber bundles consisting of intergrowths of grunerite, ferroactinolite, and ferrian sepiolite. Ross and colleagues propose that the formation of these minerals occurred as the result of secondary processes, acid solutions percolating through faults and shear zones in the ore body. Processing of ores with these minerals results in the disaggregating of the fiber bundles and their dispersal as individual fibers. The authors stress that these minerals constitute very much less than one-percent of the total ore body mass.

Cummingtonite, grunerite, actinolite, and their chemical variations, occur throughout the Peter Mitchell pit. Fibrous mineral growth is not found in the undeformed rocks along the entire extent of the mine. Some fibers are found as secondary minerals altered in the main from pre-existing amphiboles. These are found in sites where deformational episodes have obviously occurred.

The authors conclude, "no asbestos of any type was found in the mine pit."

Given that the above conclusions are correct, the issue returns to the nature of the small fibrous objects observed in air and water samples, i.e., are these cleavage fragments, are these asbestos fragments (Ross and colleagues say "no"). Regardless of form, are they biologically active?

As the hunt for asbestos minerals in the environment and workplace increased in intensity, driven in large measure by the presence of disease that some consider peculiar to specific forms of asbestos, new minerals have been found occurring with the asbestos habit [Ross et al. and Langer, this volume]. The chemistry section in these contributions clearly shows that cation substitution within the amphibole structure is so common that many minerals constitute this mineral group. Some of them have been found with the asbestiform habit, i.e., winchite, richterite, arfvedsonite, and fluor-edenite. These authors failed to find amphibole asbestos in the Peter Mitchell Pit although non-asbestiform mineral fibers do occur.

The contribution by Axten and Foster, *Analysis of Airborne and Waterborne Particles around a Taconite Ore Processing Facility*, underscores the need to distinguish among the elongated particles found in samples of dust derived from mining and milling operations. The taconite ores of the northeastern Mesabi Range contain amphibole minerals whose names were listed, absent mineral habit, in the federal asbestos standard. The amphibole "fibers" found in the air and water samples in and around the taconite processing plant in Silver Bay were not characterized further than the OSHA definitional criteria. The authors note that distinguishing between asbestos fiber and elongate cleavage fragment was not an integral part of the assays when environmental studies began in the 1970s.

As time progressed, the methods for particle collection, filter preparation, instrument required for mineral visualization, for particle identification and counting, had evolved so that samples obtained in one period of time could not be directly compared with samples collected over another period of time. As Axten and Foster state, the only "known" in the sampling datasets was that air measurements for particles were low. Despite these limitations a large dataset exists and estimations of risk may be made within some defined set of assumptions.

Sampling air and water had been carried out since the early 1970s and thousands of these measurements have been made. Early analyses followed the then existing OSHA definition of asbestos. Prismatic cleavage fragments were imbedded in the standard so that mineral name, particle length, and aspect ratio alone determined what the analyst called asbestos. For the purpose of risk calculation, one may assume that these elongate mineral particles

that conform to the 1972 OSHA Asbestos Standard definition possess identical toxicities to asbestos. Read Wilson and colleagues' contribution, this volume.

The issue is not academic to the state health agencies or the people of Minnesota. Based on these measurements, mineral types (names without habits), and their concentrations in air, and assuming that these particles are "medically significant", allow such a risk calculation to be made. Axten and Foster report particles of actinolite, tremolite and grunerite in the air in and around the facility at Silver Bay where taconite ore is processed. These are shown to steadily decrease in concentration over time. Wilson and colleagues use an average value of 0.00014 f/cc of air for their risk calculation (this volume).

Injecting earlier analyses into the mix, Langer et al. (1979) reported that only a small percentage of "fibrous particles" (derived from the gangue minerals during ore processing at Silver Bay) found in water samples drawn from Lake Superior were morphologically, chemically, and structurally indistinguishable from similar particles found in an amosite population. The assay instrument was the analytical transmission electron microscope. Not having any reason to believe that the population of the amphibole particles in the air of the taconite processing plant would be different from the particles in the tailings dumped into the containment dam in Lake Superior, the "worst-case" risk calculations for mesothelioma are lower.

Axten and Foster report that several of the ambient air samples obtained in Silver Bay were significantly lower than the fiber levels measured in the air in St. Paul, Minnesota. The fiber levels in the waters of Lake Superior have also declined to values observed in the natural runoff of rivers that empty into the lake.

It may be noted that the Minnesota Department of Health (2007) (MDH) is still concerned with exposures in Silver Bay because of mesothelioma occurrence among some 72,000 current and former taconite miners and millers in the state (Brunner et al., 2008) and within the state itself (Minnesota Department of Health Report, 2007). Parenthetically, the mesothelioma concentration in northeastern Minnesota also includes the town of Cloquet and the population of workers formerly employed at Cloquet's Wood Conversion, then Conwed, ceiling tile-manufacturing facility in town. Twenty-five mesotheliomas have been confirmed in this cohort of workers and three more cases are suspected to have occurred (MDH, 2007). From 1958–1964, inclusive, more than 3100 tons of amosite was used in the manufactured fire-rated ceiling tiles; from 1965–1974, almost 6800 tons of chrysotile was consumed at the site for the same purpose (Conwed Corporation, 1965–1974 documents). The mesothelioma diagnoses peaked with five cases reported in 1996, 35 years from the peak of amosite consumption in that facility in 1961. Other important exposures to asbestos have occurred in trades outside of the taconite environment and the MDH must consider the importance of these separately.

The Ross et al. and Axten and Foster papers presented in this session bring to discussion critical issues: First, is it known with certainty what it is that the analyst is measuring; secondly, has the analyst accurately distinguished between asbestos and cleavage fragment; and lastly, do the risk calculations reflect what is actually known? Wilson and colleagues avoid the problem of mineral characterization and assume that the amphiboles found in the air samples, regardless of source, have the same carcinogenic potency as the asbestos minerals.

Zanko, Niles and Oreskovich push the characterization envelope further with a proposal to explore the use of coarse taconite tailings as construction aggregate for high bearing-load applications, i.e., roads and highways. The issue is of pragmatic importance. The suggestion made is based on detailed mineral analysis and physical characterization of the tailings ("*Mineralogical and microscopic evaluation of coarse taconite tailings from Minnesota taconite operations*"). The materials in question are coarse tailings, size characterized by standard sieving technique. The population of particles appears to have dimensions greater than 10 microns.

Cumulative frequency particle-size curves of the western Mesabi samples show the 50th percentile for all to lie between 400 and 1000 μ (0.4–1.0 mm). The lack of respirable dust is explained as the result of a "washing step" in the ore extraction process. To begin with, the samples do not possess a respirable particle population.

Based on the analysis of five groups of coarse taconic tailings samples from the western Mesabi Range, areas far removed from the thermal and metasomatic effects of the Duluth Gabbro, no amphibole minerals have been found. The taconite is characterized as principally quartz and magnetite with other iron oxides (e.g., hematite), iron carbonate (siderite) and iron silicates present in abundance. Low-temperature iron silicates characterize the western Mesabi Range. Fibers in the Biwabik Iron Formation are principally talc and minnesotaite, the iron analog of talc. The authors stress that both particle size and mineralogy of the particle population suggest that the material may be used as an asbestos-free aggregate.

Far up northeast into the Eastern Mesabi, within the metamorphic aureole of the gabbro, amphiboles occur in abundance. Some of these carry the same name as the asbestos minerals described in the initial OSHA Asbestos Standard in 1972. The issue the authors focus upon is the form of the amphibole (asbestiform or cleavage fragment). Employing polarized light and electron optical techniques, the amphiboles appear to crush to form fragments. Zanko et al. state that some portion of these fragments is morphologically difficult to distinguish from asbestiform fibers.

The authors concluded their paper with the following "points:" respirable taconite dust is generated at the mine site and that the wet extraction techniques "wash" the crushed ores of fine particles; the result is that the amount of fine dust found in tailings is small to nil; the tailings are found to resist abrasion may be incorporated into matrices reducing the potential for post-application exposure.

Although tailings removed from the amphibole area of the Eastern Mesabi do not have asbestiform minerals, the authors recommend the materials be handled with diligence and care. They are concerned with the presence of crystalline silica (quartz) in all the tailings samples.

References

- Brunner, W.M., Williams, A.N., Bender, A., 2008. Investigation of exposures to commercial asbestos in northeastern Minnesota iron miners who developed mesothelioma. *J. Reg. Toxicol. Pharmacol.* 42, S116–S120.
- Conwed Corporation, 1965–1974. Mr. Robert Brownson, national litigation counsel, provided documents regarding asbestos consumption at the Cloquet plant.
- Langer, A.M., Maggiore, C.M., Nicholson, W.J., Rohl, A.N., Rubin, I.B., Selikoff, I.J., 1979. The contamination of Lake Superior with amphibole gangue minerals. *Ann. NY Acad. Sci.* 330, 549–572.
- Minnesota Department of Health, 2007. Mesothelioma in northeastern Minnesota and two occupational cohorts: 2007 update. December 7, 2007. p. 16.

Health effects of amosite mining and milling in South Africa

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Abstract

This study focuses on the amosite mining region in South Africa and associated health effects, compared to other mined asbestos fiber types. Historically, dust and fiber levels were high in the amosite mills and mines, and many miners and members of the surrounding communities were exposed to the fibers. Research has shown that amosite produces both benign and malignant disease. Nevertheless, the mesotheliomagenic potential of amosite is several fold lower than crocidolite. The risk of disease associated with amosite exposure is difficult to quantify. Reasons for this include the scarcity of available information, including fiber measurements, and case ascertainment, as well as the juxtaposition of the amosite and crocidolite asbestos seams in South Africa.

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Keywords: Amosite; Mesothelioma; Crocidolite; South Africa; Asbestos

1. Introduction

South Africa is unique in that all three commercially important types of asbestos occur and have been mined and widely exported from this country. South Africa was the world's main commercial source of amosite (grunerite), the name of which is derived from “asbestos mines of South Africa”.

South Africa was at the forefront of the asbestos mining industry. However, there is a lack of research and documentation monitoring asbestos mines and mills. What little information that is in the public domain needs to be interpreted with knowledge of the background to geography, geology and demographics. The Pneumoconiosis Research Unit (PRU), now the National Institute for Occupational Health (NIOH), in Johannesburg participated in many of the published studies, and also carried out some unpublished work. This information has been drawn on for interpretation of the available literature.

Historically, there were two amphibole asbestos mining areas in South Africa. Cape Crocidolite was mined in the Northern Cape Province asbestos field, which extends for a length of about 540 km (Fig. 1). No amosite was mined in this area. Five hundred kilometers away, in the north eastern part of the country, is the Pietersburg asbestos field (in Limpopo Province), where both Transvaal crocidolite and amosite were mined. This field is around 100 km long and lies along the Olifants River and its tributaries (Webster, 1973). There was very little movement of population between these regions, although more senior mine officials were sometimes transferred between the different mines and mining regions.

Many small mines and mills operated in the Pietersburg asbestos field, from about 1920, producing Transvaal crocidolite and amosite from deposits in which seams of the two amphiboles often overlapped. Crocidolite mining here (which was in the form of addits) however, never reached the production levels of those in the Northern Cape. The deposits were small and scattered, and were considered to be of poorer grade than those in the Northern Cape.

The largest and most important mine in the Pietersburg asbestos field was the Penge group of mines (comprising

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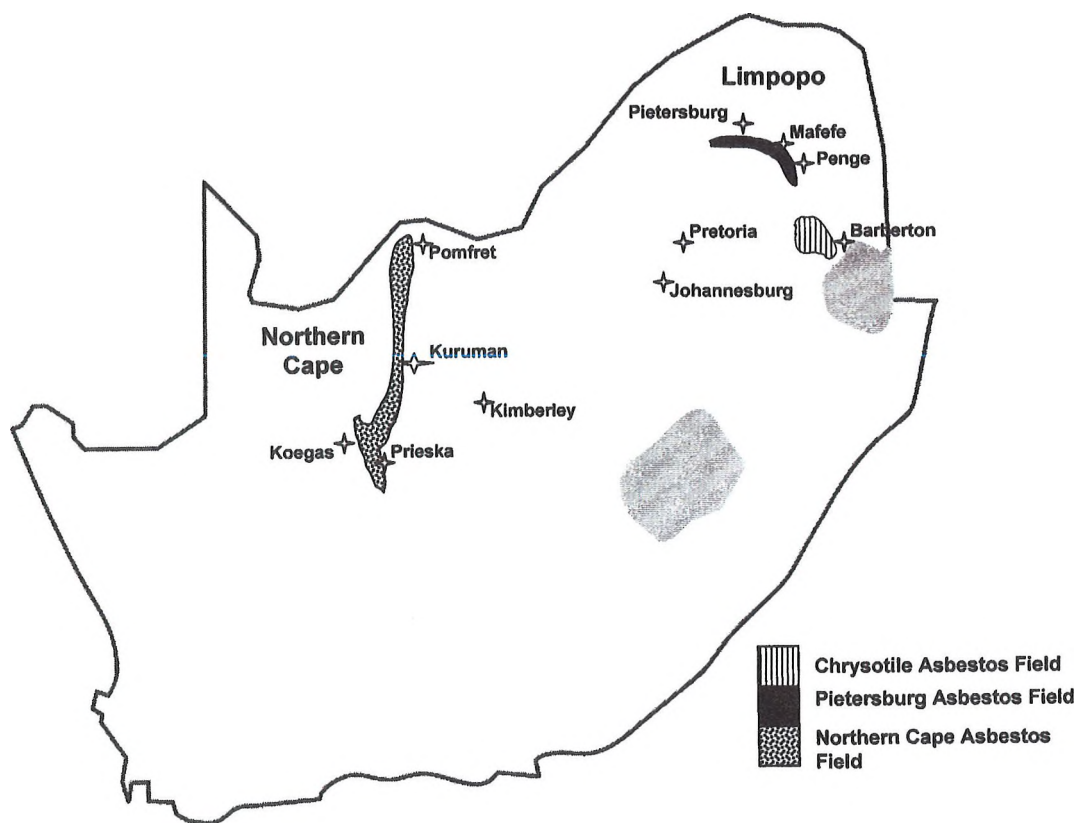


Fig. 1. Map of asbestos mining areas in South Africa. Wagner et al. (1960) reported a cluster of mesotheliomas associated with the Northern Cape asbestos fields west of Kimberley.

Penge, Weltevrede and Kromellembog mines) on the south-eastern extremity, where only amosite was mined (Coetzee et al., 1976). Penge was the only mine in the region that had deep mine shafts. Amosite production began in 1914 at Penge and continued for more than 70 years, until 1992 (Felix, 1997). This became the largest mine in the area and, from about 1976 until it closed, the world's only commercial source of amosite. Production peaked at 100,000 tons in 1970 (Fig. 2) when 7000 workers were employed; at this time around 13,000 workers were employed in the Northern Cape (crocidolite) asbestos field

(Rees et al., 1999). Some of the reasons for the popularity of amosite were the extent of the ore body and the relative ease with which the deposits could be mined. Amosite production exceeded that of Cape crocidolite until the early 1960s (Fig. 2).

In the early 1960s Europe and North America were the major importers of South African asbestos. The picture had changed radically by the late 1980s. At this stage, the Far East was importing 90% of the chrysotile stocks, 70% of amosite and 40% of crocidolite (Harrington and McGlashan, 1998). In 1988 the Japanese government regulated against the use of amosite and, by 1991, amosite had been phased out completely. The collapse of this Far East market led to the closure of the Penge mine in June 1992.

Almost all the smaller operations had closed by 1976. However, chrome, platinum, andalusite, vanadium and iron continue to be mined in the region.

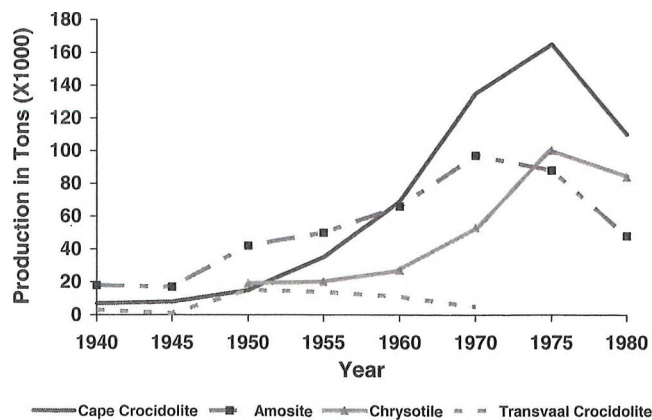


Fig. 2. Asbestos production in South Africa, 1940–1980.

2. Exposure

“It is difficult to recover the exposure story of South Africa’s asbestos mines. The official record is incomplete, and the accounts from the mining companies, and to a lesser extent from the Department of Mines, are not always reliable. Often they give a distorted picture of dust levels” (McCulloch, 2002).

In 1949, Schepers visited Penge mine as part of the first official government radiological and clinical survey of the Pietersburg asbestos field. He encountered deplorable working conditions:

“Exposures were crude and unchecked. I found young children, completely included within large shipping bags, trampling down fluffy amosite asbestos, which all day long came cascading down over their heads. They were kept stepping lively by a burly supervisor with a hefty whip. I believe these children to have had the ultimate of asbestos exposure” (Schepers, 1965).

2.1. Fiber measurements

Despite the fact that measurements were few and far between, historical scientific evidence (sparse as it was), plus anecdotal evidence, clearly indicates that the levels of asbestos fibers in and around the Penge mining area were exceptionally high.

What measurements were made had their own inherent problems; they were often averaged for the mine and the mill, and then for groups of mines, or over time. At varying times measurements were made using Konimeters or thermal precipitators, and strategic and personal samplers. It was, furthermore, not always clear what was being measured, viz. particles and/or fibers. The definition of a fiber is determined by the ratio of its length to diameter and the measurement of the diameter itself. This definition was not constant; the fiber length: diameter ratio was changed from two to three in 1965, and the diameter from five to three microns in 1970 (du Toit, 1989).

In 1947, measurements in the Penge mills ranged from 162 to 720 p/ml, and underground, from 80 to 228 p/ml (Sluis-Cremer, 1965) (Table 1). Levels appeared to increase in the 1950s, probably due to mechanization, when 30% of the counts in the mills were above 780 p/ml (Sluis-Cremer,

1965). Rendall, using personal samplers, recorded counts of up to 327 f/ml in the mills and more than 100 f/ml in a range of other surface jobs (Rendall, 1971); underground levels were <5 f/ml. In the 1980s the fiber counts at Penge ranged from 0.1 to 6.5 f/ml in the mills, and from 0.2 to 1.0 f/ml underground (Department of Minerals and Energy, personal communication).

2.2. The amosite work force/occupational exposure to amosite

Penge was a purpose-built town which developed only as a consequence of the mining activity. There was a high labor turnover, perhaps because of the lack of a stable, entrenched community, at times close to 100% per annum (McCulloch, 2002). Many of the workers came from neighboring countries, returning home when they became ill or when they left their jobs for other reasons.

There were very few white miners in the area, and most of them worked at Penge. The black miners were more dispersed within the Pietersburg asbestos field, and thus may have been exposed to both amphiboles. This may have been one of the reasons why some of the studies were limited to the white ethnic group. However, they comprised a small proportion of the Penge work force: in 1963 Penge had 360 white and 6500 black workers (McCulloch, 2002).

There were many small mills in the Penge area, in addition to two mills at Penge mine. They were of basic design and caused extensive environmental pollution in the valleys (McCulloch, 2002). The workers themselves were exposed to extremely high fiber levels, as sweepers, sorters and packers.

Cobbing, whereby the fiber was loosened from the rock, was done primarily by women and children at Penge, as well as at the smaller operations. In 1940, 25% of the Penge workforce were boys younger than 16 (McCulloch, 2002). The employment of children younger than 16 years of age was only prohibited in 1973. Even when a new second mill was built at Penge in the mid-60s, extensive hand cobbing continued because the ‘new mill’ broke down often, primarily because they continued to process large quantities of iron stone.

2.3. Environmental exposure to amosite

Fiber exposure was not confined to the immediate vicinity of the mines and mills. Van Sittert and Rendall (1998) demonstrated during the operation of the Penge mill, that fibers were detectable at a distance of up to 100 km from Penge.

There was also contamination from water. There was, and still is, no piped water in the rural areas where black people are living. Tailings, deliberately put into the rivers and streams, washed down to the Penge area. In the dry season, the rivers dried up, leaving fibers on the banks. These were then blown about by the strong prevailing winds. Water-borne fiber exposure was compounded when

Table 1
Fiber measurements at Penge

Source	Year	Site	Particles/cc	Fibers/ml
Sluis-Cremer et al. (1992)	1945	Surface		150
		Underground		14
Sluis-Cremer (1965)	1947	Mills	162–720	
		Underground	80–228	
		Mills	30% >780	
Sluis-Cremer et al. (1992)	1960	Surface		56
		Underground		6
Sluis-Cremer et al. (1992)	1970	Surface		40
		Underground		4
Rendall (1971)	1970	Mills		1.4–326.7
		Other surface jobs		0.2–113.4
		Underground		<5
Department of Minerals and Energy, personal communication	1986	Mills		0.1–6.5
		Underground		0.2–1.0

the rivers were used for domestic use such as drinking, bathing and laundry. Children were especially vulnerable as they often played on tailings dumps or on playgrounds covered with asbestos fibers. Asbestos was also used by the community for, amongst other things, brick making and decorating houses (Felix, 1997).

In 1988, some 12 years after the closure of the last addits in the region, personal and strategic sampling was performed in the Mafeke district, which is in very close proximity to the site of Penge mine (Felix, 1997). Children were exposed to the highest concentrations (mean 0.02 f/ml; range 0.002–0.090 f/ml).

2.4. Size of exposed population in Pietersburg asbestos field

In 1965 the number of persons employed at Penge was around 10,000, similar to the Northern Cape asbestos field (Sluis-Cremer, 1965). The estimates for miners in 1970 were around 13,000 in the Northern Cape and 7000 at Penge (Rees et al., 1999). The numbers employed in the chrysotile mines were always fewer; in 1970, there were 1200 employees. One can only estimate the sizes of the populations at risk of environmental exposure. The Northern Cape comprised a larger geographical area, but the population density was higher in the Pietersburg asbestos field. Felix (1997) identified 64% of 611 randomly selected adults in the Mafeke district of the Pietersburg asbestos field with a history of environmental asbestos exposure.

3. Health effects of amosite exposure in South Africa

Studies of asbestos-related diseases in South Africa began with the work on chrysotile miners (Slade, 1931). This work was not continued into the 1940s, however, perhaps as a consequence of World War II. Webster revived the issue of asbestos and health in the 1950s, contributing significantly to the discovery of the link between exposure to crocidolite and the development of mesothelioma (Webster, 1954). Following the publications of Wagner in the 1960s (Wagner et al., 1960), research activity focused on crocidolite in the Northern Cape Province. Despite intensive mining of amosite in South Africa for more than 70 years, relatively little research has been done in the country on the health effects of exposure to this fiber type. One reason could be the juxtaposition of the seams of amosite and crocidolite in the Pietersburg asbestos field. Crocidolite was mined in close proximity to Penge mine. Thus it was, and still is, very difficult to identify, with absolute certainty, individuals who were exposed to only amosite.

3.1. Non-malignant amosite-associated disease

The research that has been done on amosite exposed workers has identified high rates of both pleural abnormalities and parenchymal lung disease (Table 2). Because of the paucity of occupational hygiene data, and also because the mines seldom maintained comprehensive employment

records, particularly for black workers, these studies generally did not have data to enable dose-response analyses.

The first research into asbestos-related disease at Penge was conducted in the 1960s by the Pneumoconiosis Research Unit (PRU), and published in 1965 (Sluis-Cremer, 1965). An autopsy series of black miners who died while employed identified asbestosis (although often of slight degree) in 80% of the Penge miners and 72% of the Cape crocidolite miners (Table 2). The mean age and service of both groups was the same, viz. 43 years and four years, respectively. A field survey of 2389 persons, identified cases of asbestos-related disease (this included both pleural abnormalities and parenchymal disease) in the Northern Cape crocidolite and Penge amosite mining regions. Sluis-Cremer (1965) found higher proportions of fiber/asbestos bodies (these terms were used interchangeably) in sputum in the Northern Cape population than in the Penge community. Likewise, the prevalence of asbestos related disease was higher in those exposed to Cape crocidolite. This held true for both occupational and environmental exposures.

Irwig et al. investigated Cape crocidolite and amosite currently employed miners for benign pleural disease and asbestosis. They found a significantly higher prevalence of pleural abnormalities in the amosite exposed workers with more than 15 years of service, compared to the crocidolite miners (34% vs. 17%). They detected no such difference for parenchymal disease (Irwig et al., 1979).

In a community-based study of a population exposed to asbestos dust in an area heavily contaminated by dust from mining, milling and uncontrolled tailings dumps, pleural changes were found in 52% of occupationally exposed subjects and in 34% of subjects with only environmental exposure (Felix, 1997).

Davies et al. (2001) studied the prevalence of asbestos disease in 770 women who had worked on asbestos mines in the Pietersburg asbestos field from 1929 to 1980; 80% were cobblers. A diagnosis of pleural and/or parenchymal asbestosis was made in 96% of cases. They ascribed the high prevalence to exposure to high levels of amphibole asbestos dust, predominantly amosite, and to the long residence time of dust in the lungs (Davies et al., 2001).

3.2. Mesothelioma

The occurrence of mesothelioma in the Pietersburg asbestos field has led to some controversy. In the 1960s, an orthodoxy developed amongst establishment scientists in South Africa that mesotheliomas did not result from exposure to amosite. This was articulated most strongly at the 1965 New York Academy of Sciences conference in papers by Sluis-Cremer (1965) and Webster (1965). Sluis-Cremer (1965) suggested real differences in the carcinogenicity of the mesothelium between amosite and crocidolite fibers.

Several factors contributed to the development of this view. The available evidence indicated a high prevalence

Table 2
Studies on benign disease in amosite exposed persons in South Africa

Author	Study design	Study population	Study period	Findings
Sluis-Cremer (1965)	Autopsy series (histology)	Current miners:	1959–1964	Asbestosis ^a
		^g PAF: 64		80%
	Field survey (radiology)	^h CCF: 87		72%
		2389 persons	1960–1962	Sputum fibers
Irwig et al. (1979)	Prevalence (radiology)	^g PAF Occ		ⁱ ARD ^b
		^g PAF Env		16%
				23%
		^h CCF Occ		42%
		^h CCF Env		28%
		Workers:	1970–1975	Pleural abnormalities ^c
Felix (1997)	Community-based (radiology)	^g PAF: 548		34%
		^h CCF: 882		17%
				Asbestosis ^d
		^g PAF: 548		23%
Davies et al. (2001)	Prevalence (radiology)	^h CCF: 882		27%
		Men and women residents of Mafefe	1988	Pleural abnormalities ^e
				Env: 34%
Davies et al. (2001)	Prevalence (radiology)	770 females ex-cobbers	1990s	Occ: 52%
				Pleural abnormalities plus asbestosis ^f

^a Parenchymal linear, reticular or nodular disease.

^b Parenchymal linear, reticular or nodular disease; or calcified pleural plaques.

^c Pleural thickening, pleural calcification or obliteration of the costophrenic angle (ILO definition).

^d Irregular opacities with profusion >1/0 (ILO definition).

^e Pleural plaques, calcified pleural plaques, pleural thickening, obliterated costophrenic angle.

^f Pleural plaques, calcified pleural plaques, pleural thickening; and parenchymal linear, reticular or nodular disease.

^g PAF, Pietersburg asbestos field (amosite/Penge).

^h CCF, Cape Crocidolite field.

ⁱ ARD, asbestos related disease.

of mesotheliomas in the Northern Cape crocidolite asbestos field (Wagner, 1960). However, there were no reports of mesothelioma from the Pietersburg asbestos field, although there was a high prevalence of benign asbestos disease (Sluis-Cremer, 1965).

Nevertheless, this view was soon challenged. The Asbestos Tumour Reference Panel was set up in 1965 at the PRU, to which all cases of mesothelioma were to be sent for expert review of the disease and confirmation of diagnosis. It was presumed that all cases of mesothelioma in South Africa were being reported to the registry. Of the first 375 subjects, only 4 (1%) had worked at amosite mines; but they had also been exposed to crocidolite elsewhere (Webster, 1973).

Since then, the evidence for low rates of mesothelioma in amosite asbestos exposed workers has been corroborated by a number of researchers. In 1992, Sluis-Cremer and colleagues published a study which examined mortality in three cohorts of amphibole miners. The cohorts were established in 1980, using employment records of white men who were employed from 1945 to 1955. There were 3212 amosite miners, 3430 Cape crocidolite miners and 675 men with exposure to both amphiboles. A total of 30 mesotheliomas were identified. Four of these cases had been exposed to pure amosite, six to both amosite and Cape crocidolite, and 20 to Cape crocidolite only.

The calculated incidence of mesothelioma, per 100,000 person-years, for exposure to Cape crocidolite was almost six times that for amosite (44.6 and 7.8, respectively). Likewise, the PMR for crocidolite exposure was much higher than that for amosite (almost eight times; PMR 4.7 vs. 0.6). Sluis-Cremer et al. (1992) stated that, while amosite can cause mesotheliomas “there can now be no question that crocidolite is far more dangerous than amosite at least in so far as mesothelioma is concerned”. There is no evidence, from South Africa, to the contrary. This gradient of mesotheliomagenic risk by fiber type is supported by other studies (Hodgson and Darnton, 2000).

Rees et al. (1999) reported on a case control study undertaken in the period 1988 to 1990. One hundred and twenty-three mesotheliomas were identified. Again, crocidolite exposure was mostly implicated in the development of mesothelioma. Three cases mined amosite and three mined both amosite and crocidolite. Of the 22 environmental mesotheliomas, 20 (91%) had exposure to Cape crocidolite, and two to both amosite and crocidolite. There were no cases associated with chrysotile exposure.

Recent pathology records from the Limpopo Province, where the Pietersburg asbestos field is located, suggest that there may be mesotheliomas that have not been included in published studies. In the 15 months from February 1989 to

April 1990, 16 mesotheliomas were diagnosed at the Pietersburg branch of the South African Institute of Medical Research (Felix, 1997).

Over the last few years only one of 50 cases that have come to autopsy at the NIOH had amosite exposure recorded.

3.3. Lung cancer

Sluis-Cremer et al. (1992) calculated the SMR due to lung cancer for crocidolite exposure to be higher than that for amosite exposure (2.03 vs. 1.38; relative toxicity 1.85). This difference, however, was much less than that for mesothelioma. Cancer registration studies have reported no excess of lung cancer for amosite exposed workers (Higginson and Oettle, 1960; Botha et al., 1986). However, lung cancer studies in asbestos workers are confounded by smoking. Only Sluis-Cremer et al., 1992 controlled for smoking.

4. Discussion and conclusions

The South African asbestos industry was large, profitable and an important source of foreign earnings (95% of production was exported). However, little was put back in terms of research, occupational hygiene and health surveillance. Currently, at the NIOH, where the lungs of deceased mine workers are examined, asbestos related diseases continue to be seen; this will continue for some decades, despite the closure of asbestos mines.

There is solid evidence of high rates of benign asbestos disease from amosite. There is no question that amosite causes mesothelioma (and lung cancer).

The burden of mesothelioma in the Pietersburg asbestos field is uncertain, but is almost certainly lower than in the Northern Cape Province, even taking into consideration problems with under ascertainment. There is no study of crocidolite miners from this area not also exposed to amosite. Nevertheless, occupationally associated cases from the Pietersburg asbestos field have been infrequently documented and, in contrast to Cape crocidolite, there are no environmental mesotheliomas attributable solely to amosite exposure.

Cumulative amosite and Cape crocidolite production levels were similar for the asbestos mining period (Harrington and McGlashan, 1998). The numbers of people exposed (workers and residents), were also comparable. Amosite was mined from the turn of the last century until 1992; the exposure periods are thus also comparable.

The juxtaposition of the seams of amosite and crocidolite in the Pietersburg asbestos field make it very difficult to identify, with absolute certainty, individuals who were exposed to only amosite. Nevertheless, the available evidence from South Africa supports the concept of a fiber gradient in mesotheliomagenic potential for South African asbestos. Those exposed to crocidolite asbestos appear to have the highest risk for developing mesothelioma, fol-

lowed by amosite; chrysotile has not been implicated in the development of this malignancy in South Africa. One explanation for this may be relative lack of contaminating tremolite, an amphibole that variably occurs with chrysotile ores (Rees et al., 2001).

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

- Botha, J.M., Irwig, L.M., Strebel, P.M., 1986. Excess mortality from stomach cancer, lung cancer, asbestosis and/or mesothelioma in crocidolite mining districts in South Africa. *Am. J. Epidemiol.* 123, 30–40.
- Coetzee, C.B., Brabers, A.J.M., Malherbe, S.J., 1976. Mineral Resources of the Republic of South Africa, fifth ed. Department of Mines, Geological Survey.
- Davies, J.C.A., Williams, B.G., Debeila, M.A., Davies, D.A., 2001. Asbestos-related lung disease among women in the Northern Province of South Africa. *S.A. J. Sci.* 97, 87–92.
- du Toit, R.S.J., 1989. The estimation of the cumulative fibre exposure of persons employed on South African asbestos mines. NCOH Report No. 4.
- Felix, M.A., 1997. Environmental asbestos and respiratory disease in South Africa, Ph.D. Thesis. University of the Witwatersrand, Johannesburg.
- Higginson, J., Oettle, A.G., 1960. Cancer incidence in the Bantu and 'Cape Coloured' races of South Africa: report of a cancer survey in the Transvaal (1953–55). *J. Nat. Cancer Inst.* 24, 589–671.
- Harrington, J.S., McGlashan, N.D., 1998. South African asbestos: production, exports, and destinations, 1959–1993. *Am. J. Ind. Med.* 33, 321–326.
- 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.
- Irwig, L.M., du Toit, R.S.J., Sluis-Cremer, G.K., Solomon, A., Thomas, R.G., Hamel, P.P., Webster, I., Hastie, T., 1979. Risk of asbestosis in crocidolite and amosite mines in South Africa. *Ann. NY Acad. Sci.* 330, 35–52.
- McCulloch, J., 2002. Asbestos Blues: Labour, Capital, Physicians and the State in South Africa. James Currey, Oxford and Indiana University Press, Indiana.
- Rees, D., Myers, J.E., Goodman, K., Fourie, E., Blignaut, C., Chapman, R., Bachman, M.O., 1999. Case-control study of mesothelioma in South Africa. *Am. J. Ind. Med.* 35, 213–222.
- Rees, D., Phillips, J.I., Garton, E., Pooley, F.D., 2001. Asbestos lung fibre concentrations in South African Chrysotile mine workers. *Ann. Occup. Hyg.* 45, 473–477.
- Rendall, R.E.G., 1971. Unpublished data, NIOH files.
- Schepers, G.W.H., 1965. Discussion following presentation by Laamanen and Raunio, observations on atmospheric air pollution caused by asbestos. *Ann. NY Acad. Sci.* 132, 240–254.
- Slade, G.F., 1931. The incidence of respiratory disability in workers employed in asbestos mining, with special reference to the type of disability caused by the inhalation of asbestos dust. MD thesis, University of the Witwatersrand, Johannesburg.
- Sluis-Cremer, G.K., 1965. Asbestosis in South Africa—certain geographical and environmental considerations. *Ann. NY Acad. Sci.* 132, 215–234.
- Sluis-Cremer, G.K., Liddell, F.D.K., Logan, W.P.D., Bezuidenhout, B.N., 1992. The mortality of amphibole miners in South Africa 1946–80. *Br. J. Ind. Med.* 49, 566–575.
- Van Sittert, G., Rendall, R.E.G., 1998. Drift of asbestos fibres from Penge. NCOH files.

- Wagner, J.C., 1960. Some Pathological Aspects of Asbestosis. In: Orenstein, A.J. (Ed.), Proceedings of the Pneumoconiosis Conference held at the University of the Witwatersrand, Johannesburg, 9–24 February 1959. J&A Churchill Ltd., London, p. 378.
- Wagner, J.C., Sleggs, C.A., Marchand, P., 1960. Diffuse pleural mesothelioma and asbestos exposure in the north west cape province. *Br. J. Ind. Med.* 17, 260–265.
- Webster, I., 1973. Asbestos and malignancy. *S. Afr. Med. J.* 47, 165–171.
- Webster, I., 1954. Some of the clinical, pathological and experimental problems of the pneumoconioses. *Proc. Transvaal Mine Med. Officers' Ass.* 34, 33–38.
- Webster, I., 1965. Mesotheliomatous tumours in South Africa: pathology and experimental pathology. *Ann. NY Acad. Sci.* 132, 623–646.

Human health effects associated with the commercial use of grunerite asbestos (amosite): Paterson, NJ; Tyler, TX; Uxbridge, UK

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Abstract

Grunerite asbestos (amosite) has been shown in epidemiological and experimental animal studies to cause lung cancer, mesothelioma and pulmonary fibrosis commonly referred to as asbestosis. An overview of the human and experimental animal studies describing the health hazards of grunerite asbestos (amosite) is presented. Of the many human studies describing the health hazards of asbestos, only three factories using mainly, if not exclusively, grunerite asbestos (amosite) have been studied. The first is a series of reports on a cohort of 820 workers from a plant located in Paterson, NJ. Among this cohort, 18.7% died of lung cancer and 17 mesotheliomas occurred. The Paterson factory closed in 1954 and moved to Tyler, Texas where it operated until 1972. Among the 1130 former workers in the Tyler plant 6 mesotheliomas were reported with 15.8% lung cancer mortality. The third grunerite asbestos (amosite) exposed cohort was an insulation board manufacturing facility in Uxbridge, United Kingdom. Here 17.1% of the workers died of lung cancer and 5 mesotheliomas occurred. The lung content from 48 Uxbridge workers was analyzed by analytical transmission electron microscopy for mineral fibers. The relationship between grunerite asbestos (amosite) concentrations in the lung correlated with grades of fibrosis and asbestos bodies and was lower than the concentration found in the cases with malignant tumors. The lung cancer cases contained more grunerite asbestos (amosite) than mesothelioma cases, and in the cases of non-malignant disease the concentrations were still lower. In both types of malignancies the concentration of grunerite asbestos (amosite) was very high—over a billion fibers per gram of dried lung tissue. Occupational exposure to airborne concentrations of between 14 and 100 fibers of grunerite asbestos (amosite) per milliliter after 20 year latency causes marked increases in lung cancer, mesothelioma and pulmonary fibrosis (asbestosis).

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1. Introduction

Asbestos occurs in nature as fine flexible fibers characterized by high thermal stability and high tensile strength (Ross et al., 2008). Asbestos was widely used in the 20th century in the production of various heat resistant materials and fabrics, insulation and friction products and as a constituent of asbestos cement (Alleman and Mossman, 1997; Ross and Virta, 2001).

Most countries regulate six commercial minerals under the asbestos standard. The predominant commercial

fiber-type is the serpentine mineral—chrysotile (white asbestos)—while the other five fiber-types are amphibole asbestos minerals. Two of the latter class – grunerite asbestos (amosite) (brown asbestos) – and riebeckite (crocidolite) asbestos (blue asbestos) – were commonly found in commerce during the last century, while anthophyllite asbestos and tremolite-actinolite asbestos were much less commonly used (Ross and Virta, 2001). Chrysotile asbestos is the only asbestos fiber-type that continues in commerce. The fibrous particles most commonly associated with talc are non-asbestos fibrous grunerite although lower concentration of non-asbestos fibrous ferroactinolite has also been reported (Wilson et al., 2008).

We will survey the asbestos-related diseases caused by occupational exposure to grunerite asbestos (amosite)

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and the relevant *in vivo* and *in vitro* studies, in order to gain some insight about the mechanisms of asbestos-related diseases. This information will provide a background for our goal of describing the health hazards from occupational exposure to grunerite asbestos (amosite) during the manufacturing of products with this asbestos fiber-type. The health hazards in the mining environment are described by Murray and Nelson (2008).

2. Mineralogical characteristics of grunerite asbestos (amosite)

Amosite asbestos was the geological name given to the mineral by Hall, a geologist, in 1907. He derived the name from the first letters of the mineral's predominant mining region commonly referred to as the asbestos mines of South Africa with the "ite" commonly given to mineral names (Hall, 1930). To simplify the diverse nomenclature of the many amphiboles, minerals, names such as amosite, were eliminated in favor of names that denote a specific elemental composition. For amosite, the amphibole name with the same elemental composition is "grunerite" followed by "asbestos" to denote the crystal form or habit. Amosite or amosite asbestos would continue to be used to describe the mineral in both commerce and the medical literature. We will use both names in this paper.

Grunerite asbestos (amosite) is a fibrous silicate mineral, with the chemical formula $(\text{Fe}^{2+}, \text{Mg})_7 \text{Si}_8 \text{O}_{22} (\text{OH})_2$. Using transmission electron microscopy, a narrow range of dimensions has been reported for this asbestos fiber-type. Airborne population of grunerite asbestos (amosite) having lengths $\geq 5 \mu\text{m}$ 12.7% and 24.6% of airborne fibers in mining and bagging, respectively (Gibbs and Hwang, 1980) while the width in bulk samples has been reported to be between 0.29 and 0.35 μm , and a little smaller 0.20–0.26 μm for airborne grunerite asbestos (amosite) (Veblen and Wylie, 1993). We have not found any size distribution data for airborne grunerite asbestos (amosite) fibers in the manufacturing environment and there is a paucity of airborne exposure information.

3. Origin of the problem

Early studies of asbestos-related disease at the end of the 19th Century focused on chrysotile asbestos, as it was the most widely used asbestos fiber-type. Manufacturing of textiles from chrysotile asbestos was very dusty causing high exposures and a significant incidence of severe asbestosis (often fatal) developing a few years after first exposure. The first grunerite asbestos (amosite) mine opened at Penge in the Transvaal Province (now referred to as the Northern Province) of South Africa in 1914. Production remained below 5000 tons per annum until World War II when it increased markedly to over 20,000 tons per annum, later peaking at 106,000 tons per annum around 1973. After 20 years of latency these exposures would produce readily detectable asbestos-related diseases

in those occupationally exposed while fabricating commercial products, leading to health hazard evaluation studies of grunerite asbestos (amosite) and other asbestos fiber-types.

4. Mechanisms and experimental studies

The mechanisms by which grunerite asbestos (amosite) exerts its pathophysiologic effects are as yet not entirely known, but aspects of the mechanism are being uncovered. Initial attention focused on fiber morphology as the principal determinant of mesothelioma potency, based on a series of experimental animal studies indicating fibers $>8 \mu\text{m}$ in length and $\leq 0.25 \mu\text{m}$ in width were commonly carcinogenic at high exposures (Stanton et al., 1981). Although these studies have never been shown to be incorrect, the artificial nature of the implantation model and the very high dose used severely limit their usefulness in evaluating human risk (Johnson, 1993; McConnell, 1995; Addison and McConnell, 2005). The Stanton morphology criteria do not explain why some fiber-types have little or no carcinogenic potential even at very high concentration in implantation studies, nor does it provide useful information on the health hazards of fibers with dimensions different for those proposed by Stanton et al. (1981), particularly fibers of greater diameter (Nolan and Langer, 1993).

In experimental animal studies, where the route of administration has been inhalation, the physical dimensions of the fibers were shown to be important for pathogenicity (Davis et al., 1986; Miller et al., 1999a,b; Searl et al., 1999), the longer fibers (often considered as those $\geq 5 \mu\text{m}$ long as a minimum) being the most pathogenic, with translocation from the lungs occurring slowly, if at all. Grunerite asbestos (amosite) translocates to extrapulmonary sites, such as omentum and mesentery, but not as rapidly as chrysotile (Dodson et al., 2000; Suzuki and Kohyama, 1991). Translocation, extremely high exposure and acid stability may account for the high incidence of peritoneal mesotheliomas among workers with occupational exposure to grunerite asbestos (amosite). Conversely, the persistence of long grunerite asbestos (amosite) fibers in the lung, compared to chrysotile, may account for amphiboles, greater facility in causing pulmonary diseases (Churg et al., 1989; Hodgson and Darnton, 2000; Britton, 2002).

More recent studies have focused on the iron in grunerite asbestos (amosite) and its potential to catalyze the formation of oxygen free radicals and cause breakage in DNA strands *in vitro* (Graham et al., 1999; Nejari et al., 1993; Lund and Williams, 1994; Kamp et al., 1995). Grunerite asbestos (amosite) has also been shown to modify the local immune response of pulmonary alveolar macrophage neutrophils (Lawrence and Fox, 1983; Graham et al., 1999; Ueki, 2001). Recent studies report changes in fiber length are associated with changes in *in vitro* properties of grunerite asbestos (amosite). Short-fibers obtained by grinding have a lower potential to damage DNA and lower *in vitro* toxicity, and are less effective at altering the redox

metabolism (Riganti et al., 2003). Simian Virus 40 (SV40) has been shown to cause mesothelioma in hamsters (Carbone, 2000), and a role for SV40 as an etiological agent in human mesotheliomas has been suggested by Gazdar et al. (2002). Nevertheless, the results of recent studies suggest this is unlikely (Lopez-Rois et al., 2004; Manfredi et al., 2005).

Among the studies conducted on animals, the most important to consider are those that target the most common route of entry of asbestos fibers into the body—inhalation (Johnson, 1993; McConnell, 1995). Inhalation studies performed on rats, hamsters and other animals indicate grunerite asbestos (amosite) can cause lung cancer, mesotheliomas and pulmonary fibrosis (asbestosis) (Davis et al., 1986; Miller et al., 1999a,b; Hesterberg et al., 1999; McConnell et al., 1999; Webster et al., 1993). Grunerite asbestos (amosite) impedes pulmonary function by decreasing compliance, and increasing tidal volume and resistance in pulmonary function tests of laboratory animals. These changes were both less pronounced and less prolonged than with chrysotile. They were also correlated with a peribronchial granulomatous reaction, but not with fibrosis (Hiett, 1978).

Intratracheal and intrabronchial instillation of suspensions of grunerite asbestos (amosite) into dogs, guinea pigs and rats showed a rapid translocation of the finer fibers from the alveolar spaces to the lung parenchyma and lymph nodes (Oberdörster and Morrow, 1988; Searl et al., 1999). Grunerite asbestos (amosite) fibers were cleared from the lungs at a slower rate than chrysotile (Churg et al., 1989).

Injecting grunerite asbestos (amosite) directly into the peritoneal cavity of rats caused an increased incidence of peritoneal mesotheliomas (Davis et al., 1986; Miller et al., 1999a). A clear dose–response has been reported (Davis et al., 1991).

Feeding studies, however, show different results. Feeding grunerite asbestos (amosite) to hamsters or rats did not cause an increase in gastrointestinal or any other malignancies (NTP, 1983, 1990).

Feeding grunerite asbestos (amosite), as well as taconite tailings, earth and water from Lake Superior containing taconite tailings to rats also failed to show an increase in gastrointestinal cancer or any other malignancies (Hilding et al., 1981).

5. Asbestos-related disease in humans

All asbestos fiber-types are pathogenic to humans (Browne, 1994; Huncharek, 1994). Asbestos dust causes short and long term changes in pulmonary function, appearance of cellular atypia and ferruginous bodies in sputum, and radiographic abnormalities (Nash and Fortson, 1981). Ferruginous bodies in sputum are commonly formed on amphibole asbestos and therefore occur more frequently in populations with exposure to these types of asbestos minerals. Short chrysotile can be coated but is

not long enough to form ferruginous bodies with the typical beaded appearance and therefore classical ferruginous bodies are not as commonly found after exposure to chrysotile asbestos. Asbestos causes pulmonary fibrosis (asbestosis), lung cancer and both pleural and peritoneal mesotheliomas with a definite dose–response (Acheson et al., 1984; Hodgson and Darnton, 2000; Seidman et al., 1986; Heller et al., 1999; Levin et al., 1998; Britton, 2002).

Asbestos exposure, whether occupational, para-occupational and environmental, is the cause of a high percentage of cases of mesothelioma. In males, occupational asbestos exposure is particularly important and the likely explanation for mesothelioma being 5-fold more common in US males than females (Price and Ware, 2004). In females, background or non-asbestos-related mesotheliomas represent a significantly higher percentage than among males (Wagner et al., 1960; Newhouse and Thompson, 1965a,b; Edward et al., 1996; McDonald and McDonald, 1996).

Exposure to riebeckite (crocidolite) asbestos and grunerite asbestos (amosite) accounts for the majority of mesothelioma cases in industrialized countries, even though chrysotile is the asbestos fiber-type most commonly used (Wagner, 1986; Roggli and Pratt, 1993; Churg and Vedal, 1994; Langer and Nolan, 1998; McDonald and McDonald, 1996; McDonald et al., 2001; Morinaga et al., 2001; Britton, 2002; Neuberger and Vutuc, 2003; Dodson et al., 2003). Asbestos has also been implicated in causing laryngeal, esophageal and gastrointestinal tumors (Clemmesen and Hjalgrim-Jensen, 1981; Raffn et al., 1989) although this has not been established (Gamble, 2008). Studies demonstrated grunerite asbestos (amosite) (as well as other types of asbestos) in colon tissue from patients with colon cancer and occupational asbestos exposure, although causation has not been convincingly shown (Ehrlich et al., 1985, 1991).

Exposure guidelines for grunerite asbestos (amosite) have been debated and modified several times over the years, and differ from country to country (Health and Safety Executive, 1988; McCullagh, 1980). The current exposure limit recommended by the US Health Research Institute, NIOSH, is 10^5 fibers/ m^3 of air (0.1 f/mL) for asbestos fibers $>5 \mu m$ in length and a length to diameter ratio of at least 3:1. The OSHA permissible exposure limit, for the 8 h time-weighted-average, is the same. The NIOSH recommendations and OSHA regulations are among the strictest in the world, although the regulations do not yet address the importance of asbestos fiber-type. Airborne asbestos fibers in the workplace are collected on a membrane filter and imaged by phase-contrast light microscopy to ensure compliance. The morphological criterion eliminates from the exposure count the fibers too narrow to be imaged with the light optics used and fibers shorter than $5 \mu m$.

Several studies have shown a gradient in the risk for lung cancer and mesothelioma between different types of asbestos, with riebeckite asbestos (crocidolite) and grunerite asbestos (amosite) conveying a greater risk than chrys-

otile (Acheson et al., 1984; Gardner and Powell, 1986; Wagner et al., 1988; Rees et al., 1999a,b,c; Hodgson and Darnton, 2000; Britton, 2002) Smoking increases the risk for lung cancer more than 10-fold, but does not increase the risk of developing mesothelioma (Acheson et al., 1984; Dufresne et al., 1996).

Not only workers with occupational exposure to asbestos are at risk; para-occupational exposure is an important cause of asbestos-related disease (Wagner et al., 1960; Newhouse and Thompson, 1965a,b; Edward et al., 1996; Rees et al., 1999a,b,c; Browne and Wagner, 2001; Neuberger and Vutuc, 2003). Para-occupational exposures to asbestos may occur through contact with the work-clothes of a family member working in the asbestos industry or through exposure to asbestos containing products, especially the more friable low density type products (Gibbs and Griffiths, 1990). Airborne grunerite asbestos (amosite) from the clothes of an asbestos worker or the demolition of an asbestos containing house has led to occult asbestos exposure (Yamada et al., 1997).

6. Cohorts occupationally exposed to grunerite asbestos (amosite)

Three cohorts of workers exposed mainly, if not exclusively, to grunerite asbestos (amosite) have been studied. We use the epidemiology reports on these three studies to summarize what is known about the health hazards of this asbestos fiber-type.

The first study establishing the carcinogenicity of grunerite asbestos (amosite) was conducted on a cohort of 820 workers, from a plant in Paterson, NJ (Selikoff et al., 1972; Seidman et al., 1979, 1986; Selikoff and Seidman, 1980; Ribak et al., 1989). The plant has been reported to have utilized almost exclusively grunerite asbestos (amosite), and the exposure period for the cohort was limited to the workers who started work between June, 1941 and December 1945 (encompassing the entire period the United States was engaged in World War II). The work force was made up almost entirely of white males, who were older than would be usual for such a work force, as the younger men were in the armed forces.

The concentrations of airborne asbestos were never measured in the Paterson factory, although it has been estimated at between 14 and 75 f/mL (see Levin et al., 1998 for a discussion). Seidman et al. (1986) estimate the average exposure at 50 f/mL while for risk assessment, Nolan et al. (1999) used 30 f/mL as a lower limit for the average exposure. Only workers hired up to 1945 were included in the cohort, so by 1975 the latency period had been a minimum of 30 years. Workers in the cohort who had asbestos exposure besides the Paterson factory were omitted, so the health hazard would relate specifically to the grunerite asbestos (amosite) exposures in the Paterson, NJ factory. Every death in the cohort was traced, and relevant clinical and pathological information was sought (Fig. 1).

In the latest update (where 740 deaths had occurred in the Paterson cohort of 820 men), cases of mesothelioma were diagnosed: eight were pleural and 9 peritoneal mesotheliomas (Table 1). The only significant difference between the pleural and peritoneal mesothelioma cases was the mean duration of employment in the factory: 25.6 months versus 43.8 months (range 2–60 months) in the pleural versus peritoneal mesothelioma groups, respectively. This might indicate that the nine peritoneal mesothelioma cases were associated with higher exposures. The mean time from first exposure to the mesothelioma diagnosis was 31 years in both groups. Chest pain was the main symptom in the pleural mesothelioma group with death occurring on average 12 months from the time of first symptom, while abdominal pain was the main symptom in the peritoneal mesothelioma group with an average of only 8 months survival from first symptom. Pulmonary insufficiency was the immediate cause of death in most pleural cases (7 out of 8) while wasting and inanition was the immediate cause of death in most peritoneal cases (7 out of 9).

The Paterson factory closed in 1954 and moved to Tyler, Texas where a cohort of 1130 workers fabricated grunerite of asbestos (amosite) containing products until February 1972 (Table 1 and Fig. 1; Levin et al., 1998). Exposures at the factory are thought to be similar to those of Paterson as both facilities were operated by the same company and used, in some cases, the very same machinery and processes. Unlike Paterson, where no airborne asbestos concentrations were ever recorded, in Tyler 170 air samples were collected starting in 1967 (13 years after the plant opened, more than 70% of the air samples collected in 1971). The concentration range was reported to be from 15.9 to 91.4 f/mL (Levin et al., 1998). More detailed exposure data specific to various tasks the workers performed are available for 1967, 1970, and 1971, and are shown in Table 2 (Hurst et al., 1979; Johnson et al., 1982).

Although not all measurements were described using an average and range, it is apparent that task-specific exposures fall into three distinctly different concentration ranges. The highest exposure occurred among the workers milling/fiberizing the asbestos fibers; the mean exposure for the 3 years in which measurements were made was about 90 f/mL. Workers employed in forming/finishing and curing/packing asbestos had similar exposures of about 37.5 and 17.5 f/mL, respectively (Table 2).

Levin et al. (1998) reported the mortality experience for 222 deaths in the cohort. The total cohort experienced an increased standard mortality ratio (SMR) for cancer of the lung, trachea and bronchus of 277 while those with less than 6 months of exposure had a slightly lower SMR of 268. Hurst et al. (1979) reported that 85% of the Tyler workers had a history of cigarette smoking; it has not been reported, though, whether any of the lung cancers occurred in non-smokers.

Six mesotheliomas occurred in the cohort: four pleural and two peritoneal (Table 1 and Fig. 1). In three of the four cases the latency exceeded 25 years, whereas in the fourth

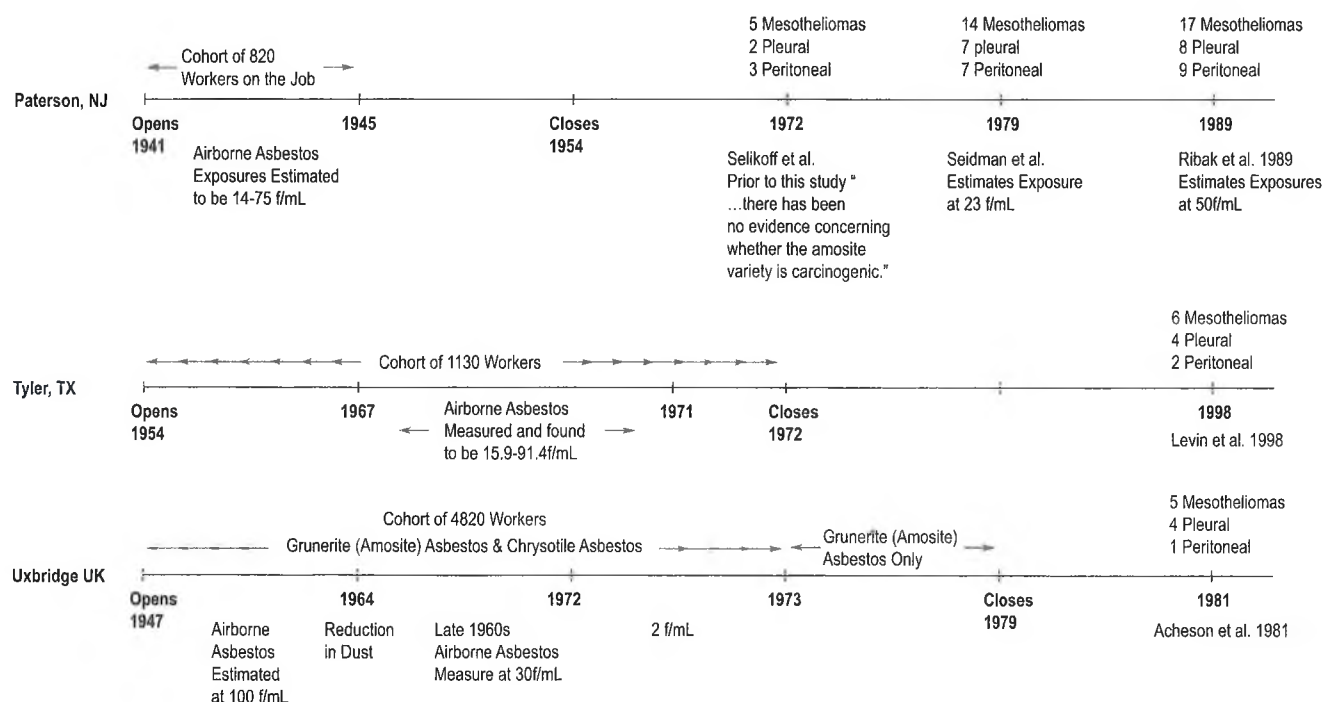


Fig. 1. Timeline for asbestos-related mesothelioma at the factories using predominantly, if not exclusively, grunerite asbestos (amosite): Paterson, NJ; Tyler, TX; and Uxbridge, UK.

Table 1

Summary of the mortality experience of three populations occupationally exposed to grunerite (amosite) asbestos

Cohort studied (reference)	No. in cohort	Deaths	No. of lung cancers	% of lung cancer	No. of mesothelioma		% of mesothelioma Deaths	No. of asbestosis cases	Asbestosis as a % of mortality
					Deaths	Ratio ^a			
Paterson, NJ (Selikoff et al., 1972)	230	105	25	23.8	5	2-3	4.8	14	13.3
Workers (Seidman et al., 1979)	820	523	93	17.8	14	7-7	2.7	30	5.7
Seidman et al. (1986)	820	593	111	18.7	17	8-9	2.9	31	5.2
Ribak et al. (1989)	820	740	NR*	NR*	17	8-9	2.3	NR*	NR*
Tyler, TX (Levin et al., 1998) workers	1130	222	35	15.8	6	4-2	2.7	3	1.4
Uxbridge, UK workers (Acheson et al., 1981, 1984)	4820	333	57	17.1	5	4-1	1.5	9	2.7

All three groups are thought to have been exposed predominately, if not exclusively, to grunerite (amosite) asbestos.

* Not reported.

^a Ratio of pleural to peritoneal.

Table 2

Results of personal air sampling for five different functions at the grunerite asbestos (amosite) factory in Tyler, Texas

Operation	Fiber/mL			Fibers/mL Mean for 3 years
	1967	1970	1971	
Milling/fiberizing	163.5	36.2	74.4	91.4
Forming	33.3	25.7	50.6	36.5
Curing	2.5	31	14.4	15.9
Finishing	44.6	34.8	39.5	39.6
Packing	16.7	17.9	22.8	19.1

The samples were analyzed by phase-contrast light microscopy; the number of fibers per milliliter with a length equal to or greater than 5 µm and with an aspect ratio of 3:1 or greater are reported.

case, the latency was over 15 years. In one case the exposure was less than 6 months, in two cases the exposures were between 1 and 5 years, and in the fourth case the exposure was greater than 5 years. There were three asbestosis deaths (representing 1.4% of the total mortality) about 3.7-fold less asbestosis mortality than in the Paterson factory (Table 1). No information was given concerning the latency or duration of exposure in the two peritoneal mesothelioma cases or the three asbestosis cases.

No information was given about the tasks performed by the six workers who developed mesothelioma (or any other asbestos-related disease). It would be particularly important to know if those who worked for a short period of time

were employed in positions with high exposures to airborne asbestos. For example, if the worker who developed pleural mesothelioma after just 6 months' exposure were milling grunerite asbestos (amosite) with an average exposure of 91.4 f/mL, his cumulative lifetime asbestos exposure would have been 45 f/mL years. This is more than 11-fold higher than the 4 f/mL years of cumulative exposure a worker would have after working 40 years at the current US exposure level of 0.1 f/mL. Six months of exposure at Tyler could have produced a cumulative exposure an order of magnitude higher than a 40-year working career by today's standard. Brief exposure at the Tyler factory could be associated with a high cumulative exposure leading to a high risk of asbestos-related disease.

The third epidemiology study focused on the use of grunerite asbestos (amosite) and chrysotile asbestos in a factory fabricating insulation boards in Uxbridge, United Kingdom (Acheson et al., 1981). Asbestos exposure at the factory begins in 1947 and ends when the factory closes in 1979. Up to 1973 both grunerite asbestos (amosite) and chrysotile asbestos were used, while for the last 6 years before the factory closed only grunerite asbestos (amosite) was used (Fig. 1). As the quantities of short-fiber chrysotile asbestos used were small when compared to grunerite asbestos (amosite), and the limited evidence for the role of a low exposure to short chrysotile in inducing human mesotheliomas, Acheson et al. (1981) concluded it was reasonable to attribute the five mesotheliomas found among the Uxbridge workers to exposure to grunerite asbestos (amosite) (Table 1). Four of the five mesothelioma cases were pleural. The single peritoneal case occurred in an individual after 28 years (including a short exposure and a long latency). The four pleural cases had exposures of 4 months, 1.5 years, 3.5 years and 9.5 years, with latencies of 22 years, 19 years, 24 years and 14 years, respectively. A fifth pleural mesothelioma was reported by Acheson et al. (1981) in an individual who started to work at the factory at 50 years of age and developed a mesothelioma 11 years later, after only 6 weeks of exposure in the factory. Due to the short latency and the brief exposure to grunerite asbestos (amosite) Acheson et al. (1981) concluded the mesothelioma was not related to exposure at the factory.

Exposures prior to 1964 were thought to be as high as 100 f/mL. Four of the mesothelioma cases were exposed to the dustiest operations such as milling or fiberizing of asbestos before 1960. Exposure estimates of Acheson et al. (1984) are almost identical to the average of 91.4 f/mL reported by Hurst et al. (1979) for milling/fiberizing at the Tyler, TX factory. In Uxbridge, employment histories of the mesothelioma cases were reported, and three of the five mesotheliomas occurred among individuals whose job included milling/fiberizing. This is also the case for the two workers who developed asbestosis and either pleural or peritoneal mesothelioma, after working for 8 years and 6 years, respectively, at milling/fiberizing. Of the three pleural mesotheliomas with less than 4 years'

exposure, two worked in milling/fiberizing and the third case with 4 months of exposure had both asbestosis and a pleural mesothelioma indicating a significant cumulative exposure during his brief period in the factory.

Riebeckite (crocidolite) asbestos was never used in the fabrication of commercial products, but had been evaluated experimentally from time to time at the Uxbridge factory. Acheson et al. (1984) reports the mortality experience for a cohort of 5969 men fabricating asbestos containing insulation board from 1947 to 1979. By the end of 1980 the cohort experienced 422 (7%) mortality. Only 4280 men worked making asbestos insulation board with only 14% of these starting works prior to 1960. The other 1689 workers made non-asbestos building materials in the same building complex. No additional mesotheliomas were reported besides the 5 reported earlier (Acheson et al., 1981). A 2-fold excess of lung cancer was reported with 57 observed while only 29 were expected with increased lung cancer mortality for those starting work both before and after 1960 (Table 1). The asbestos exposed cohort also had 9 asbestosis deaths an intermediate number between Paterson and Tyler (Table 1). All of the 9 worker with the asbestosis had started work prior to the dust reduction in 1964, and 7 of them started before 1960.

No significant excess of any other cancer (including gastrointestinal cancer and non-Hodgkin's lymphomas) was reported. The excess mortality was limited to diseases of the lung and pleura, with 28 excess lung cancer and 4 excess pleural mesothelioma deaths out of a total of 61 deaths. All of the excess lung cancer mortality occurred among workers who were smokers or ex-smokers. The Uxbridge cohort had three excess lung cancer deaths for every asbestosis death, similar to the Paterson factory. The Tyler factory had almost 8 excess lung cancers for each asbestosis death. Among the other workers in the Tyler complex who did not work directly with asbestos, but did share some facilities and worked in close proximity, no mesotheliomas or increased mortality from lung cancer was found.

In addition to the mortality study, a lung tissue content study was done on 48 workers from the Uxbridge, UK plant (Gibbs et al., 1994). Asbestos fiber-types and concentration in the lung parenchyma were investigated in each individual, and compared to the lung pathology in that case. Fourteen cases of lung cancer and five pleural mesotheliomas were identified among the 48 samples studied. Gibbs et al. (1994) are silent on the relationship between their cases and those mesothelioma cases described by Acheson et al. (1981). Analytical transmission electron microscopy was used for the lung content analysis. All fibers with 3:1 aspect ratios of any length were counted. Large amounts of grunerite asbestos (amosite) (mean = 785 million fibers per gram dried lung tissue) and relatively small amounts of chrysotile (mean = 12 million fibers per gram dried lung tissue) were consistently found, strengthening the conclusions of Acheson et al. (1981) – that the mesothe-

liomas were caused by grunerite asbestos (amosite). The grunerite asbestos (amosite) concentration in the 14 lung cancer specimens was 40% higher than in the 5 mesothelioma cases. A definite dose–response was demonstrated between grunerite asbestos (amosite) concentrations in the lung parenchyma and lung cancer and mesothelioma. Mesothelioma cases contained more grunerite asbestos (amosite) than the remaining cases without malignant disease.

The degree of interstitial fibrosis and number of asbestos bodies were graded. A positive relationship was found between the concentration of grunerite asbestos (amosite) and the grade of fibrosis and asbestos bodies. This observation hints that exposure to grunerite asbestos (amosite) was the cause of asbestosis rather than the chrysotile asbestos exposure. Duration of exposure affected the grades of fibrosis and the number asbestos bodies to a lesser extent. Chrysotile asbestos concentrations did not seem to affect the fibrosis grades, perhaps owing to its relatively small amounts.

Eleven subjects, including one of the mesothelioma cases, had significant amounts of riebeckite (crocidolite) asbestos in their lungs. This could have been acquired outside this plant. Grunerite asbestos (amosite) concentration in lung parenchyma examined verified the high level of exposure to this asbestos fiber-type in the factory.

7. Conclusions

The epidemiology studies of the three factories producing grunerite asbestos (amosite) products provide consistent evidence for this asbestos fiber-type producing asbestosis and increased risk of lung cancer and mesothelioma in both the pleura and peritoneum (Table 1). The highest mortality from asbestosis and peritoneal mesothelioma was in the cohort exposed in Paterson, NJ indicating it is likely to have the highest cumulative asbestos exposure of the three grunerite asbestos (amosite) exposed cohorts (Table 1). The results of the air sampling in the Tyler, TX factory found the mean asbestos exposures associated with milling/fiberizing to be 91.4 f/mL. The other four processes for which exposure information was gathered at the Tyler factory also indicate the workers had high asbestos exposures (Table 2). The increased risk of asbestos-related disease after brief exposure in all these factories may be related to the very high exposures.

In all three factories some pleural mesotheliomas occurred in workers with exposures of less than 1 year, and one pleural mesothelioma occurred in a worker from Tyler and another from Uxbridge with less than 6 months, exposure. The peritoneal mesothelioma cases were generally associated with higher cumulative exposures. Exposure conditions in all three factories appear to have been rather similar, possibly leading to an accumulated exposure of 45 f/mL year in as little as 6 months, significantly increasing the risk of pleural mesothelioma in all three cohorts.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

- Acheson, E.D., Bennett, C., Gardiner, M.J., Winter, P.D., 1981. Mesothelioma in a factory using amosite and chrysotile asbestos. *The Lancet* 2, 1403–1406.
- Acheson, E.D., Gardiner, M.J., Winter, P.D., Bennett, C., 1984. Cancer in a factory using amosite asbestos. *International Journal of Epidemiology* 13 (1), 3–10.
- Addison, J., McConnell, E.E., 2005. A review of carcinogenicity studies of asbestos and non-asbestos tremolite and other amphiboles. In: *Proceedings of the International Symposium on the Health Hazard Evaluation of Fibrous Particles Associated with Taconite and the Adjacent Duluth Complex*. St. Paul, Minnesota, March 30–April 1, 2003.
- Alleman, J., Mossman, B.T., 1997. Asbestos revisited. *Scientific American* 277, 70–75.
- Britton, M., 2002. The epidemiology of mesothelioma. *Seminars in Oncology* 29 (1), 18–25.
- Browne, K., 1994. Asbestos-related disorders. In: Parkers, W.R. (Ed.), *Occupational Lung Disorders*, third ed. Butterworth-Heinemann, Ltd., Oxford, pp. 411–504.
- Browne, K., Wagner, J.C., 2001. Environmental exposure to amphibole-asbestos and mesothelioma. In: Nolan, R.P., Langer, A.M., Ross, M., Wicks, F.J., Martin, R.F. (Eds.), *In: Health Effects of Chrysotile Asbestos: Contribution of Science to Risk Management Decisions*, vol. 5. The Canadian Mineralogist Special Publication, pp. 21–28.
- Carbone, M., 2000. Simian virus 40 and human tumors: it is time to study mechanisms. *Journal of Cellular Biochemistry* 76 (2), 189–193.
- Churg, A., Wright, J.L., Gilks, B., DePaoli, L., 1989. Rapid short-term clearance of chrysotile compared with amosite asbestos in the guinea pig. *American Review of Respiratory Disease* 139 (4), 885–890.
- Churg, A., Vedal, S., 1994. Fiber burden and patterns of asbestos-related disease in workers with heavy mixed amosite and chrysotile exposure. *American Journal of Respiratory and Critical Care Medicine* 150 (3), 633–669.
- Clemmesen, J., Hjalgrim-Jensen, S., 1981. Cancer incidence among 5686 asbestos cement workers followed from 1943 through 1976. *Ecotoxicology and Environmental Safety* 5, 15–23.
- Davis, J.M., Addison, J., Bolton, R.E., Donaldson, K., Jones, A.D., Smith, T., 1986. The pathogenicity of long versus short fibre samples of amosite asbestos administered to rats by inhalation and intraperitoneal injection. *British Journal of Experimental Pathology* 67 (3), 415–430.
- Davis, J.M., Bolton, R.E., Miller, B.G., Niven, K., 1991. Mesothelioma dose–response following intraperitoneal injection of mineral fibres. *International Journal of Experimental Pathology* 72 (3), 263–274.
- Dodson, R.F., O'Sullivan, M.F., Huang, J., Holiday, D.B., Hammar, S.P., 2000. Asbestos in extrapulmonary sites: omentum and mesentery. *Chest* 117 (2), 486–493.
- Dodson, R.F., O'Sullivan, M., Brooks, D.R., Hammar, S.P., 2003. Quantitative analysis of asbestos burden in women with mesothelioma. *American Journal of Industrial Medicine* 43, 188–195.
- Dufresne, A., Begin, R., Masses, S., Dufresne, C.M., Loosereewanich, P., Perrault, G., 1996. Retention of asbestos fibers in lungs of workers with asbestosis, asbestosis and lung cancer, and mesothelioma in asbestos township. *Occupational and Environmental Medicine* 53 (12), 801–807.
- Edward, A.T., Whitaker, D., Browne, K., Pooley, F.D., Gibbs, A.R., 1996. Mesothelioma in a community in the north of England. *Occupational and Environmental Medicine* 53 (8), 547–552.
- Ehrlich, A., Rohl, A.N., Holstein, E.C., 1985. Asbestos bodies in carcinoma of colon in an insulation worker with asbestosis. *Journal of the American Medical Association* 254 (20), 2932–2933.
- Ehrlich, A., Gordon, R.E., Dikman, S.H., 1991. Carcinoma of the colon in asbestos-exposed workers: analysis of asbestos content in colon tissue. *American Journal of Industrial Medicine* 19 (5), 629–636.

- Gamble, J.F., 2008. Risk of gastrointestinal cancer from inhalation and ingestion of amphibole asbestos. *Regulatory Toxicology and Pharmacology* 52, S124–S153.
- Gardner, M.J., Powell, C.A., 1986. Mortality of asbestos cement workers using almost exclusively chrysotile fiber. *Journal of the Society of Occupational Medicine* 36 (4), 124–126.
- Gazdar, A.F., Butel, J.S., Carbone, M., 2002. SV40 and human tumours: myth, association or causality? *Nature Review Cancer* 2, 951–964.
- Gibbs, G.W., Hwang, C.Y., 1980. Dimensions of airborne asbestos fibres. In: Wagner, J.C. et al. (Eds.), *Biological Effects of Mineral Fibers*. International Agency for Research in Cancer, vol. 1. IARC Scientific Publication No. 30, pp. 69–78, 30.
- Gibbs, A.R., Griffiths, D.M., 1990. Comparison of fibre types and size distributions in lung tissues of paraoccupational and occupational cases of malignant mesothelioma. *British Journal of Industrial Medicine* 47 (9), 621–626.
- Gibbs, A.R., Gardner, M.J., Pooley, F.D., Griffiths, D.M., Blight, B., Wagner, J.C., 1994. Fiber levels and disease in workers from a factory predominantly using amosite. *Environmental Health Perspectives* 102 (5), 261–263.
- Graham, A., Higinbotham, J., Allan, D., Donaldson, K., Beswick, P.H., 1999. Chemical differences between long and short amosite asbestos: differences in oxidation state and coordination sites of iron, detected by infrared spectroscopy. *Occupational and Environmental Medicine* 56 (9), 606–611.
- Hall, A.L., 1930. Asbestos in the Union of South Africa. Geological Survey Memoir No. 12. Union of South Africa, Pretoria, Department of Mines and Industry.
- Health and Safety Executive, 1988. Asbestos: exposure limits and measurement of airborne dust concentrations. HMSO Publication Center, P.O. Box 276, London SW8 5DT, United Kingdom.
- Heller, D.S., Gordon, R.E., Clement, P.B., Turnnir, R., Katz, N., 1999. Presence of asbestos in peritoneal malignant mesotheliomas in women. *International Journal of Gynecological Cancer* 9 (6), 452–455.
- Hesterberg, T.W., Axten, C., McConnell, E.E., Hart, G.A., Müller, W., Chevalier, J., Everett, J., Thevenaz, P., Oberdörster, G., 1999. Studies on the inhalation toxicology of two fibreglasses and amosite asbestos in the Syrian Golden Hamster. Part I. Results of a subchronic study and dose selection for a chronic study. *Inhalation Toxicology* 11 (9), 747–784.
- Hiett, D.M., 1978. Experimental asbestosis: an investigation of functional and pathological disturbances. *British Journal of Industrial Medicine* 35 (2), 129–145.
- Hilding, A.C., Hilding, D.A., Larson, D.M., Aufderheide, A.C., 1981. Biological effects of ingested amosite asbestos, taconite tailings, diatomaceous earth and Lake Superior waters in rats. *Archives of Environmental Health* 36 (6), 298–303.
- Hodgson, J.T., Darnton, A., 2000. The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure. *Annals of Occupational Hygiene* 44 (8), 565–601.
- Huncharek, M., 1994. Asbestos and cancer: epidemiological and public health controversies. *Cancer Investigation* 12 (2), 214–222.
- Hurst, G.A., Spivey, C.G., Matlage, E.T., Miller, J.M., Faulk, G., McLarty, J.W., Greenberg, S.D., 1979. The tyler asbestos workers Program. I. A Medical surveillance model and method. *Archives of Environmental Health* 34, 434–439.
- Johnson, N.F., 1993. The limitations of inhalation, intratracheal, and intracelomic routes of administration for identifying hazardous fibrous minerals. In: Warheit, D.B. (Ed.), *Fiber Toxicology*. Academic Press, San Diego, pp. 43–72.
- Johnson, W.M., Lemen, R.A., Hurst, G.A., Spiegel, R.M., Liu, F.H.Y., 1982. Respiratory morbidity among workers in an amosite insulation plant. *Journal of Occupational Medicine* 24, 994–999.
- Kamp, D.W., Israbian, V.A., Preusen, S.E., Zhang, Z.X., Weitzman, S.A., 1995. Asbestos causes DNA strand breaks in cultured pulmonary epithelial cells: role of iron-catalyzed free radicals. *American Journal of Physiology* 268 (3), L471–L480.
- Langer, A.M., Nolan, R.P., 1998. Asbestos in the lungs of persons exposed in the USA. *Monaldi Archives of Chest Diseases* 53, 168–180.
- Lawrence, E.C., Fox, T.B., 1983. Effects of amosite asbestos on human pulmonary alveolar macrophage function. *American Review of Respiratory Disease* 127 (4), 61.
- Levin, J.L., McLarty, J.W., Hurst, G.A., 1998. Tyler asbestos workers: mortality experience in a cohort exposed to amosite. *Occupational and Environmental Medicine* 55 (3), 155–160.
- Lopez-Rois, F., Illei, P.B., Rusch, V., Ladanyi, M., 2004. Evidence against a role of SV40 in human mesothelioma and a high risk of false-positive PCR results owing to the presence of SV40 sequences in common laboratory plasmids. *The Lancet* 364, 1157–1166.
- Lund, L.G., Williams, M.G., 1994. Iron associated with asbestos bodies is responsible for the formation of single strand breaks in PHI X174 RFI DNA. *Occupational and Environmental Medicine* 51 (3), 200–204.
- Manfredi, J.J., Dong, J., Liu, W., Resnick-Silverman, L., Qiao, R., Chahainian, P., Saric, M., Gibbs, A.R., Phillips, J.I., Murray, J., Axten, C.W., Nolan, R.P., Aaronson, S.A., 2005. Evidence against a role for SV40 in human mesothelioma. *Cancer Research* 65, 2602–2609.
- McConnell, E.E., 1995. Advantages and limits of in vitro screening tests. *The Annals of Occupational Hygiene* 39, 727–735.
- McConnell, E.E., Axten, C., Hesterberg, T.W., Chevalier, J., Müller, W.C., Everitt, J., Oberdörster, G., Chase, G.R., Thevenaz, P., Kotin, P., 1999. Studies on the inhalation toxicology of two fibreglasses and amosite asbestos in the Syrian golden hamster. Part II. Results of chronic exposure. *Inhalation Toxicology* 11 (9), 785–835.
- McCullagh, S.F., 1980. Amosite as a cause of lung cancer and mesothelioma in humans. *Journal of the Society of Occupational Medicine* 30, 153–156.
- McDonald, J.C., McDonald, A.D., 1996. The epidemiology of mesothelioma in historical context. *European Respiratory Journal* 9 (9), 1932–1942.
- McDonald, J.C., Armstrong, B.G., Edwards, C.W., Gibbs, A.R., Lloyd, H.M., Pooley, F.D., Ross, D.J., Rudd, R.M., 2001. Case-referent survey of young adults with mesothelioma: I. Lung fibre analyses. *Annals of Occupational Hygiene* 45 (7), 513–518.
- Miller, B.G., Searl, A., Davis, J.M., Donaldson, K., Cullen, R.T., Bolton, R.E., Buchanan, D., Soutar, C.A., 1999a. Influence of fiber length, dissolution and biopersistence on the production of mesothelioma in the rat peritoneal cavity. *Annals of Occupational Hygiene* 43 (3), 155–166.
- Miller, B.G., Jones, A.D., Searl, A., Buchanan, D., Cullen, R.T., Soutar, C.A., Davis, J.M., Donaldson, K., 1999b. Influence of characteristics of inhaled fibers on development of tumors in the rat lung. *Annals of Occupational Hygiene* 43 (3), 167–179.
- Morinaga, K., Kishimoto, T., Sakatani, M., Akira, M., Yokoyama, K., Sera, Y., 2001. Asbestos-related lung cancer and mesothelioma in Japan. *Industrial Health* 39 (2), 65–74.
- Murray, J., Nelson, G., 2008. Health effects of amosite mining and milling in South Africa. *Regulatory Toxicology and Pharmacology* 52, S75–S81.
- National Toxicology Program, 1983. Lifetime carcinogenesis studies of amosite asbestos in Syrian golden hamsters (feed studies) Research Triangle Park. NTP Publication 84-2505 (NTP TR 249).
- National Toxicology Program, 1990. Toxicology and Carcinogenesis Studies of Amosite Asbestos in F344/N Rats (Feed Studies). NTP Publication 91-172312 (NTP TR 279).
- Nash, D.R., Fortson, N.G., 1981. Serum protein concentrations and respiratory tract abnormalities following short-term exposure to amosite: a comparison between former asbestos workers and unexposed controls. *Journal of Toxicology and Environmental Health* 7 (5), 733–744.
- Nejjari, A., Fournier, J., Pezerat, H., Leanderson, P., 1993. Mineral fibers: correlation between oxidizing surface activity and DNA base hydroxylation. *British Journal of Industrial Medicine* 50 (6), 501–504.

- Neuberger, M., Vutuc, C., 2003. Three decades of pleural cancer and mesothelioma registration in Austria where asbestos cement was invented. *International Archives of Occupational Health* 76, 161–166.
- Newhouse, M.L., Thompson, H., 1965a. Mesothelioma of the pleural and peritoneum following exposure to asbestos in the London Area. *British Journal of Industrial Medicine* 22, 261–269.
- Newhouse, M.L., Thompson, H., 1965b. Epidemiology of mesothelial tumors in the London Area. *Annals of the New York Academy of Sciences* 132, 579–588.
- Nolan, R.P., Langer, A.M., 1993. Limitations of the stanton hypothesis. In: Guthrie, G., Mossman, B.T. (Eds.), *Health Effects of Mineral Dusts*. Mineralogical Society of America, Washington, DC, pp. 309–326.
- Nolan, R.P., Langer, A.M., Wilson, R., 1999. A risk assessment for exposure to grunerite asbestos (amosite) in an iron ore mine. *Proceedings of the National Academy of Sciences of the United States of America* 96, 3412–3419.
- Price, B., Ware, A., 2004. Mesothelioma trends in the United States: an update based on SEER data for 1973 through 2003. *American Journal of Epidemiology* 159, 107–112.
- Oberdörster, G., Morrow, P.E., 1988. Size dependent lymphatic short term clearance of amosite fibers in the lung. *Annals of Occupational Hygiene* 32 (1), 149–156.
- Rees, D., Goodman, K., Fourie, E., Chapman, R., Blignaut, C., Bachmann, M.O., Myers, J., 1999a. Asbestos exposure and mesothelioma in South Africa. *South African Medical Journal* 89 (6), 627–634.
- Rees, D., Goodman, K., Fourie, E., Chapman, R., Blignaut, C., Bachmann, M.O., Myers, J., 1999b. Asbestos exposure and mesothelioma in South Africa. *South African Medical Journal* 89 (6), 627–634.
- Rees, D., Myers, J.E., Goodman, K., Fourie, E., Blignaut, C., Chapman, R., Bachmann, M.O., 1999c. Case-control study of mesothelioma in South Africa. *American Journal of Industrial Medicine* 35 (3), 213–222.
- Raffin, E., Lynge, E., Juel, K., Korsgaard, B., 1989. Incidence of cancer and mortality among employees in the asbestos cement industry in Denmark. *British Journal of Industrial Medicine* 46 (2), 90–96.
- Ribak, J., Seidman, H., Selikoff, I.J., 1989. Amosite mesothelioma in a cohort of asbestos workers. *Scandinavian Journal of Work Environment and Health* 15, 106–110.
- Riganti, C., Aldieri, E., Bergandi, L., Tomatis, M., Fenoglio, I., Costamagna, C., Fubini, B., Bosia, A., Ghigo, D., 2003. Long and short fiber amosite alters at a different extent the redox metabolism in human lung epithelial cells. *Toxicology and Applied Pharmacology* 193, 106–115.
- Roggli, V.L., Pratt, P.C., 1993. Asbestos fiber type in malignant mesothelioma: an analytical scanning electron microscopic study of 94 cases. *American Journal of Industrial Medicine* 23 (4), 605–614.
- Ross, M., Virta, R., 2001. Occurrence, production and uses of asbestos. In: *The Health Effects of Chrysotile-Asbestos: Contribution of Science to Risk-Management Decisions*. Canadian Mineralogist, Special Publication 5, pp. 79–88.
- Ross, M., Langer, A.M., Nord, G.L., Nolan, R.P., Lee, R.J., Van Orden, D., Addison, J., 2008. The mineral nature of asbestos. *Regulatory Toxicology and Pharmacology* 52, S26–S30.
- Searl, A., Buchanan, D., Cullen, R.T., Jones, A.D., Miller, B.G., Soutar, C.A., 1999. Biopersistence and durability of nine mineral fibre types in rat lungs over 12 months. *Annals of Occupational Hygiene* 43 (3), 143–153.
- Seidman, H., Selikoff, I.J., Hammond, E.C., 1979. Short-term asbestos work exposure and long-term observation. *Annals of the New York Academy of Sciences* 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. *American Journal of Industrial Medicine* 10 (5/6), 479–514.
- Selikoff, I.J., Hammond, E.C., Churg, J., 1972. Carcinogenicity of amosite asbestos. *Archives of Environmental Health* 25, 183–186.
- Selikoff, I.J., Seidman, H., 1980. Mortality effects of cigarette smoking among amosite asbestos factory workers. *Journal of the National Cancer Institute* 65 (3), 507–513.
- Stanton, M.F., Layard, M., Tegeris, A., Miller, E., May, M., Morgan, E., Smith, A., 1981. Relation of particle dimension to carcinogenicity in amphibole asbestos and other fibrous minerals. *Journal of the National Cancer Institute* 67, 965–976.
- Suzuki, Y., Kohyama, N., 1991. Translocation of inhaled asbestos fibers from the lung to other tissues. *American Journal of Industrial Medicine* 19 (6), 701–704.
- Ueki, A., 2001. Biological effects of asbestos fibers on human cells in vitro—especially on lymphocytes and neutrophils. *Industrial Health* 39 (2), 84–93.
- Veblen, D.R., Wylie, A.G., 1993. Amphiboles and 1:1 layer silicates. In: Guthrie, G.D., Mossman, B.T. (Eds.), *Health Effects of Mineral Dusts*. Reviews in Mineralogy, vol. 28. Mineralogical Society of America, Washington, DC, pp. 61–137.
- Wagner, J.C., Sleggs, C.A., Marchand, P., 1960. Diffuse pleural mesothelioma and asbestos exposure in the northwestern Cape Province. *British Journal of Industrial Medicine* 17, 260–271.
- Wagner, J.C., 1986. Mesothelioma and mineral fibres. In: Fortner, J.G., Rhoads, J.E. (Eds.), *Accomplishments in Cancer Research* 1985. Lippincott, Philadelphia.
- Wagner, J.C., Newhouse, M.L., Corrin, B., Rossiter, C.E.R., Griffiths, D.M., 1988. Correlation between fiber content of the lung and disease in east London asbestos factory workers. *British Journal of Industrial Medicine* 45 (5), 305–308.
- Webster, I., Goldstein, B., Coetzee, F.S.J., Van Sittert, G.C.H., 1993. Malignant mesothelioma induced in baboons by inhalation of amosite asbestos. *American Journal of Industrial Medicine* 24 (6), 659–666.
- Wilson, R., McConnell, E.E., Ross, M., Axten, C.W., Nolan, R.P., 2008. Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. *Regulatory Toxicology and Pharmacology* 52, S232–S245.
- Yamada, H., Hashimoto, H., Akiyama, M., 1997. Talc and amosite/crocidolite preferentially deposited in the lungs of nonoccupational female lung cancer cases in urban areas of Japan. *Environmental Health Perspectives* 105 (5), 504–508.

Rapporteur's Report Session 3: Exposure to grunerite asbestos (amosite): Historical perspectives of the health effects: Graham W. Gibbs

The development of information concerning mesothelioma in South Africa started with the 1959 finding of Dr. J. Christopher Wagner of cases of mesothelioma in persons living in the vicinity or working in crocidolite mines in Cape Province. After more than 40 years, the data from South Africa now provide important insights into the differences in mesothelioma risk associated with different asbestos fiber-types. Three case series reports and one analytical report were reviewed in this session. In total, information on 504 proven cases was presented. There were 28% of cases arising from occupational exposure in mining, 35% from non-mining occupations, 23% from environmental exposures; 14% where no exposure was established and 9% where the exposure was unknown. Among the 129 cases for which occupational exposure and asbestos fiber-type were established, 115 cases were associated with occupational exposure to Cape crocidolite; 1 case associated with occupational exposure to Transvaal crocidolite and 9 cases with occupational exposure to amosite (grunerite asbestos) and 4 cases with occupational exposure to mixed fiber-types. There were *no* cases associated with chrysotile asbestos. There were 33 cases of environmental mesothelioma linked to Cape crocidolite exposure and 2 to exposure to amosite and crocidolite but *none* to Transvaal amosite alone or to chrysotile. The evidence shows that amosite is capable of causing mesothelioma but that the major risk in South Africa is associated with Cape crocidolite.

In a second paper the mortality experience at two factories in the US, (Paterson and Tyler) and one in the UK

(Uxbridge) manufacturing insulation products was reviewed. It was clear that all had increased proportional mortality (PMRs) from mesothelioma with the ratios ranging from 1.5% in the UK plant to 4.8% in one study at the Paterson plant. It is noteworthy that approximately 50% of the US and 20% of the UK cases were peritoneal tumors. Asbestosis mortality (while not always the most reliably recorded outcome) together with exposure estimates did seem to be in accord with the occurrence of peritoneal mesothelioma requiring higher exposure. Estimates of exposure in the US and UK plants, based on some measurements, ranged up to about 100 f/ml. PMRs for lung cancer (which are not the most reliable for examining risk), were sufficiently high in all cohorts to conclude that lung cancer risks were clearly increased. It is interesting to note that the PMR for mesothelioma in amosite miners in South Africa was reported to be 0.6% while in the manufacturing facilities it ranged up to 4.8%. Unfortunately data to compare production and manufacturing levels of exposure were not available. However, in the manufacturing process amosite was further fiberized and it might be hypothesized that this may be a factor of importance in relation to the apparently higher mesothelioma risk associated with amosite in processing as compared to mining.

Overall, it is evident that grunerite asbestos can increase the risk of lung cancer and mesothelioma. Cape crocidolite asbestos poses a far greater risk of mesothelioma and chrysotile asbestos, based on the South African evidence *may not* cause mesothelioma.

South African experience with asbestos related environmental mesothelioma: Is asbestos fiber type important?

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Abstract

South Africa (SA), a country in which all three commercially important asbestos minerals have been mined and milled, has retained proven cases of mesothelioma linked with environmental exposure to asbestos. This study illustrates the importance of fiber type in the occurrence of environmental mesothelioma. Four studies have reviewed the source of occupational or environmental asbestos exposure in 504 histologically proven cases of mesothelioma in South Africa. One hundred and eighteen cases (23%) were thought to be related to environmental exposure to asbestos. In the vast majority of these cases, exposure was linked to crocidolite mining activities in the Northern Cape Province. Two cases were thought to have occurred in relation to amosite and Transvaal crocidolite exposure in the Limpopo Province. In the balance of cases there was some uncertainty. No cases were reported with exposure to South African chrysotile. Consequently, in the vast majority of cases of mesothelioma, environmental exposure to asbestos occurred in the Northern Cape Province, in proximity to mines, mills and dumps where crocidolite was processed. Crocidolite appears to be far more mesotheliomagenic than amosite, and chrysotile has not been implicated in the disease. This is true for both occupationally and environmentally exposed individuals. © 2007 Elsevier Inc. All rights reserved.

Keywords: Crocidolite; Mesothelioma; Chrysotile; Amosite; South Africa

1. Introduction

All three of the major commercial forms of asbestos, viz. crocidolite (blue asbestos), amosite (brown asbestos) and chrysotile (white asbestos) occur and have been mined and milled in South Africa. Crocidolite was mined in the Northern Cape Province (Cape crocidolite) and in Limpopo Province (Transvaal crocidolite). Amosite was mined in close proximity to Transvaal crocidolite and chrysotile in Mpumalanga Province. Both amosite and crocidolite belong to the amphibole group of asbestos minerals, whereas chrysotile is a serpentine asbestos mineral.

Mining of asbestos in South Africa began in the 19th century and reached its zenith in 1977 when South

Africa exported more than 380,000 tons of asbestos, making it the 3rd largest supplier in the world in that year (Harington and McGlashan, 1998). Production declined steadily thereafter and by 1992 South Africa was only the 7th largest world supplier of asbestos. By 2002 asbestos mining in South Africa had ceased completely.

A variety of transnational companies dominated asbestos mining in South Africa. From the onset of the scientific examination of the health effects of asbestos mining in South Africa, it became apparent that the primitive technologies employed in mining and particularly milling, ignorance about the health effects of asbestos and lack of enforcement by responsible government departments created widespread opportunities for environmental contamination and subsequent exposure of people who were not employed in the industry.

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2. History of mesothelioma in South Africa

During the 1959 Pneumoconiosis conference in Johannesburg, South Africa, Dr. J. Christopher Wagner gave the first public presentation of five cases of mesothelioma connected with exposure to asbestos. During his presentation, he suggested that a fuller investigation be conducted to examine the relationship between mesothelioma and asbestos (Wagner, 1960).

A year later, in 1960, Wagner, Sleggs and Marchand published their renowned article in the British Journal of Industrial Medicine documenting 33 cases of mesothelioma, 32 of whom had proven exposure to Cape crocidolite. Eight of the 33 cases had evidence of occupational exposure; 20 were born or lived near the mines as children. This was the first evidence implicating a specific fiber (Cape crocidolite) in the development of mesothelioma (Wagner et al., 1960). What became one of the greatest occupational health discoveries of the 20th century was based principally on cases drawn from outside the workplace. By 1961, Wagner had collected 89 cases in South Africa.

Despite this strong evidence, Wagner's work had little impact on work practices in South Africa, and workers and communities alike continued to be exposed to high fiber levels. More than 25 years passed before the first asbestos regulations were promulgated in South Africa.

During the 1961/1962 survey undertaken by the Pneumoconiosis Research Unit (now the National Institute for Occupational Health), disease rates in 2389 residents of Prieska, Koegas, Kuruman (Cape crocidolite mining areas) and the Penge group of mines (amosite) were compared with those in a control group living in a town 200 km from the asbestos mining areas (Pneumoconiosis Research Unit, 1964). The results identified a hazard for every person living in these four small-town communities. The four mesothelioma cases detected in Prieska translated into a much higher than expected rate of the disease. No cases were reported in Penge residents. In an interim report the Pneumoconiosis Research Unit stated: "people who live or have lived in the areas of Prieska, Koegas, Kuruman and Penge are in danger of contracting asbestosis even though they have no industrial exposure to asbestos dust inhalation" and "an alarmingly high number of cases with mesothelioma of the pleura has been discovered among people who live or have lived in the north western Cape area (now the Northern Cape Province)

and that there is evidence to suggest that this condition is associated with an exposure to asbestos dust inhalation which again need not be industrial" (Pneumoconiosis Research Unit, 1962).

Exposure to asbestos occurred primarily through community use of the fibers. Tailings were used for many purposes, including road surfacing, golf courses, and brick and plaster making. Fibers were used as insulation material in residential ceilings and children played on fiber-rich waste ground. This association of mesothelioma with residential asbestos exposure has been borne out by more recent work in towns like Koegas and Prieska in the Northern Cape (Kielkowski et al., 2000).

This paper reviews the South African experience of mesotheliomas in relation to environmental asbestos exposure.

3. Review of the literature

Despite the fact that South Africa has uniquely mined, transported and used crocidolite, amosite and chrysotile, and that mesothelioma rates are relatively high, there is a paucity of local epidemiological studies of this disease.

Four studies detail the occupational and environmental exposure of 504 histologically proven cases of mesothelioma in South Africa (Webster, 1973; Cochrane and Webster, 1978; Solomons, 1984; Rees et al., 1999). Two further studies add to the estimate of the overall risk of environmental mesothelioma (Zwi et al., 1989; Kielkowski et al., 2000), and the reports of the South African National Cancer Registry (SANCR) enable some estimation of the overall burden of mesothelioma in South Africa until 1992. All sources indicate that there is under-reporting of mesothelioma to official sources of data collection, as well as to workers' compensation authorities. It is also evident that there are marked differences in mesothelioma rates by race and geographic origin.

Sources suggest that incidence rates of mesothelioma in the white female population give some indication of occurrence of mesothelioma related to environmental exposures (Zwi et al., 1989), as most of the workers employed in the mining industry were men, as well as black and colored women and children.

Table 1 gives standardized incidence rates of mesothelioma in the population of South Africa at two time periods, by race and sex. For whites, for whom data are most reliable, incidence rates increased from the 1976 to 1984 period

Table 1
Standardized incidence rates per million population aged 15 years and over for mesothelioma in South Africa by race and gender

	White		Colored		Black	
	Male	Female	Male	Female	Male	Female
Overall 1976–84 ^a	32.9	8.9	24.8	13.9	7.6	3.0
95% CI 1976–84 ^a	22.7–46.4	2.5–15.8	16.2–36.9	7.7–23.5	3.5–15.8	0.6–8.8
1992 ^b	54.0	20.8	5.2	2.4	6.4	6.0

^a Zwi et al., 1989.

^b National Cancer Registry of South Africa.

Table 2

Summary of occupational and environmental asbestos exposure in 504 histologically proven cases of mesothelioma in South Africa

Exposure source	Webster (1973)	Cochrane and Webster (1978)	Solomons (1984)	Rees et al. (1999)	Total
Mining	79 (34%)	16 (23%)	15 (19%)	35 (28%)	145 (28%)
Non-mining occupational	23 (10%)	39 (57%)	53 (66%)	62 (50%)	177 (35%)
Environmental	76 (32%)	13 (19%)	7 (9%)	22 (18%)	118 (23%)
No exposure	32 (14%)	1 (1%)	5 (6%)	3 (2%)	41 (8%)
Exposure not known	22 (9%)	—	—	1 (1%)	23 (5%)
Total cases	232	69	80	123	504

and then through 1992. The 1992 white female mesothelioma incidence increased from 8.9 to 20.8 per million per year. These data suggest that there is an increasing incidence of mesothelioma as a consequence of both environmental and occupational exposure.

Table 2 is a summary of occupational and environmental asbestos exposure in 504 histologically proven cases of mesothelioma in South Africa. The first three papers are case-series reports; the only analytical study was conducted by Rees et al. (1999). The overall proportion of cases resulting from environmental exposure to asbestos in the four studies in Table 2 is high at 23%.

In the earliest review by Webster (1973), a significant proportion of cases had either unknown exposure or no exposure identified. Subsequently, there has been better ascertainment of exposure and fewer cases in these categories. Webster identified 76 (32% of a total of 232 cases) environmentally exposed cases of mesothelioma in the period 1955–1970. Mining and non-mining occupationally exposed cases comprised 44% of the mesotheliomas.

Cochrane and Webster (1978) studied 70 cases of mesothelioma diagnosed before 1978. Thirteen of the 69 for whom there was substantive evidence of asbestos exposure had only environmental exposure, defined as a minimum of three years residence in a mining area, or in a town where exposure occurred from playing on “asbestos fields” or tailings dumps as a child.

Solomons' (1984) identified eighty cases of histologically confirmed mesothelioma in the period from 1977 to 1983. In 89% of cases, he elicited a positive history of exposure. His definition of environmental exposure included childhood, domestic, neighborhood or any other definite expo-

sure that was not occupational. Seven of the eight cases had a history of only environmental exposure.

Rees et al. (1999) conducted a multi-centre case control study over the period 1988–1990. In total, 123 cases of histologically confirmed mesothelioma were identified. Twenty-two (18%) of these cases had exclusively environmental exposure in the Cape crocidolite asbestos mining region, i.e. exposure due to contamination of the general environment by asbestos mining, milling and related activities (Table 3). The remaining two environmentally exposed cases had mixed fiber (amosite and Transvaal crocidolite) exposures.

Unfortunately, not all the authors provided the same detail on the specific fiber types to which individuals were exposed, especially with regard to environmental exposure. Table 3 provides a more detailed picture of fiber-specific exposure, for those studies for which this information was provided. Exposures are defined as occupational or environmental, according to the authors' definitions. Webster (1973) defined environmental cases as those who had lived (or spent time) in the neighborhood of an asbestos mine or mill, or in geographical areas suggestive of possible asbestos exposure. Cochrane and Webster (1978) classified cases as environmentally exposed if they had lived in an asbestos mining or milling area for a minimum of three years. Solomons' (1984) definition included childhood, domestic, neighborhood or other definite exposure which was not occupational. In the study conducted by Rees et al. (1999), 22 environmentally exposed cases were exposed in one of the three main asbestos mining regions. Domestic exposure to asbestos was not included under environmental exposure. Apart from Rees et al. (1999),

Table 3

Fiber types implicated in the development of mesothelioma

Fiber type	Webster (1973)		Cochrane and Webster (1978)		Solomons (1984)		Rees et al. (1999)		All	
	Occ	Env	Occ	Env	Occ	Env	Occ	Env	Occ	Env
Cape crocidolite	75	—	—	13	17	—	23	20	115	33
Transvaal crocidolite	—	—	—	—	—	—	1	—	1	—
Amosite	2	—	—	—	4	—	3	—	9	—
Chrysotile	—	—	—	—	—	—	—	—	—	—
Mixed fiber type	1 ^a	—	—	—	—	—	3	2 ^b	4	2
Undetermined	1	76	16	—	47	7	—	—	64	83
Total	79	76	16	13	68	7	30	22	193	118

^a Amosite + Cape crocidolite.^b Transvaal crocidolite + amosite.

none of the authors were able to provide information on the geographical regions from which the cases originated or in which they may have lived.

In a separate study, not depicted in Table 2, Zwi et al. (1989) identified 1347 cases for the period 1976–1984. Only 17% (96) of cases occurring in men (where asbestos exposure was documented) were environmental; in women, 124 of 176 cases (70%) were considered to be solely due to environmental exposure.

Many questions about mesothelioma in South Africa remain unanswered. Among them are the relative contribution each variety of asbestos makes to the case load, the extent and nature of asbestos exposure in a representative group of cases (e.g. the proportion of cases with purely environmental exposure), and the relative risks associated with the different fiber types and exposure settings.

Webster (1973) was able to ascertain the fiber type in 78 of the 79 occupationally exposed cases. Amosite was implicated in three and Cape crocidolite in 75 of these cases. He did not report fiber types in any of the 76 environmentally exposed cases. Cochrane and Webster (1978) did not identify the fiber type to which any of the occupational cases had been exposed, but Cape crocidolite was implicated in all 13 of the environmentally exposed cases. Solomons (1984) was able to implicate fiber type in 21 of the 68 occupationally exposed cases; 17 of these were due to Cape crocidolite and four to amosite exposure. There was no information on fiber types given for the environmentally exposed group.

Rees et al. (1999) however, provided information on fiber type (where it could be elicited) for both occupationally and environmentally exposed individuals. Amosite exposure was reported in three miners (10%), but in none of those environmentally exposed. In 23 (77%) of those occupationally exposed and 20 (91%) of those environmentally exposed, Cape crocidolite was identified as the responsible fiber. There were no cases of mesothelioma where exposure (occupational or environmental) was to chrysotile only.

Rees et al. (1999) also calculated relative risks for mesothelioma in response to different fiber types. The relative risks associated with environmental exposure to Cape crocidolite were larger than those associated with environmental exposure to a mixture of amosite and Transvaal crocidolite, viz. 21.9 and 7.1, respectively, when compared with cancer controls, and 50.9 and 12.0, respectively, when compared with medical controls.

4. Discussion

South Africa, as a former asbestos mining country, in common with many other countries in the world, has high incidences of mesothelioma (Table 1). A high proportion of mesothelioma cases solely of environmental origin (23%) is unique to South Africa. The only comparable example is Australia, the only other country to have mined crocidolite asbestos in significant amounts.

Ferguson et al. (1987) found that, in 726 cases of mesothelioma registered in Western Australia from 1980 to 1985, 43 cases (6%) had environmental exposure only, and only in six (less than 1%) was environmental asbestos exposure due to residence in an asbestos mining region.

No confirmed cases of mesothelioma have been detailed in the literature with relation to South African chrysotile mining. There is a high prevalence of cases from the Cape crocidolite mining region. The lower number of reported cases from Limpopo Province (where amosite and Transvaal crocidolite were mined) is not linked to the sizes of the two workforces. At the height of production, the numbers employed in the amosite and Cape crocidolite mines were comparable (Sluis-Cremer, 1965).

The association between amosite exposure and mesothelioma is evident. However, this review of environmental association of asbestos with mesothelioma in South Africa suggests that crocidolite is considerably more mesotheliomagenic than amosite. Fiber type was determined in 35 of the 118 environmentally exposed cases reported in these four papers. Of these, 33 (94%) had been exposed to Cape crocidolite. Only two cases had environmental exposure to amosite; both had also been exposed to crocidolite. In a study of the causes of death in a cohort of South African amphibole miners, the proportional mortality ratio for mesothelioma was 4.7% in the crocidolite miners, compared to 0.6% in amosite miners (Sluis-Cremer et al., 1992).

Past occupational exposures in the mining industry in South Africa, given the imperfect historical record, were at times astonishing by modern standards. These exposures conferred an enormous risk of malignant and non-malignant asbestos related disease on workers employed by the asbestos mining industry, as well as on residents in the mining areas.

5. Conclusion

In conclusion, a review of the fiber associations of environmental mesothelioma indicates that asbestos fiber type is important. There have been no reported cases associated with chrysotile in South Africa. Amphiboles occurring in the Limpopo Province of South Africa, namely amosite and Transvaal crocidolite, have been linked to environmental mesothelioma in the papers reviewed. The vast majority of environmental mesothelioma cases in South Africa, where fiber type is known, have occurred in relation to crocidolite mining activities in the Northern Cape Province and, consequently, at the low dose range of exposure, it must be concluded that this fiber type represents the greatest hazard to human health.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

- National Cancer Registry of South Africa. Cancer in South Africa, 1986–1992. South African Institute for Medical Research, Johannesburg.
- Cochrane, J.C., Webster, I., 1978. Mesothelioma in relation to asbestos fiber exposure. *S. Afr. Med. J.* 54, 279–281.
- Ferguson, D.A., Berry, G., Jelihovsky, T., Andreas, S.B., Rogers, A.J., Fung, S.C., Grimwood, A., Thompson, R., 1987. The Australian mesothelioma surveillance program 1979–1985. *Med. J. Aust.* 147, 166–172.
- Harington, J.S., McGlashan, N.D., 1998. South African asbestos: production, exports, and destinations, 1959–1993. *Am. J. Ind. Med.* 33, 321–326.
- Kielkowski, D., Nelson, G., Rees, D., 2000. Risk of mesothelioma from exposure to crocidolite asbestos: a 1995 update of a South African mortality study. *Occup. Environ. Med.* 57, 563–567.
- Pneumoconiosis Research Unit, 1964. Field survey in the North Western Cape and at Penge in the Transvaal (asbestosis and mesothelioma). Report No. 1.
- Pneumoconiosis Research Unit, 1962. Report on the progress of mesothelioma survey. South African Council for Scientific and Industrial Research, unpublished.
- Rees, D., Myers, J.E., Goodman, K., Fourie, E., Blignaut, C., Chapman, R., Bachman, M.O., 1999. Case-control study of mesothelioma in South Africa. *Am. J. Ind. Med.* 35, 213–222.
- Sluis-Cremer, G.K., 1965. Asbestosis in South Africa – certain geographical and environmental considerations. *Ann. NY Acad. Sci.* 132, 215–234.
- Sluis-Cremer, G.K., Liddell, F.D.K., Logan, W.P.D., Bezuidenhout, B.N., 1992. The mortality of amphibole miners in South Africa 1946–80. *Br. J. Ind. Med.* 49, 566–575.
- Solomons, K., 1984. Malignant mesothelioma—clinical and epidemiological features: A report of 80 cases. *S. Afr. Med. J.* 66, 407–412.
- Wagner, J.C., 1960. Some pathological aspects of asbestosis. In: Orenstein, A.J. (Ed.), *Proceedings of the Pneumoconiosis Conference held at the University of the Witwatersrand, Johannesburg, 9–24 February 1959*. J&A Churchill Ltd., London, pp. 373–382.
- Wagner, J.C., Sleggs, C.A., Marchand, P., 1960. Diffuse pleural mesothelioma and asbestos exposure in the North West Cape Province. *Br. J. Ind. Med.* 17, 260–265.
- Webster, I., 1973. Asbestos and malignancy. *S. Afr. Med. J.* 47, 165–171.
- Zwi, A.B., Reid, G., Londau, S.P., Kielkowski, D., Sitas, F., Becklake, M.R., 1989. Mesothelioma in South Africa, 1976–84 Incidence and case characteristics. *Int. J. Epidemiol.* 18, 320–329.

Exposure to airborne amphibole structures and health risks: Libby, Montana

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Abstract

Libby, Montana is the site of a large vermiculite deposit that was mined between 1920 and 1990 to extract vermiculite for commercial applications such as insulation, gardening products, and construction materials. The Libby vermiculite deposit also contains amphibole minerals including tremolite, actinolite, richterite, and winchite. Historically, Libby mine workers experienced high exposures to amphibole structures, and, as a group, have experienced the health consequences of those occupational exposures. It has been suggested that Libby residents also have been and continue to be exposed to amphibole structures released during the vermiculite mining operations and therefore are at increased risk for disease. The Agency for Toxic Substance and Disease Registry (ATSDR) conducted two epidemiological-type studies of residents living in Libby and the surrounding areas to assess these risks. The Environmental Protection Agency (EPA) collected and analyzed exposure data in Libby and used those data to project risks of asbestos-associated disease for Libby residents. The EPA has placed the Libby Asbestos Site, which includes the mine and the town of Libby, on its National Priority List of hazardous waste sites in need of clean up. This article presents a review of the exposure studies conducted in Libby and an analysis of health risks based on the data collected in those studies. Libby mine workers have experienced elevated levels of asbestos-associated disease as a consequence of their occupational exposures to amphibole structures. Libby residents' exposures typically are substantially lower than mine workers' historical exposures, and the health risk projections for residents are, accordingly, substantially lower.

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Keywords: Libby; Montana; Vermiculite; Amphibole minerals; Asbestos; Asbestos-associated disease

1. Introduction

Libby, Montana gained the attention of the U.S. government health agencies in 1999 when the Seattle Post Intelligencer ran an article by Andrew Schneider titled "A town left to die". The article associated high rates of respiratory disease in Libby with exposure to amphibole particles released into the air from the vermiculite mine located in Libby.

Vermiculite is the mineralogical name given to hydrated laminar magnesium–aluminum–iron silicate that resembles mica in appearance. When subjected to heat, vermiculite has the unusual property of exfoliating or expanding into worm-like pieces. This characteristic of exfoliation is the

basis for commercial use of vermiculite in applications such as insulation, gardening products, and construction materials.

Commercially useful vermiculite is found in Australia, Brazil, China, Kenya, South Africa, the U.S., and Zimbabwe. In the U.S., vermiculite is mined at Enoree, South Carolina and Libby, Montana. The Libby mine, which operated from 1920 to 1990, may have produced as much as 80% of the world's supply of vermiculite.

The Libby vermiculite deposit contains amphibole minerals. It has been suggested that the amphibole component of the ore deposits at the vermiculite mine has unique characteristics that make its potency for asbestos-associated disease different than other asbestos minerals. "Libby Asbestos" (LA), a term coined by the United States Environmental Protection Agency (EPA) and the Agency for Toxic Substance Disease Registry (ATSDR), is a collection

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of amphibole minerals including tremolite, actinolite, anthophyllite, richterite, and winchite. LA is a combination of asbestiform structures (i.e., fibers) and non-asbestiform structures known also as cleavage fragments.

High-level exposure to LA has been associated with various diseases including lung cancer, mesothelioma, asbestosis, and other non-malignant respiratory diseases (McDonald et al., 1986; Amandus et al., 1987a; Amandus and Wheeler, 1987b). This article presents a review of the exposure studies conducted in Libby and an analysis of health risk based on the data collected in those studies. Libby mine workers have experienced elevated levels of asbestos-associated disease as a consequence of their occupational exposures to amphibole particles. Libby residents' exposures typically are substantially lower than mine workers' historical exposures and the health risk projections for residents are, accordingly, substantially lower.

2. Chronology of health studies and regulatory actions in Libby

The vermiculite mining operation in Libby between 1920 and 1990 consisted of ore extraction, processing, and shipping. Until the 1960s, mine workers often were exposed to high levels of LA, which co-existed with the vermiculite ore. In the mid-1980s, W.R. Grace and the National Institute for Occupational Safety and Health (NIOSH) conducted separate epidemiology studies of mine workers to assess health risks associated with exposure to LA in vermiculite mining (McDonald et al., 1986; Amandus et al., 1987a; Amandus and Wheeler, 1987b). ATSDR and EPA initiated studies of respiratory disease among Libby residents in 1999. In 2000, ATSDR released a report describing the results of its study of asbestosis mortality in Libby (ATSDR, 2000). The report stated that the asbestosis mortality rate in Libby was 40–60 times greater than the national average asbestosis mortality rate. During the summer of 2000, ATSDR initiated a medical testing program and Screening Study. ATSDR's report on the Screening Study, released in 2001, stated that Libby residents experienced a high rate of pleural abnormalities (ATSDR, 2002b). Also in 2001, the EPA summarized an exposure analysis it had conducted in Libby stating that exposure to asbestos in Libby constituted an "imminent and substantial endangerment to public health" (Weis, 2001). In 2002, EPA placed Libby on the National Priorities List of the Superfund Program, which established it as a hazardous waste site requiring clean-up. Also in 2002, ATSDR revised its asbestosis mortality study, updated its Screening Study, reported on a pilot study of environmental cases of pleural abnormalities, and issued a Public Health Assessment for vermiculite (ATSDR, 2002a; ATSDR, 2002b; ATSDR, 2002c; ATSDR, 2002d). The studies addressing the rate of pleural abnormalities among Libby residents were summarized and published with comments in Environmental

Health Perspectives (Peipins et al., 2003a,b; Price, 2004). The remainder of this article contains a review of the mine worker and Libby resident studies and regulatory actions concerning Libby. Included are re-analyses of data in order to evaluate concerns about the health risk of low-level environmental exposure to LA.

3. Morphology characterization of LA

LA is a collection of amphibole minerals that have been identified as tremolite, actinolite, soda tremolite, richterite, and winchite (Meeker et al., 2001). A typical sample of LA also contains acicular cleavage fragments. Because LA is a mixture of pure fibers and acicular morphologies, in the remainder of this report LA particles are referred to as structures rather than fibers. The toxicities of the mineral components of LA have not been thoroughly studied. Cleavage fragments, in particular, are at the center of a controversy concerning their toxicity for asbestos-associated disease. Currently, The Occupational Safety and Health Administration (OSHA), excludes cleavage fragments from the mineral fibers it regulates under its asbestos exposure standard (57 FR 24310). The relative toxicity of cleavage fragments, which tend to be thicker and shorter than fibers, although uncertain, is generally considered to be less than the asbestiform analogue (Ilgren, 2004; Davis et al., 1991; Wylie et al., 1993; ATS, 1990). Notwithstanding the specific toxicity uncertainties associated with cleavage fragments, it is generally accepted that inhalation of long, thin fibers (longer than 5 μm with diameters less than 0.50 μm) have greater potential to cause disease than shorter, thicker fibers (ATSDR, 2003a; EPA, 2003).

Table 1 contains a summary of data concerning the size distribution of LA. Amandus et al. (1987a) summarized lengths and widths separately based on light microscopy inspection of 599 LA structures collected in air samples. Amandus reported results only for structures longer than 5 μm and thicker than 0.45 μm . Seventy four percent (74%) of the structures were longer than 10 μm , 11% were longer than 40 μm , and 93% had diameters between 0.45 and 0.90 μm . McDonald et al. (1986) provides preliminary results of an electron microscopy study to characterize the structure size distribution of LA conducted by the Institute of Occupational Health and Safety at McGill University. McDonald's results indicate that 62% of LA structures were longer than 5 μm . Additional results from McGill based on three air samples confirm McDonald's result (McGill University, 1983). Ten percent (10%) of the structures were longer than 20 μm and 73% were thinner than 0.50 μm . The McGill data also provides information about the two-dimensional distribution of structures. Focusing on structures no thicker than 0.50 μm , 38.9% were longer than 5 μm ; 13.1% were longer than 10 μm ; and 2.7% were longer than 20 μm .

ADL (1983) used electron microscopy to determine the percentage of structures typically counted by light micros-

Table 1
Fiber sizes: asbestos from the Libby vermiculite mine^a

Phase contrast microscopy (PCM)		Transmission electron microscopy (TEM)					
Amandus et al., 1987a,b		McDonald et al., 1986		McGill University, 1983 ^b		ADL, 1983	
Length	Percent	Length	Percent (%)	Number	Percent (%)	Number	Percent (%)
<5.0	N/A	<5.0	38	80	36	N/A	N/A
5–10	27%	5–10		82	37	93	46
10–20	37%	10–20	62	38	17	85	42
20–40	26%	20–40		17	8	21	10
>40	11%	>40		4	2	2	1
Width		Width					
<0.25	N/A	<0.25		86	39	56	28
0.25–0.45	N/A	0.25–0.50		76	34	95	47
0.45–0.90	93%	0.50–0.90	100	33	15	37	18
0.90–1.25	5%	0.90–1.25		10	5	10	5
1.25–2.00	2%	1.25–2.00		16	7	3	1
>2.00		>2.00	0	0	0	0	0

^a The samples underlying these data were not collected according to a formal statistical design. Therefore, the data are not necessarily representative of LA and should be interpreted only as information about the size distribution of LA, but not as a formal characterization of the size distribution.

^b Width frequencies are approximations.

copy that were tremolite. The results, based on analysis of two samples, indicate that 50–75% of optically visible structures were tremolite. ADL also reported the structure size distribution. However, the ADL results cannot be compared to the McGill results because ADL did not include counts of structures shorter than 5 μ m.

Recently, air sampling was conducted in Libby to determine the potential LA exposures of Libby residents. Brattin (2002) and RJ Lee Group (2002) discuss the structure size distribution of these data. The air samples were collected: (1) at the location of a former export/screening plant; (2) in residential and commercial properties; and (3) from attics with vermiculite attic insulation (Brattin, 2002). Based on average length, width, and aspect ratio, Brattin (2002) concludes that current samples of LA have the same structure size distribution as samples collected when the mine was operating. The RJ Lee Group (2002) analysis indicates that a high percentage of the current airborne structures, possibly 80%, are cleavage fragments.

Information about LA structure type and size distributions is important in estimating exposure and risk for Libby residents. The scientific literature indicates that cleavage fragments are most likely less carcinogenic than asbestos fibers, and short structures (e.g., lengths less than 5 μ m) are less carcinogenic than long, thin fibers (Ilgren, 2004; ATSDR, 2003b; EPA, 2003; Wylie et al., 1993; OSHA, 1992). Based on available data, LA appears to consist of amphibole minerals in many size ranges including long, thin amphibole structures. Therefore, environmental exposures, if sufficiently high, could increase the risk of disease for Libby residents.

4. Epidemiology studies of Libby mine workers

Two retrospective epidemiological studies of Libby mine workers have been conducted (McDonald et al., 1986;

Amandus et al., 1987a; Amandus and Wheeler, 1987b) to assess the risk of asbestos-associated disease from LA. Recently, McDonald reported results on an update of his study that included the vital status of the worker cohort through 1999 (McDonald, 2001; McDonald et al., 2002, 2004).

The Amandus and McDonald studies differ in three respects that may affect interpretation of the results. First, McDonald's cohort consisted of 406 workers versus 575 workers in the Amandus study. Second, McDonald's follow-up period continued through December 31, 1999, which accounted for 285 deaths among the 406 cohort members. Amandus followed workers through December 31, 1981, which accounted for 161 deaths among 575 cohort members. Finally, McDonald's external reference group for standard mortality ratio (SMR) calculations was white males in Montana. Amandus used white males in the U.S as the external reference group for SMR calculations.

SMRs indicated excess lung cancer and excess non-malignant respiratory disease (NMRD) in both studies. The SMRs from the two studies are not directly comparable because the two studies used different external reference groups to determine the numbers of expected cases. Exposure-response analyses of these data restricted to subjects with latency greater than 20 years (i.e., time since hire greater than 20 years), discussed below, show the excess in lung cancer occurs primarily at the higher exposure levels.

Mesothelioma cases were observed in both studies. Amandus recorded 2 cases. The proportional mortality ratio (PMR) for the Amandus cohort was 1.2%. Based only on deaths for workers with latency greater than 20 years, the PMR was 2.2%. Amandus stated that the minimum exposure for the mesothelioma cases was 300 f-yr/cc. McDonald recorded 12 mesotheliomas for a PMR equal to 4.2%. The average exposure for these 12 cases was 48.1 f-yr/cc.

4.1. Lung cancer

This section describes an investigation of the relationship between LA exposure and lung cancer risk. The data reported by Amandus and Wheeler (1987b) and McDonald et al. (McDonald et al., 1986; McDonald, 2001; McDonald et al., 2002) have been used to re-estimate the relationship between lung cancer risk and exposure, and to expand upon the interpretation of the results that the authors reported.

4.1.1. Lung cancer risk models

McDonald et al. (1986) and Amandus and Wheeler (1987b) use a linear risk model for lung cancer identical to the model employed by EPA. In this model, SMR, which is the ratio of observed lung cancer cases (O) in the cohort to the expected number of cases (E) based on an appropriate reference population, is represented as a linear function of lifetime cumulative exposure (f-yr/cc). E , also referred to as the background rate of lung cancer, varies with age, sex, and smoking history. The model may have one or two parameters. The principal parameter is K_L , referred to as the “slope” parameter, which measures the potency of asbestos for lung cancer. The role of K_L is shown in the single parameter model Eq. (1):

$$\text{SMR} = 1 + K_L \cdot (\text{f-yr/cc}). \quad (1)$$

In this one-parameter version of the model, if the asbestos exposure level is zero, SMR is equal to 1.0. Using Eq. (1) and the definition of SMR, the incremental number of lung cancer cases associated with exposure to asbestos is: $I = E \cdot K_L \cdot (\text{f-yr/cc})$.

The two-parameter version of this model allows for differences between the study cohort and the external reference group in lung cancer risk factors other than asbestos exposure. The two-parameter model may be stated either as:

$$\text{SMR} = \alpha + K_L \cdot (\text{f-yr/cc}); \quad (2)$$

or

$$\text{SMR} = \alpha \cdot [1 + K_L \cdot (\text{f-yr/cc})]. \quad (3)$$

In both forms of the model, α measures the difference in lung cancer mortality between the internal control group (i.e., study cohort members who were not exposed to asbestos) and the external reference group. For example, if the only lung cancer risk factor in addition to asbestos exposure were smoking, α measures the difference in smoking effect between the study cohort and the external reference group.

In EPA (1986), the relationship between lung cancer and exposure was analyzed using Eq. (2) for a number of different epidemiology studies.¹ EPA used the results to develop the lung cancer component of the quantitative risk assess-

ment published in its Integrated Risk Information System (IRIS).² Berman and Crump (2003), working with EPA's Superfund Program, updated the asbestos lung cancer risk analysis using Eq. (3).

The Amandus and McDonald data, which are displayed in Fig. 1, were used to estimate each of the three alternative models. Fig. 1 includes 99% confidence limits for the SMRs for each exposure category. The plots show that although SMR has an increasing trend with exposure, the increase is determined principally by the highest exposure group. In addition, the increase in lung cancer due to asbestos exposure is not statistically significant for the low exposure categories. The parameter estimates for the three models are summarized in Table 2 and discussed below.

4.1.2. Amandus study

As indicated in Table 2, each of the three models provides an adequate description of the Amandus data (i.e., deviance p -value greater than 0.05). Based on the value of α in Models 2 and 3, which has a value less than 1.0, the internal control group appears to have fewer lung cancer cases than the external reference group. The range of asbestos potency for lung cancer, K_L , based on the Amandus data is 0.006–0.0077 (f-yr/cc)^{−1}. These values are less than, but near, the asbestos potency value EPA currently employs in its asbestos risk assessment, 0.01 (f-yr/cc)^{−1} (EPA, 1986).

The parameter estimates obtained with the Amandus data also were used to provide additional interpretation of the relationship between LA exposure and lung cancer. The exposure level required to double lung cancer risk versus the external reference group and the incremental risk of lung cancer associated with LA exposure to 25 f-yr/cc were calculated. The “risk-doubling” exposures all exceed 150 f-yr/cc. The incremental risk associated with 25 f-yr/cc is less than 0.20.

4.1.3. McDonald study

The results in Table 2 indicate that EPA's primary lung cancer model Eq. (1) is not consistent with McDonald's data (p -value less than 0.05). The results for Models 2 and 3 indicate an excess of lung cancer cases among the internal controls relative to the external reference group. McDonald used Montana white males as the external reference group. Models 2 and 3 provide an adequate representation of the data. It is not possible to differentiate statistically between Model 2 and Model 3, however, Model 1 does not fit the data. The results for models 2 and 3 suggest a potency value less than 0.006, which is less than EPA's potency value of 0.01 used to develop its IRIS risk assessment in 1986. The “risk doubling” exposures calculated from these models are not meaningful because the

¹ The Libby mine worker data were not included in EPA's 1986 report.

² The quantitative risk relationship in the IRIS asbestos file addresses total cancer risk (i.e., the sum of lung cancer and mesothelioma risks).

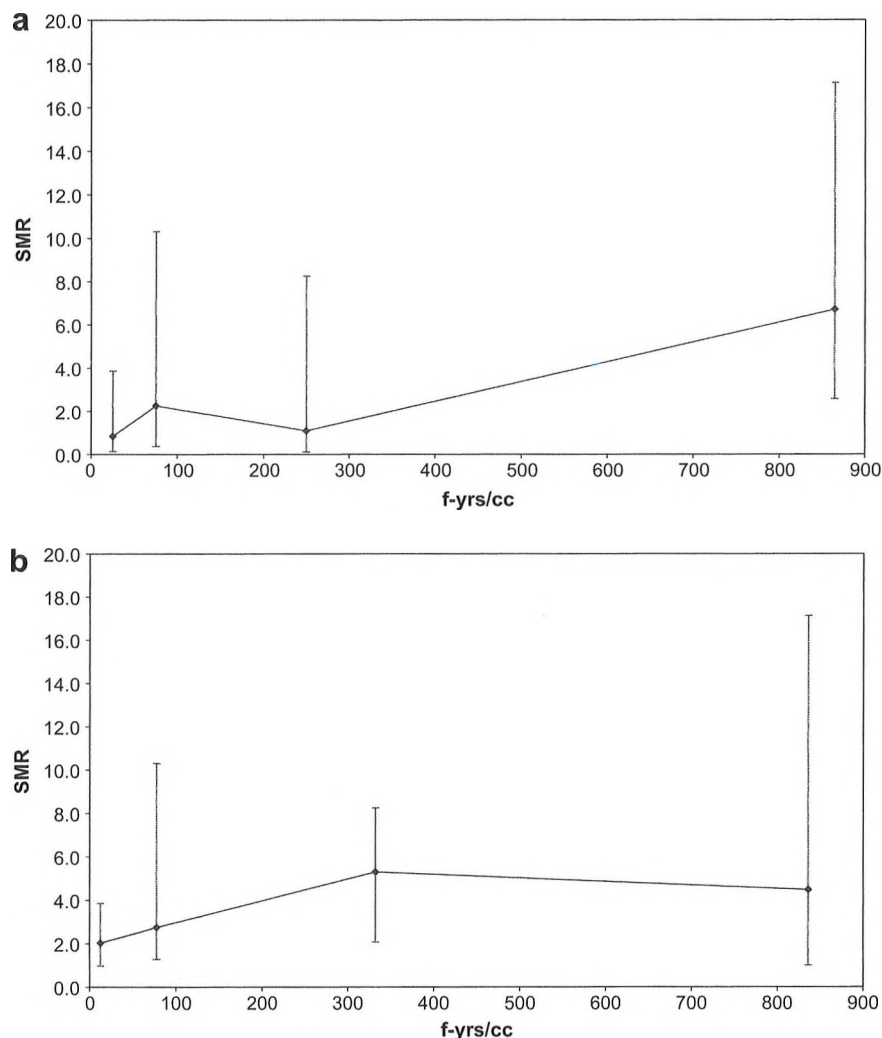


Fig. 1. Lung cancer SMR and 99% confidence limits: (a) Libby Miners (Amandus, 1987b) and (b) Libby Miners (McDonald, 2001).

internal controls have a lung cancer risk greater than two times the reference group risk. The incremental lung cancer risk associated with exposure to 25 f-yr/cc is less than 0.14.

4.1.4. Lung cancer summary of Libby mine worker studies

Based on a linear exposure–response assumption, data published by Amandus and McDonald estimate LA unit risk for lung cancer between $0.0025 \text{ (f-yr/cc)}^{-1}$ and $0.0077 \text{ (f-yr/cc)}^{-1}$. McDonald et al. (2004) includes an estimate of Model 1 based on miner cohort follow-up data through 1999. The estimate of unit risk for these data was 0.0036.³ These values are less than the unit risk employed by EPA in its IRIS risk assessment. Therefore, following the EPA risk assessment approach, LA is not more potent for lung cancer than other asbestiform amphiboles.

³ This unit risk factor was statistically different from zero (p -value = 0.02). McDonald applied Poisson regression to estimate the unit risk factor. The data used by McDonald were not available for re-analysis.

4.2. Mesothelioma

Data concerning mesothelioma reported in the two epidemiology studies are insufficient to estimate risk models that could be used to assess the relative potency of LA for mesothelioma. Amandus and McDonald report mesotheliomas among the study cohorts. Amandus and Wheeler (1987b) found two mesothelioma cases for a proportional mortality ratio (PMR) of 1.2%. McDonald (McDonald, 2001; McDonald et al., 2002, 2004) found 12 mesotheliomas (PMR = 4.2%). As expected, due to the relatively high exposure levels experienced by mine workers, these PMRs are substantially larger than the U.S. male PMR for mesothelioma. Based on SEER data for the year 2000, the estimated U.S. PMR for male mesothelioma is approximately 0.2%.

Amandus and Wheeler (1987b) stated that both cases he reported had exposures that exceeded 300 f-yr/cc. Cumulative exposure for 11 of the 12 mesotheliomas reported by McDonald had exposures exceeding 11.7 f-yr/cc. McDonald reports exposure for the remaining mesothelioma case as a range between zero and 8.6 f-yr/cc.

Table 2

SMR versus exposure for Libby vermiculite miners: summary of regression modeling

Study	Model	α	Slope (K_L)	Deviance p -value	Exposure level for SMR = 2.0 (f-yr/cc)	Contribution to SMR due to asbestos exposure of 25 f-yr/cc
Amandus et al. (1987a,b)	Model 1	1.00	0.0058	0.22	173	0.14
Amandus et al. (1987a,b)	Model 2	0.85	0.0060	0.50	192	0.15
Amandus et al. (1987a,b)	Model 3	0.81	0.0077	0.50	155	0.19
McDonald (2001)	Model 1	1.00	0.0108	<0.01	93	0.27
McDonald (2001)	Model 2	2.15	0.0055	0.51	N/A	0.14
McDonald (2001)	Model 3	2.16	0.0025	0.51	N/A	0.06

Note. Model 1—Eq. (1): $SMR = 1 + K_L \cdot (f\text{-yr/cc})$.

Model 2—Eq. (2): $SMR = \alpha + K_L \cdot (f\text{-yr/cc})$.

Model 3—Eq. (3): $SMR = \alpha \cdot [1 + K_L \cdot (f\text{-yr/cc})]$.

p -value: A p -value greater than 0.05 indicates an adequate fit to the data.

N/A: The data indicate that lung cancer incidence for the internal controls was more than double the incidence for external controls, therefore the calculation provides no information.

The range of cumulative exposures for the mesothelioma cases is particularly significant for assessing mesothelioma risk for Libby residents. EPA has estimated lifetime cumulative exposures to LA for Libby residents for various activities. The maximum of these lifetime cumulative exposures is 0.04 f-yr/cc (Ref. Table 8 and Weis, 2001, 2002).⁴ No broadly accepted threshold exposure limit for mesothelioma exists that could be used to evaluate the significance of exposures of 0.04 f-yr/cc.⁵ However, Price and Ware (2004), based on mesothelioma incidence trends in the U.S., argue that such a threshold exists, and, in addition, suggest a background risk level for mesothelioma (i.e., the risk of mesothelioma absent exposure to asbestos). The lowest exposure among the Libby mine worker mesothelioma cases suggested by the McDonald data, the midpoint of the exposure range for the lowest exposure group, 4.3 f-yr/cc, is a candidate for the mesothelioma exposure threshold for LA. However, the size of the Libby mine worker cohort is insufficient to adopt this value for all risk management purposes. Ambient exposure for an 80-year lifetime would be an extremely conservative lower bound for the mesothelioma exposure threshold. If the long-term average ambient concentration of asbestos were 0.005 f/cc, lifetime cumulative exposure would be 0.40, 10 times greater than the maximum lifetime cumulative exposure projected for a Libby resident (Ref. Table 8). In addition, if EPA's current risk assessment methodology (EPA, 1986) were used to estimate lifetime risk of mesothelioma for the maximally exposed resident of Libby, the risk would be 1.1×10^{-4} , less than the background risk of

mesothelioma estimated by Price and Ware (2004).⁶ Therefore, by any reasonable assessment, the likelihood of mesothelioma for the maximally exposed resident of Libby would be negligible.

5. ATSDR health consultation

In December 2000, ATSDR, in cooperation with the Montana DPHHS, released an analysis of mortality in Libby–Montana for the years 1979–1998 (ATSDR, 2000). The analysis, based on a review of death certificate data, was conducted to develop information about mortality potentially associated with asbestos exposure in Libby. Six geographic boundaries with increasing areas were used for the analysis. The smallest area was Libby city limits—1.1 square miles. This area was increased in steps to the final area, central Lincoln County—a 314-square mile circular area with a 10-mile radius centered in downtown Libby. Each decedent was classified into an area and SMRs were calculated for each area. The study population initially consisted of 419 decedents. ATSDR updated the study (ATSDR, 2002a) by adding death certificates for decedents that would have been included in the initial analysis if they had been discovered during the initial search. The revision analyzed data for 542 decedents and provided a clearer picture of causes of mortality than the initial report.

The initial report stated that mortality due to asbestosis in Libby was 40–80 times greater than expected. The report failed to mention that virtually all the asbestosis deaths, as well as other deaths associated with asbestos, were found

⁴ Air samples were analyzed by electron microscopy. A structure was included in the count only if it was longer than 5 μm , thicker than 0.25 μm , had an aspect ratio of at least 3:1, and was asbestos. This counting protocol has the same structure dimension criteria as the standard measurement method based on Phase Contrast Microscopy (PCM) used by OSHA. The method, which includes only asbestos structures, is referred to as Phase Contrast Microscopy Equivalent (PCME).

⁵ "Threshold," as it is used in this article, means an exposure level where the probability of incremental mesotheliomas is small enough to characterize the risk as negligible.

⁶ Price and Ware (2004) estimate background lifetime mesothelioma risk between 3 and 4 per 10,000 (3.4×10^{-4}). Mesothelioma risk based on the EPA method was calculated from Table 7 in EPA (1986). The table evaluates risk based on lifetime average daily exposure equal to 0.01 f/cc. Exposure for the maximally exposed Libby resident is 0.04 f-yr/cc divided by 70 years (assumed lifetime for these calculations). The result, 5.7×10^{-4} , was applied to the first row in the table for males (exposure beginning at birth and continuing for a lifetime). The risk, 1.1×10^{-4} , was calculated as $(5.7 \times 10^{-4}/0.01) \times 192.8 \times 10^{-5}$.

among former workers at the Libby mine. This information is critical input for risk management decisions and public policy because it indicates the excess mortality due to asbestos exposure occurred in an occupational group that experienced extremely high asbestos exposures. Such a result is not unexpected. Absent this information, a reader of the ATSDR report would be likely to conclude that all residents of Libby, not only the group of mine workers who experienced high levels of occupational exposure to asbestos, were at increased mortality risk based simply on being a resident of Libby. A discussion of ATSDR's principal results follows.

5.1. Asbestosis

Asbestosis mortality in Libby was 40 times greater than expected in comparison to the state of Montana reference population, and 80 times greater than expected when compared to the U.S. reference population. These results were based on 12 asbestosis deaths; 11 were males previously employed in the Libby mine. The remaining one female was a household contact of a former mine worker who was employed at the mine for 20 years (ATSDR, 2001). The high multiples of asbestosis deaths relative to the number of asbestosis deaths expected in the reference populations are misleading. The mine workers would have experienced high exposures to asbestos over extended time periods whereas the average inhabitant, whether of Montana or the U.S., would most likely have only background asbestos exposure. It is unclear how the household contact would have experienced exposures high enough to cause asbestosis. A threshold exposure for asbestosis between 25 f-yr/cc and 100 f-yr/cc has been suggested (Churg and Green, 1998; EPA, 1986). Therefore, the correct interpretation of the asbestosis mortality rates reported by ATSDR should be—a typical resident of Libby or its surrounding areas who was not a mine worker would not be at increased risk of death due to asbestosis.

5.2. Lung cancer

The ATSDR results show a statistically significant excess of lung cancer for males relative to the male Montana population, but not relative to the male U.S. population. Females showed no statistically significant excesses relative to either reference group.

The statistically significant excess for males would be misleading if it were interpreted as a characterization of lung cancer for typical Libby residents for a number of reasons. First, the primary cause of lung cancer is smoking and no data were analyzed to adjust for smoking. Second, females, because they typically did not work at the mine, would provide the best information on lung cancer risk for Libby residents with environmental exposure to LA. Females showed no statistically significant excess of lung cancer relative to either of the reference populations. Third, 21 lung cancer decedents were formerly mine employees.

These decedents would have had occupational exposures to LA. To properly judge the impact of asbestos-associated lung cancer risk for Libby residents, it would be appropriate to exclude these workers from the risk calculations. Although the ATSDR report does not indicate the number of males and females among these 21 decedents, it is reasonable to expect that they were all male. Assume that all were male and the age distribution of this group of former mine workers was approximately the same as the age distribution of the total group of male lung cancer decedents. Then, after excluding these 21 workers from the risk calculations for males, the resulting SMRs do not indicate statistically significant excesses of lung cancer (ATSDR, 2002a, Tables 7 and 8).

6. Medical testing and Screening Study

In July 2000, ATSDR initiated a medical testing program for Libby residents. Testing was conducted from July to November 2000, and again during the summer of 2001. Participation was voluntary. Subjects either were recruited directly by ATSDR or responded to media advertising. The medical tests included a three-view chest radiograph—posterior–anterior (P–A), right anterior oblique, and left anterior oblique—and a spirometry test. Subjects eligible for testing included former WRG mine workers, and people who had lived, worked, or played in Libby for at least 6 months prior to December 31, 1990. The principal goal of the testing program was to identify asbestos-associated health effects of subjects exposed to asbestos from the mine and, where indicated by the test results, refer them for further medical evaluation. Each subject's test results were evaluated by an on-site radiologist, who determined if a follow-up evaluation was warranted.

ATSDR combined the testing program with a statistical analysis, referred to as a Screening Study, to investigate relationships between radiographic abnormalities and exposure to LA from the mine. Each X-ray film was interpreted by two or three radiologists certified as B-readers,⁷ who focused on identifying pleural and interstitial abnormalities. ATSDR classified a subject as a pleural "case" if pleural abnormalities were identified by at least two B-readers using a combination of the oblique and P–A views. An interstitial "case" required at least two B-readers to identify an interstitial abnormality using the P–A view. In addition, ATSDR conducted in-person interviews to obtain demographic and health-related information including age, sex, weight, height, residential history, occupational history, recreational activities and other potential vermiculite-LA exposure pathways, smoking status, medical history (e.g., chest injury or surgery), and self-reported symptoms and illnesses.

⁷ Every film was evaluated by at least two B-readers. A third B-reader was employed only if the first two B-readers disagreed on the presence of a pleural abnormality.

In August 2001, ATSDR released a report about the Screening Study that covered results for the first round of testing (6149 subjects). The report described various statistical analyses relating pleural abnormalities to asbestos exposure pathways and potential confounders. ATSDR has not updated its statistical analysis to include results for the 1158 additional subjects during the summer of 2001. Instead, the Agency issued a brief summary of results in September 2002 that covered all subjects who had recent X-rays (ATSDR, 2002b). ATSDR's results included:

- 1186 of the 6668 subjects with chest X-rays (17.8%) had pleural abnormalities.
- The prevalence of pleural abnormalities was highest in WR Grace workers (51%).
- Most subjects reported multiple routes of exposure (household contact, occupational, recreational, and other) and the prevalence of pleural abnormalities increased with the number of exposure pathways.
- 6.7% of the subjects who reported no asbestos exposure pathways had pleural abnormalities.
- Factors associated with higher rates of pleural abnormalities identified through statistical modeling and analysis included: being a WR Grace worker; having household contact with a WR Grace worker; military asbestos exposure; increasing age; being male; smoking; duration of residence in Libby; played in vermiculite piles; higher Body Mass Index.

ATSDR determined the percentage of pleural abnormalities among medical testing participants, 17.8%, and the percentage of participants with pleural abnormalities who claimed no identifiable exposure to asbestos, 6.7%. ATSDR also reported a range of background pleural abnormality rates from other regions of the U.S., 0.02–2.3%. Although not explicitly stated, ATSDR tacitly implied through the juxtaposition of these rates that residence in Libby was a significant risk factor for asbestos-associated pleural disease.

ATSDR's implied conclusion is questionable for two reasons. First, the majority of pleural cases are former mine workers or others who, due to their special activities, were likely to have experienced high level exposures to asbestos. These subjects make up a significant fraction of the 17.8% cases reported by ATSDR, but they are not typical of the majority of residents of Libby. Second, another fraction of the 17.8% may have been identified as cases due to errors in interpreting X-ray films. The potential for misreading pleural fat as a pleural abnormality on X-rays is well documented (Sargent et al., 1984; Proto, 1992; ATSDR, 2003a). Errors of this type may be a contributing factor to the relatively high rate of pleural abnormalities reported for subjects in the Screening Study. In addition, defects in the study design, including the absence of control films and the fact that readers were aware that every film belonged to a subject who had lived in Libby, lead to other potential biases that favor positive diagnoses even where

radiographic evidence may not be conclusive. Using a data file prepared by ATSDR that contained the screening data, we investigated: (1) the correlation between LA exposure levels and employment at the mine and (2) factors that play a role in misdiagnosis of pleural abnormalities.

6.1. Asbestos exposure levels

Frequencies and percentages of pleural abnormality diagnoses were compiled for three exposure groups:

- Group 1.* Participants who were employed by WRG at the Libby mine;
- Group 2.* Participants who were not employed at the Libby mine, but either had other occupational exposures or domestic exposures⁸; and
- Group 3.* Participants who had neither occupational nor domestic exposures (also referred to as environmental exposures).

The results are shown in Table 3. Group 1 had the largest percent of pleural cases (51.0%), followed by Group 2 (19.9%), and Group 3 (9.1%). Overall, of the 1186 pleural abnormality cases reported by ATSDR, 971 (81.9%) were in the first two exposure groups—mine workers and other occupationally and domestically exposed participants. These results indicate a correlation between the prevalence of pleural abnormalities and asbestos exposure. Former mine workers, Group 1, would have experienced occupational exposures that were substantially higher than exposures in the other groups. The exposure levels for Group 2, other occupational exposure and domestic exposure, would be expected to be lower as a group average than mine workers' exposures. Group 3 exposures would have been much lower than Group 1 or Group 2 exposures.

These data not only indicate a correlation between pleural abnormalities and asbestos exposure, but also suggest that the prevalence of pleural abnormalities associated with low-level environmental exposures (Group 3) is near the internal background rate, 6.7%, for the Screening Study. These findings, however, may be strengthened or weakened depending on the rate of false positive diagnoses, which may be substantial. The following sections describe analyses of the data that address the false positive issue.

6.2. Adipose tissue and detection of pleural abnormalities

6.2.1. The "FAT?" box on B-reader forms

As a partial solution to misreading sub-pleural fat as pleural thickening or a pleural plaque, the B-reader forms used in the Screening Study included a section for commenting on pleural fat. This section contains a box labeled "FAT?" that provides B-readers with an opportunity to

⁸ Domestic exposure occurred where a participant, such as a spouse, shared living quarters with a mine worker and cared for his work clothes.

Table 3

Radiographic identification of pleural abnormalities for three exposure groups in the ATSDR Screening Study in Libby, Montana

	Pleura diagnosis				Total
	Abnormal		Normal		
	Number	Percent (%)	Number	Percent (%)	
Group 1: employed by WRG at the Libby Mine	186	51.0	179	49.0	365
Group 2: other occupational or domestic exposure ^a	785	19.9	3151	80.1	3936
Group 3: no occupational or domestic exposure	215	9.1	2152	90.9	2367
Total	1186	17.8	5482	82.2	6668

^a "Other Occupational" means occupational exposure, but not at the Libby mine. "Domestic Exposure" means exposure of a spouse or other household contact of an individual with occupational exposure.

Table 4

B-reader "Fat?" breakdown for the ATSDR Screening Study in Libby, Montana—all readers

"FAT?" box checked	B-reader forms that identify pleural abnormalities	
	Number	Percent (%)
Yes	893	36.2
No	1574	63.8
Total	2467	100.0

Note. The final category on the B-reader form was labeled "FAT?". A check mark in this box indicated the reader's concern that the abnormalities identified on the form also may be explained by pleural fat.

record their concerns that the observed abnormalities may be explained alternatively as adipose tissue.

Tables 4 and 5 contain a summary of the "FAT?" box results. Table 4 displays results for all B-reader evaluations that indicated a pleural abnormality. Although agreement between two readers led to 1186 pleural cases, a total of 2467 B-reader evaluations identified pleural abnormalities. Of these 2467 evaluations, 893 (36.2%) included a check in the "FAT?" box. Limiting this analysis to the 1186 cases, the "FAT?" box was checked by at least one of the B-readers for 399 subjects, or 28.6% (Table 5). These results suggest that the false positive rate for pleural abnormalities in the Screening Study population may be near 30%.

Table 6 shows that the correlation between sub-pleural fat and a positive diagnosis for pleural abnormalities exists in each of the three exposure groups defined earlier. The data show that the percentage of cases with "FAT?" checked is lowest for mine workers (18.3%) compared to slightly greater than 30% for the other exposure groups. This differential is expected because the mine workers would have had the highest asbestos exposures and, therefore, would have

Table 5

B-reader "Fat?" breakdown for the ATSDR Screening Study in Libby, Montana—cases

"FAT?" box checked	Pleural abnormality cases	
	Number	Percent (%)
Yes (by at least one B-reader)	339	13.7
No	847	34.3
Total	1186	48.1

See note to Table 4.

experienced a higher percentage of pleural abnormalities that should not have been confused with sub-pleural fat.

6.2.2. Correlation between Body Mass Index and pleural abnormalities

A further assessment of the potential for pleural fat as a source of false positive diagnoses involved investigating the relationship between Body Mass Index (BMI)⁹ and the diagnosis of pleural abnormalities for the three exposure groups introduced above.

For each exposure group, Table 7 displays the number and percent of positive and negative diagnoses by BMI category—obese, overweight, normal, and underweight.¹⁰ For Group 1, WRG mine workers, there is no correlation between BMI and the diagnosis. The percentages of subjects in each BMI category are statistically the same for those diagnosed with pleural abnormalities as those diagnosed as normal (p -value = 0.86).

For Group 2, which consists of subjects with other occupational and domestic exposure, BMI is correlated with the diagnosis outcome (p -value < 0.001). A larger percentage of BMI-obese subjects have positive diagnoses in comparison to negative diagnoses (48.5% versus 30.2%) and a smaller percentage of BMI-normal subjects have positive diagnoses in comparison to negative diagnoses (13.8% versus 29.3%).

For Group 3, which consists of subjects with no occupational and no domestic exposure, BMI also is correlated with diagnosis (p -value < 0.001). The pattern of percentages for the BMI categories is similar to the pattern for Group 2: 51.2% of BMI-obese subjects have positive diagnoses versus 30.8% with negative diagnoses; 18.1% of BMI-normal subjects have positive diagnoses versus 33.5% with negative diagnoses.

The results in Table 7 suggest that body mass, absent high level exposures to asbestos, influences positive pleural

⁹ Calculated values of BMI were not included in the electronic database received from ATSDR. The height and weight data recorded for each participant was used to calculate BMI. According to the Centers for Disease Control and Prevention, BMI = (weight in kilograms)/(height in meters)².

¹⁰ The BMI categories are defined as follows: obese—BMI greater than 30; overweight—BMI between 25 and 30; normal—BMI between 18.5 and 25; underweight—BMI less than 18.5 (CDC).

Table 6

B-reader "Fat?" breakdown for the ATSDR Screening Study in Libby, Montana by exposure group—pleural abnormality cases

"FAT?" box checked		Exposure group			Total
		1	2	3	
Yes (by at least one B-reader)	Count	34	236	69	339
	Percent	18.3%	30.1%	32.1%	28.6%
No	Count	152	549	146	847
	Percent	81.7%	69.9%	67.9%	71.4%
Total		186	785	215	1186

Notes. Exposure Group 1—WRG mine workers.

Exposure Group 2—other occupational exposure or domestic exposure (i.e., living in the household of an occupationally exposed subject).

Exposure Group 3—environmental exposure (i.e., no occupational or domestic exposure).

Table 7

Correlation between radiographic identification of pleural abnormalities and body mass in the ATSDR medical testing program for Libby, Montana

BMI	Pleural abnormality		Pleura normal	
	Number	Percent (%)	Number	Percent (%)
<i>Group 1: worked at WRG = 365</i>				
Obese	76	40.9	66	36.9
Overweight	74	39.8	72	40.2
Normal	34	18.3	38	21.2
Underweight	0	0.0	0	0.0
BMI N/A	2	1.1	3	1.7
Total	186	100.0	179	100.0

Test result: no correlation between BMI and identification of pleural abnormality

Chi square 0.8

p-value 0.86*Group 2: other occupational or domestic exposure = 3936*

Obese	381	48.5	951	30.2
Overweight	281	35.8	1238	39.3
Normal	108	13.8	923	29.3
Underweight	7	0.9	23	0.7
BMI N/A	8	1.0	16	0.5
Total	785	100.0	3151	100.0

Test result: statistically significant correlation between BMI and identification of pleural abnormality

Chi square 123.0

p-value < 0.001*Group 3: no occupational or domestic exposure = 2367*

Obese	110	51.2	663	30.8
Overweight	60	27.9	726	33.7
Normal	39	18.1	720	33.5
Underweight	1	0.5	32	1.5
BMI N/A	5	2.3	11	0.5
Total	215	100.0	2152	100.0

Test result: statistically significant correlation between BMI and identification of pleural abnormality

Chi square 43.1

p-value < 0.001

abnormality diagnoses. For mine workers, there is no difference in the distribution of BMI between those diagnosed with pleural abnormalities and those diagnosed as normal. This result is consistent with the hypothesis that pleural abnormalities in mine workers are principally a consequence of high asbestos exposure levels. However, in the

two other exposure groups, where asbestos exposure was likely to have been much lower, the group diagnosed as positive has a higher percentage of obesity than the group diagnosed as normal. These data suggest that higher Body Mass Index influences the pleural abnormality diagnoses in a way that could engender false positives.

Table 8
Estimated cumulative lifetime exposure and IRIS risk estimates for Libby residents

Estimated cumulative lifetime exposures and IRIS risk estimates for E1001 residents							
Description		PCM			PCME		
		Average level (f/cc)	Estimated lifetime cumulative exposure (f-yr/cc)	EPA IRIS risk	Average level (f/cc)	Estimated lifetime cumulative exposure (f-yr/cc)	EPA IRIS risk
<i>Scenario 1</i>							
Routine activity	Ave	0.0040	0.1023	3.4×10^{-04}	0.0001	0.0026	8.4×10^{-06}
Resident	Max	0.0140	0.3580	1.2×10^{-03}	0.0010	0.0256	8.4×10^{-05}
<i>Scenario 2</i>							
Routine cleaning	Ave	0.0900	0.0411	1.4×10^{-04}	0.0050	0.0023	7.5×10^{-06}
Resident	Max	1.0170	0.4644	1.5×10^{-03}	0.0930	0.0425	1.4×10^{-04}
<i>Scenario 3</i>							
Remodeling	Ave	0.4543	0.0249	8.2×10^{-05}	0.2380	0.0130	4.3×10^{-05}
Resident	Max	1.6200	0.0888	2.9×10^{-04}	0.7040	0.0386	1.3×10^{-04}
Contractor	Ave	0.4543	0.2489	8.2×10^{-04}	0.2380	0.1304	4.3×10^{-04}
	Max	1.6200	0.8877	2.9×10^{-03}	0.7040	0.3858	1.3×10^{-03}
<i>Scenario 4</i>							
Rototilling	Ave	0.1136	0.0083	2.7×10^{-05}	0.0332	0.0002	8.0×10^{-06}
Resident	Max	0.2272	0.0166	5.5×10^{-05}	0.0664	0.0049	1.6×10^{-05}

Source: Average level (f/cc) from Weis (2001, 2002).

Estimated cumulative lifetime exposure and EPA IRIS risk calculated by PAI using factors provided in Weis (2001).

7. EPA exposure and risk analysis

In 2002, EPA added the Libby Asbestos Site to the General Superfund Section of the National Priorities List (NPL), which established Libby as a hazardous waste site requiring clean-up (67 FR 65315 October 24, 2002). As part of the support for the NPL listing, EPA conducted an analysis of exposure and risk for Libby residents and concluded that "... asbestos contamination in various types of source materials at residential and commercial areas in and around the community of Libby, Montana" poses "... an imminent and substantial endangerment to public health" (Weis, 2001).

The analysis was based on air samples collected by EPA associated with four types of activities referred to as Scenarios 1–4. The activities were: Scenario 1—routine activities by a resident; Scenario 2—active cleaning by a resident; Scenario 3 (two parts) a—extensive contact with vermiculite by a contractor, and b—limited contact with vermiculite by a resident; Scenario 4—rototilling a home garden by a resident.¹¹

Exposure estimates and risk calculations for the scenarios are displayed in Table 8. The design used for collecting the data was not sufficiently detailed to claim that the results are representative of exposures for Libby residents. Therefore, interpretation and projections based on these results are speculative at best. Nevertheless, EPA argued that the results supported a finding of imminent and substantial endangerment to public health. However, basic interpretation of the results, even without concern about

how well they represent residents of Libby, does not suggest a public health crisis. Generally, the risks for residents are within the range considered acceptable by EPA's Superfund program (1×10^{-6} to 1×10^{-4}).

Exposure is reported in Table 8 by PCM and PCME analysis. PCM is the measurement method used by OSHA to enforce its permissible exposure limit (PEL) for asbestos (59 FR 40964 August 10, 1994). PCM cannot distinguish non-asbestos structures that are morphologically similar to asbestos structures. Nevertheless, PCM is appropriate for measuring exposure in an occupational setting where the airborne structures are predominantly asbestos. PCME, which differentiates asbestos from non-asbestos structures, is valuable for measuring airborne concentrations in non-occupational settings where the non-asbestos component of airborne fibers may be substantial. The PCME counting protocol has the same dimension criteria for structures as the PCM method, but includes only asbestos structures (see footnote 4 for details).

The risk estimates in Table 8 represent total cancer (i.e., lung cancer plus mesothelioma) in accordance with the EPA's risk assessment methodology presented in IRIS. Risks calculations are displayed for both PCM and PCME exposure estimates. The difference in exposure and risk between the two methods can be substantial. For most of the scenarios, the reduction in exposure and risk for PCME relative to PCM is approximately a factor of 10.

The risk estimates in Table 8 are very likely higher than the true risks because of EPA's conservative approach to risk assessment. EPA does not consider threshold exposure limits and employs straight-line risk extrapolation from high occupational exposures to low environmental exposures. EPA's conservatism is seen by considering the life-

¹¹ EPA (2001) contains details about the scenarios.

time cumulative exposures estimated for Libby residents (Table 8). The maximum of these exposure estimates, excluding the Scenario 3b Contractor, which should be assessed as an occupational exposure, is 0.0425 f-yr/cc. This exposure is substantially less than the risk doubling exposure estimates for lung cancer in Table 1 (93–173 f-yr/cc), the lifetime occupational exposure allowed by OSHA's PEL (4.0–4.5 f-yr/cc),¹² and an estimate of lifetime background exposure of 0.40 f-yr/cc. Based on these comparisons, the health risks associated with Libby resident exposure to LA are negligible.

8. Conclusions

Reports prepared by EPA and ATSDR imply, and the news media asserts, that the typical Libby resident is at substantial risk for asbestos-associated disease due to exposure to LA. Upon closer inspection, however, the excess risk projections apply to Libby mine workers who experienced historical high level occupational exposures when the mine was operating. Estimated lifetime cumulative exposures for Libby residents who were not mine workers based on recent air sampling conducted by EPA are low. There is no evidence that LA is more potent for asbestos-associated disease than other types of asbestos. The studies conducted at Libby have not produced sufficient evidence to support the claim that environmental exposures to LA independent of occupational exposures of miners are associated with increased pleural or parenchymal abnormalities, lung cancer, or mesothelioma.

Conflict of Interest

The author has consulted with and conducted studies for W.R. Grace & Co. on various issues concerning asbestos exposure and health risk, including exposure at Libby, Montana. Also, at the request of W.R. Grace & Co., the author has testified in court as a paid expert about results of my studies on asbestos exposure and health risk.

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References

- ADL, 1983. Letter report from ET Peters, ADL, to Julie Yang, WR Grace, August 8, 1983. Administrative Record—Libby Asbestos Superfund Site.
- Amandus, H.E., Wheeler, R., Jankovic, J., Tucker, J., 1987a. The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. Part I: exposure estimates. *American Journal of Industrial Medicine* 11 (1), 1–14.
- Amandus, H.E., Wheeler, R., 1987b. The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite. Part II: mortality. *American Journal of Industrial Medicine* 11, 15–26.
- American Thoracic Society (ATS), 1990. American thoracic society: health effects of tremolite. *Am. Rev. Resp. Dis.* 142, 1453–1458.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2000. Health consultation: mortality from asbestosis in Libby, Montana, 1979–1998. ATSDR December 12, 2000.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2002a. Mortality in Libby, Montana, 1979–1998. Update to health consultation: mortality from asbestosis in Libby, Montana, 1979–1998.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2002b. Preliminary Findings of Libby, Montana Asbestos Medical Testing. Available from: <<http://www.atsdr.cdc.gov/asbestos/02-1023-CombinedTesting.pdf>>. Accessed September, 2002.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2002c. Review of asbestos-associated abnormalities among a group of patients from Libby, Montana: a pilot study of environmental cases. ATSDR, August, 2002.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2002d. Public health assessment: Libby Asbestos NPL Site. ATSDR 2002.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2003. Report on the expert panel on health effects of asbestos and synthetic vitreous fibers: the influence of fiber Length. Prepared by Eastern Research Group for ATSDR, March 17, 2003.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2003. Case studies in environmental medicine: asbestos toxicity. Available from: <http://www.atsdr.cdc.gov/HEC/CSEM/asbestos/clinical_evaluation.html>. Accessed April, 2003).
- Berman W.D., Crump K.S., 2003. Technical support document for a protocol to assess asbestos-related risk. EPA Office of Solid Waste and Emergency Response 2003. Available from: <<http://www.epa.gov/superfund/programs/risk/asbestos/index.htm>>.
- Brattin, B., 2002. Memorandum: issues regarding cleavage fragments. Bill Brattin, Syracuse Research Corporation, May 9, 2002 Administrative Record—Libby Asbestos Superfund Site.
- Churg, A., Green, F.H.Y., 1998. *Pathology of Occupational Lung Disease*, second ed. Williams and Wilkins, Europe.
- Davis, J.M.G., Addison, J., McIntosh, C., Miller, B.G., Niven, K., 1991. Variations in the carcinogenicity of tremolite dust samples of differing morphology. *Annals of the New Academy of Sciences* 643, 473–490.
- Environmental Protection Agency (EPA), 1986. Airborne asbestos health assessment update. EPA 600/8-84-003F.
- Environmental Protection Agency (EPA), 2001. Phase 2 sampling and quality assurance project plan (Revision 0) for Libby, Montana. Environmental monitoring for asbestos. Evaluation of exposure to airborne fibers during routine and special activities. Prepared by USEPA Region 8 with technical support from Syracuse Research Corporation.
- Environmental Protection Agency (EPA), 2003. Report on the peer consultation workshop to discuss a proposed protocol to assess asbestos-associated risk. Prepared by Eastern Research Group, EPA Contract 68-C-98-148, May 30, 2003.
- Ilgren, E.B., 2004. The biology of cleavage fragments: a brief synthesis and analysis of current knowledge. *Indoor and Built Environment* 13, 343–356.
- McDonald, J.C., Harris, J., Armstrong, B., 1986. Cohort study of mortality of vermiculite miners exposed to tremolite. *British Journal of Industrial Medicine* 43, 436–444.

¹² The PEL limits exposure to 0.1 f/cc as a time-weighted average over 8 h. For a 40- or 45-year working lifetime, the lifetime cumulative exposure would be between 4.0(=0.10 × 40) and 4.5(=0.10 × 45) f-yr/cc.

- McDonald, C., 2001. Carcinogenicity of fibrous tremolite in workplace and general environments. Summary of paper to be presented at EPA Asbestos Health Effects Conference, Oakland, CA, May 24, 2001.
- McDonald, J.C., Harris, J., Armstrong, B., 2002. Cohort mortality study of vermiculite miners exposed to fibrous tremolite: an update. *Annals of Occupational Hygiene* 46 (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. *Occupational and Environmental Medicine* 61 (4), 363–366.
- McGill University, 1983. Analysis of analytical transmission electron microscopy of fibrous particles in Libby's air samples: preliminary results. Patrick Sebastien, Institute of Occupational Health and Safety. Administrative Record—Libby Asbestos Superfund Site.
- Meeker, G.P., Brownfield, I.K., Clark, R.N., Vance, J.S., Hoefen, T.M., Sutley, S.J., Gent, C.A., 2001. The Chemical Composition and Physical Properties of Amphibole from Libby, Montana: A Progress Report, Abstract, 2001 Health Effects of Asbestos, Oakland, CA.
- Occupational Safety and Health Administration (OSHA), 1992. Occupational Exposure to Asbestos, Tremolite, Anthophyllite and Actinolite. 57 FR 24310 June 6, 1992.
- Peipins, L.A., Lewin, M., Campolucci, S., Lybarger, J.A., Miller, A., Middleton, D., Weis, C., Spence, M., Black, B., Kapil, V., 2003a. Radiographic abnormalities and exposure to asbestos-contaminated vermiculite in the community of Libby, Montana, USA. *Environmental Health Perspectives* 111 (14).
- Peipins, L.A., Lewin, M., Campolucci, S., Lybarger, J.A., Miller, A., Middleton, D., Weis, C., Spence, M., Black, B., Kapil, V., 2003b. Radiographic Abnormalities: Response from Peipins et al.. *Environmental Health Perspectives* 112 (2), November 2004.
- Price, B., 2004. Radiographic abnormalities and asbestos exposure: Libby Montana. *Environmental Health Perspectives* 112 (2).
- Price, B., Ware, A., 2004. Mesothelioma trends in the United States: an update based on surveillance, epidemiology, and end results program data for 1973–2003. *American Journal of Epidemiology* 159, 107–112.
- Proto, A.V., 1992. Conventional chest radiographs: anatomic understanding of newer observations. *Radiology* 183, 593–603.
- RJ Lee Group, 2002. Memorandum, February 21, 2002. Administrative Record—Libby Asbestos Superfund Site.
- Sargent, E.N., Boswell, W.D., Ralls, P.W., Markowitz, A., 1984. Subpleural fat pads in patients exposed to asbestos: distinction from non-calcified pleural plaques. *Diagnostic Radiology* 152, 273–277.
- Weis, C., 2001. Memorandum from Chris Weis, USEPA to Paul Peronard, USEPA. Subject: Amphibole Mineral Fibers in Source Materials in Residential and Commercial Areas of Libby Pose an Imminent and Substantial Endangerment to Public Health. December 20, 2001.
- Weis, C., 2002. Memorandum from Chris Weis, USEPA to Paul Peronard, USEPA. Subject: Revised Screening Risk Estimates. November 22, 2002.
- Wylie, A.G., Bailey, K.F., Kelse, J.W., Lee, R.J., 1993. The importance of width in asbestos carcinogenicity and its implications for public policy. *American Industrial Hygiene Association Journal* 54, 239–252.

Environmental mesothelioma associated with tremolite asbestos: Lessons from the experiences of Turkey, Greece, Corsica, New Caledonia and Cyprus

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Abstract

Mediterranean regions such as Greece, Turkey, Cyprus, Corsica and New Caledonia have experienced epidemics of malignant mesothelioma as a result of non-occupational, “domestic” exposure to tremolite asbestos and fibrous erionite. This exposure to tremolite asbestos and fibrous erionite is typified “domestic” due to its prevalence in regions with natural deposits of tremolite asbestos (or fibrous erionite) where the material from tremolite asbestos or fibrous erionite is used for domestic applications such as whitewashing. However, these exposures may be useful in examining the potential consequences of even small amounts of amphibole asbestos fibers in the ambient air. It can also elucidate the effects of fibers that behave like amphibole asbestos. However, this type of exposure is not useful for studying the potential effects of small amounts of asbestos in the ambient air of big cities due to the differing nature of the fiber types and modes of exposure between the regions.

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Keywords: Tremolite asbestos; Erionite; Domestic; Environmental; Exposure

1. Introduction

More than 20 years ago, in 1981, when the Medical School of Ioannina, NW Greece, was established we encountered for the first time chest roentgenograms of usually healthy individuals with extensive, patchy, bilateral calcifications (Fig. 1). Much to our surprise, these obviously pleural calcifications were known to local health authorities. Everyone seemed to agree that: (1) they are typical of inhabitants of Metsovo (a mountainous village sixty kilometers east of Ioannina (population 5000)), (2) they are a result of previous tuberculous pleurisy and (3) they cause “no health effects” and therefore, there is nothing to worry about.

We could not agree that this was just an innocent result of previous tuberculosis and started investigating the phenomenon. Our initial questions were: (1) are these calcifications really so frequent? (2) are they really confined to the Metsovo area and most importantly (3) if not tuberculosis, what is their cause?

It soon became obvious that indeed the calcifications were quite frequent (almost in half the adult population) and occurred only among Metsovites (Constantopoulos et al., 1985). The cause became obvious when, in the same month of 1981 we had two unfortunate patients with huge pleural effusions that proved to be malignant pleural mesothelioma; both were from Metsovo (Constantopoulos et al., 1987a,b). Mesothelioma and pleural calcifications can only be attributed to asbestos exposure. It was therefore no surprise when Dr. A. Langer and Dr. R. Nolan, then at Mount Sinai Hospital in New York, where we sent transbronchial biopsies of Metsovites, found tremolite

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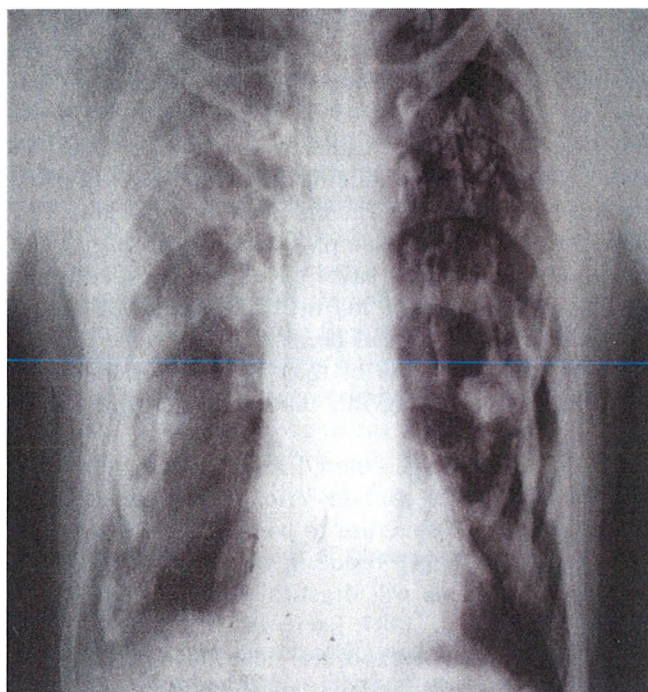


Fig. 1. In 1981, we found chest roentgenograms of usually healthy individuals from Metsovo with extensive, patchy, bilateral pleural calcifications.

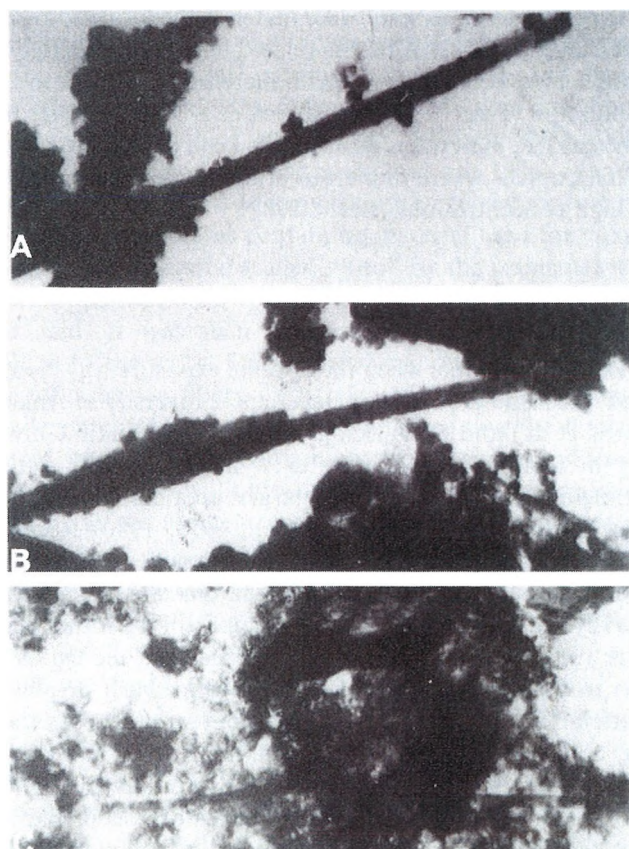


Fig. 2. Tremolite asbestos fibers were found by analytical transmission electron microscopy in small needle biopsy specimens.

asbestos fibers in most specimens in spite of the very small tissue samples (Constantopoulos et al., 1985) (Fig. 2).

However, where was the asbestos coming from? Metsovo is an idyllic village, up in the mountains of Pindos with no industries or mines around. The closest asbestos mine is around 200 km away. While looking for the source of the asbestos we became aware of the fascinating work of I. Baris and others in Turkey relating to the environmental exposure to tremolite asbestos and fibrous erionite resulting in epidemics of mesothelioma (Baris et al., 1975, 1978, 1981; Yazicoglu et al., 1978, 1980). A gathering of the villagers produced the source of the tremolite asbestos. It was a material used in the past as a whitewashing. It was good for waterproofing and especially to keep walls from getting “black from the fire” (amiantos in Greek = not getting dirty). The material was sent to Mount Sinai and its chemical composition was found to be identical to that of the transbronchial biopsies (tremolite asbestos) (Fig. 3) (Constantopoulos et al., 1987a).

This work has put Metsovo in the map of environmental asbestos exposure areas together with Turkey, Cyprus, Corsica and lately, New Caledonia. But is this exposure really environmental? And is it the same in all of these areas? To answer these questions we must first define and classify the different types of asbestos exposure.

Asbestos exposure can be classified as (Peters and Peters, 1998): (1) occupational, (2) para-occupational/domestic, (3) para-occupational/neighborhood, (4) para-occupational/macroenvironmental or (5) non-occupational domestic.

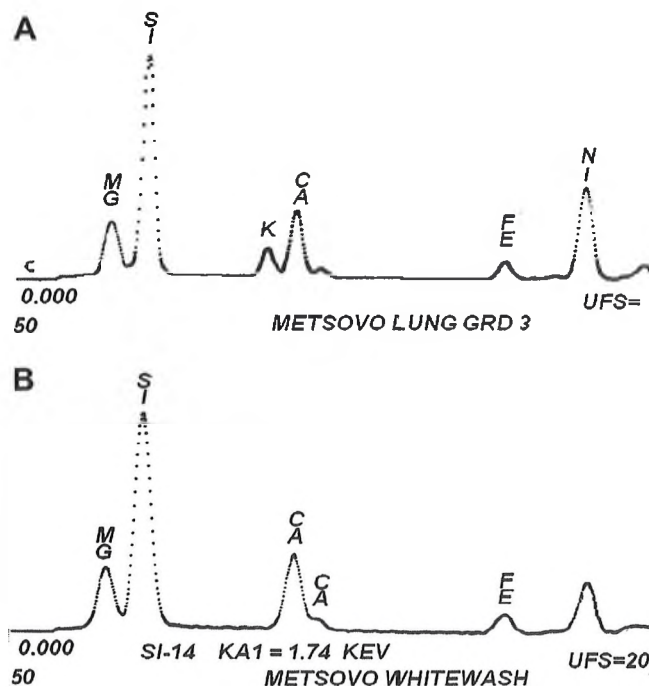


Fig. 3. Two energy dispersive spectra showing the tremolite asbestos found in the biopsies of individuals from Metsovo (A) is identical that in the whitewash (B). The potassium in the lung sample is an artifact from the tissue preparation.

1. *Occupational exposure*: occurs in workers of asbestos mines or any other workers of the extremely various asbestos exploitation factories or small family enterprises. It is a firmly proven exposure; the main cause of mesothelioma (Hillerdal, 1983).
2. *Para-occupational domestic exposure*: occurs in family members of asbestos through the dust from the workers clothes. This can create quite high levels of exposure and many cases of mesothelioma have been reported from this phenomenon (Gardner and Saracci, 1989).
3. *Para-occupational neighborhood exposure*: Several studies from many countries have shown sporadic cases of mesothelioma in residents living a few kilometers away from asbestos mines or factories. Crocidolite was the offending agent in most instances. Some of the cases from Cyprus and Corsica that we will examine in detail must have resulted from neighborhood exposure.
4. *Para-occupational macro-environmental*: Mesothelioma background incidence in non-exposed populations has been estimated to be one case per million living people per year (Hillerdal, 1983). In 2003 the US mesothelioma mortality was 2560 deaths among total US of 2,448,288 (Price and Ware, 2004). There is however, no evidence of increased risk of mesothelioma from general environmental exposure (macro-environmental exposure) in countries with asbestos factories or mines (Gardner and Saracci, 1989).
5. *Non-occupational, domestic exposure*: This is the only exposure that is neither a direct or indirect result of asbestos presence at the work place. On the contrary, it is a result of asbestos exposure inside the house, from domestic use of asbestos. The exposure can result either from continuous dust from the walls (Gardner and Saracci, 1989; Baris et al., 1987; Osman et al., 2007) or from processing of the asbestos containing material (Constantopoulos et al., 1985, 1987a,b; Sichletidis et al., 2006).

2. Cappadokia, Turkey and erionite

The first and best known environmental asbestos exposure is not really exposure to asbestos but to erionite. Indeed, the fact that exposure to this asbestos like material (a zeolite) has resulted in epidemics of mesothelioma, worse than any occupational asbestos exposure has taught us that it is not so much the chemical composition of the fiber but its aerodynamic characteristics that cause mesothelioma. In fact, erionite behaves aerodynamically exactly like a long thin amphibole asbestos fiber. Aerodynamic properties of fibers are factors driving aerosol stability, inhalation potential, etc. They are therefore factors driving biological potential but not, in and of themselves, causal factors.

The study of the effects of erionite exposure started in the 1970s by Baris and others (Baris et al., 1975), after reports of unusually high rates of cancer deaths from Karain, a small village in Cappadokia. Their study revealed that in Karain and three neighboring villages, mesotheli-

oma was the cause of death in half of the inhabitants and corresponded to an incidence 1000 times higher than expected in a non-asbestos exposed population (Baris et al., 1987; Selcuk et al., 1992). The offending agent was easy to detect since the villagers lived in houses (caves) built inside volcanic rocks containing erionite. Samples collected from the house dust, soil and ambient air of Karain all contained erionite. Indoor samples obtained during cleaning operations inside family caves gave the highest concentrations of erionite (up to 1.38 f/mL) (Baris et al., 1981). This was what the villagers had been breathing since birth and was obviously the cause of their mesothelioma. There is no mention of handling this material or crushing it, like in Metsovo.

Most Karain villagers now live in modern houses, but since the whole area contains erionite a re-settlement has been suggested; most refuse to comply. Either way, since the villagers no longer reside in caves it is believed that the number of cases will drastically decrease in the next decades (Baris et al., 1987; Baris, 1987).

The hypothesis of exposure since birth to erionite is strengthened by the fact that most mesotheliomas have occurred when exposed residents are between 35 and 55 years of age, in contrast with occupational mesotheliomas where exposures begin later in life and disease develops between 50 and 70 years of age (Hillerdal, 1983; Baris, 1987).

Finally, the hypothesis that exposure to erionite is akin to exposure to an asbestos like material is confirmed by the fact that most other asbestos related benign and malignant entities have been observed with increased incidence in this population (Firat, 1983; Karakoca et al., 1997). That this asbestos like material is erionite has been proven by studies of lung tissues where numerous erionite fibers were found in high concentrations (Baris, 1987).

3. Turkey and tremolite

At the same time when the erionite exposure was discovered, the same group from Hacettepe University in Ankara (Baris et al.) and S. Yazicioglu from Diyarbakir University in Southeastern Turkey drew attention to a similar problem concerning a much larger area in Eastern and Central Anatolia (Yazicoglu et al., 1978, 1980). Recently Osman et al., 2007 suggest similar environmental exposure continue to be health hazard in the Gaziantep region of Turkey. In this area, a similar number of mesotheliomas were reported again in the 1980s. This time the exposure was to tremolite asbestos, used as a whitewash or plaster material. It was sold from one village to another, but there was no large scale industrial exportation (Peters and Peters, 1998; Baris, 1987). There are no details available as to how the whitewash was prepared and the hypothesis of Baris is that the exposure was secondary to dust originating from the whitewashed walls, most probably since birth. This explains the peak age of mesothelioma similar to that of

erionite (40–60 years) (Peters and Peters, 1998; Selcuk et al., 1992).

There is a sex difference between fibrous erionite and tremolite asbestos. In tremolite asbestos there is a male preponderance (2:1 vs. 1:1 to fibrous erionite). This cannot be attributed to different exposure patterns between men and women, except if the effects of tremolite asbestos exposure (and not erionite) are enhanced by smoking. A similar male to female ratio is seen in Metsovo. The big difference however, between erionite and tremolite asbestos exposure in Turkey is that, although the population exposed to tremolite asbestos is around twenty times larger, the reported cases of mesothelioma were similar in a study between 1980 and 1988 (erionite 58 cases, tremolite asbestos 77 cases) showing clearly that erionite is a much more potent agent for mesothelioma (Selcuk et al., 1992).

4. Metsovo (and other areas of Greece) and tremolite asbestos

As mentioned in the introduction, the previous experience of Baris and others in Turkey was very crucial for the understanding of a similar outbreak in Metsovo, NW Greece. During the antituberculosis campaign in 1969 (Constantopoulos et al., 1985; Bazas et al., 1981) it was noted for the first time that many, otherwise healthy individuals from Metsovo presented with extensive pleural calcifications. This was further studied by Bazas et al. (Bazas et al., 1981, 1985) who found pleural plaques in 24% of examined Metsovites, but no mesothelioma, “The agent responsible for this rather benign condition was not identified” (Bazas et al., 1985). Our work in the area has shown that (Constantopoulos et al., 1985, 1987a,b, 1991, 1992; Peters and Peters, 1998; Sakellariou et al., 1996; Manda-Stachouli et al., 2004) Metsovites were exposed since birth to a tremolite asbestos containing material used for whitewashing. The material (called “luto” by the residents) was outcropped from nearby hills, shaped in the form of a ball and sold. It was then crushed, boiled over night and applied to the walls. During crushing, an high concentration of asbestos fibers were released (>200 f/mL), while smaller amounts were released while cleaning the floor of an old unused house containing the material (1–4 f/mL) and scratching its walls (20–40 f/mL). There is no tremolite asbestos in the ambient area of Metsovo. The procedure was repeated once or twice every year (Constantopoulos et al., 1991; Sakellariou et al., 1996).

More significantly, it is impossible to tell whether inhabitants were inhaling daily air with small concentrations of tremolite asbestos or once/twice a year air containing huge quantities of tremolite asbestos. What we can safely suggest is that after 1975–1980 “luto” is no longer used and Metsovites are practically free of exposure. We can claim this because Metsovo is outside the “Pindos serpentine zone” and Metsovites were traveling to nearby hills inside the zone to find “luto”. “Luto” was used by everyone until 1940–1950 and gradually abandoned. In 1980, it was used

by 10% of the population and now it is no longer in use (Constantopoulos et al., 1987a,b).

Like in Turkey, this tremolite asbestos whitewash has caused an epidemic of mesotheliomas and very high incidence of pleural calcifications in Metsovo (about half of the adult population) (Constantopoulos et al., 1985). Both epidemics have followed the decline in the use of “luto”. Thus, in our first study we reported seven mesotheliomas from Metsovo between 1981 and 1985. Seven mesotheliomas in five years in a population of 5000 is about 300 times higher than expected in non-asbestos exposed population (Hillerdal, 1983). The situation had changed ten years later. The incidence of mesothelioma between 1986 and 1995 had dropped to one-third (Sakellariou et al., 1996) reflecting the abandonment of “luto”. The same is true for the pleural calcifications. In our first study (Constantopoulos et al., 1985) about half of the adult population had plaques. When we repeated the study (Manda-Stachouli et al., 2004) we found similar overall incidence but a much lower prevalence among younger Metsovites, 30–36 years of age. If our hypothesis is correct, we expect to see a slow end to the mesothelioma epidemic in Metsovo by 2020–2030.

Metsovo is not the only area of Greece with a tremolite asbestos exposure problem. Several clusters of small villages, all in the “Pindos serpentine zone” have similar problems of much smaller scale and in some, tremolite asbestos has been incriminated (Constantopoulos et al., 1991; Sichletitis et al., 1992, 2006).

As we mentioned, Metsovites have increased incidence of both, mesothelioma and pleural plaques. The interesting finding is that these two do not occur necessarily in the same individuals. In our first report (Constantopoulos et al., 1987a) we had already mentioned that the first five Metsovites with mesothelioma had no plaques. Further studies confirmed that the population with plaques had less frequent mesothelioma (Constantopoulos et al., 1992). Not only that, bronchoalveolar lavage revealed that, those with plaques have a lymphocytic alveolitis and evidence of macrophage activation (Constantopoulos et al., 1992; Galani et al., 2002) as if they have a response to the tremolite asbestos “protecting” them from neoplasia. This intriguing hypothesis is further studied.

5. Cyprus and tremolite asbestos

There is a chrysotile mine in Troodos Mountain, Central Cyprus that has been functioning for decades. It is supposed to produce pure chrysotile and, since there are no other asbestos sources in Cyprus, this mine offered an ideal opportunity to study if pure chrysotile can cause mesothelioma.

Everyone was therefore, surprised, when mesothelioma was diagnosed in an elderly female who was not a miner but lived in a nearby village (McConnochie et al., 1987). The surprise was bigger when the fibers found in her lungs were not chrysotile but tremolite asbestos (McConnochie

et al., 1987, 1989). This prompted a large scale study of the area to address the question of whether mesotheliomas in Cyprus are related to the mine or to domestic/environmental exposure to tremolite asbestos.

The authors evaluated 12 cases of confirmed mesotheliomas that occurred around 1970–1980. Only five were asbestos miners. There were however, three wives of miners and two living in nearby villages. Two more were living in Nicosia and their mesotheliomas were unrelated to the mine directly or indirectly. The authors suggest in their first report (McConnochie et al., 1987), that since tremolite asbestos was found in domestic and outdoor dust samples, the environmental exposure to tremolite asbestos is equal if not more important to that of the mine as a cause of mesothelioma in Cyprus. They also mention however, that there are tremolite asbestos intrusions in the ore body of the mine and that these fibers were separated by “wind is lifting” after their primary crushing and then blown away by the wind (McConnochie et al., 1987). The distance this cloud of tremolite asbestos was traveling cannot be ascertained. It is also of interest that tremolite asbestos was found in stucco specimen from houses in three nearby villages but there are no details regarding this event.

It appears then, that in Cyprus we have had mesotheliomas in asbestos miners, wives of asbestos miners and inhabitants of nearby villages. The offending agent was, in all cases, tremolite asbestos. The miners’ exposure is, of course, occupational and the exposure of their wives para-occupational-domestic. The exposure of the villagers can either be classified as non-occupational-domestic like in Metsovo or in Turkey from use of tremolite asbestos stucco or, more likely, para-occupational neighborhood exposure (Viallat et al., 1991; Newhouse and Thompson, 1965; Haine et al., 1974; MacDonald, 1985) thus, indirectly related to the mine.

6. Corsica and tremolite asbestos

In North-East Corsica, a chrysotile asbestos mine was operating near the village of Canari until 1965. When the miners were examined for pleural plaques the most interesting finding was the prevalence rate of plaques in the control population (3.8%) (Rey et al., 1993). The answer for this became obvious after a look at the geological map of North-East Corsica. Near the village of Canari, where the mine is located, there are several zones with surface deposit of asbestos. The village of Murato is located inside such a zone. Rey et al. (Rey et al., 1993, 1994) examined 108 individuals of Murato and compared the prevalence of pleural plaques with those found in the neighboring village of Vezzani located outside these zones. In Murato, 41% of the examined population had pleural plaques. A sizable percentage of Vezzani (7.5%) also presented with bilateral plaques. The explanation offered by the authors was the proximity of surface asbestos deposits (Rey et al., 1994).

It is clear then, that if we exclude mines, the asbestos exposure in North-Eastern Corsica today is not related to the old asbestos mine. It could however, be considered para-occupational/neighborhood exposure, since it involves villagers living a few kilometers from the mine. It is however, not the mine itself but the surface deposits of asbestos near the mine that constitute the source of asbestos.

7. New Caledonia and tremolite asbestos

In New Caledonia, a French territory in South Pacific, a high incidence of malignant pleural mesothelioma was reported that could not be attributed to occupational exposure (Luce et al., 2000). It was explained however, by non-occupational-domestic exposure, like that of Metsovo. In the high mesothelioma areas, native Melanesians were using a very friable rock from local outcroppings as a whitewash. The rock was ground by hand to a powder, suspended in water and applied to the walls. Samples of rock and whitewash (called “Pö”) showed that it consists of pure tremolite asbestos similar to “luto” in Metsovo. Like “luto”, “Pö” has been replaced by modern materials, but is still in use in some villages. Like Metsovoites, native Melanesians are exposed since birth and the result is a very high incidence of malignant pleural mesothelioma. All but one of the fifteen mesotheliomas diagnosed between 1993 and 1995 occurred in Melanesians exposed to “Pö”. Lung cancer risk was also increased significantly among Melanesian women using “Pö”. There is no mention of pleural plaques or other benign asbestos related disorders (Luce et al., 2000).

8. Conclusions

Environmental exposure to tremolite asbestos (and fibrous erionite) has caused epidemics of malignant mesothelioma, mainly in Mediterranean countries but also in other parts of the world (New Caledonia). This exposure is non-occupational but cannot be characterized “environmental” in the sense of macro-environmental air pollution. It is better characterized as “domestic” since it occurs in areas with natural deposits of tremolite asbestos (or fibrous erionite) only when the material from these deposits is used (mainly for whitewashing and other domestic purposes). This type of exposure cannot serve as an example for the possible effects of small amounts of asbestos in the ambient air of big cities (micro-environmental) since: (1) the fiber is different (amphibole), (2) the exposure starts from birth and (3) the exposure is, at times, very high. It can however, serve to study possible effects of even small amounts of amphibole asbestos fibers in the ambient air, or even fibers that behave like amphibole asbestos.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

- Baris, Y.I., 1987. Asbestos and Erionite Related Chest Diseases. Semih Ofset Matbaacilik Ltd., Ankara-Turkey.
- Baris, Y.I., Ozesmi, M., Kerse, I., Ozen, E., Saahin, A., Kolacan, B., Ogankulu, M., 1975. An outbreak of pleural mesothelioma in the village of Karain/Urgup in Anatolia. *Kanser* 5, 1–4.
- Baris, Y.I., Sahin, A.A., Ozesmi, M., Kerse, I., Ozen, E., Kolacan, B., Altinors, M., Goktepe, A., 1978. An outbreak of pleural mesothelioma and chronic fibrosing pleurisy in the village of Karain/Urgup in Anatolia. *Thorax* 33, 181–192.
- Baris, Y.I., Saracci, R., Simonato, L., Skidmore, J.W., Artvinli, M., 1981. Malignant mesothelioma and radiological chest abnormalities in two villages in central Turkey. *Lancet* 1, 984–987.
- Baris, Y.I., Simonato, M., 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.
- Bazas, T., Bazas, B., Viitas, D., Gilson, J.C., McDonald, J.C., 1981. Pleural calcification in North-West Greece. *Lancet* 1, 254.
- Bazas, T., Oakes, D., Gilson, J.C., Bazas, B., McDonald, J.C., 1985. Pleural calcification in North-West Greece. *Environ. Res.* 38, 239–247.
- Constantopoulos, S.H., Dalavanga, Y.A., Sakellariou, C.S., Goudevenos, J., Kotoulas, O.B., 1992. Lymphocytic alveolitis and pleural calcification in non-occupational asbestos exposure; protection against neoplasia. *Am. Rev. Resp. Dis.* 146 (6), 1363–1370.
- Constantopoulos, S.H., Goudevenos, J.A., Saratzis, N., Langer, A.E., Selikoff, I.J., Moutsopoulos, H.M., 1985. Metsovo lung: pleural calcifications and restrictive lung function in North-West Greece: environmental exposure to mineral fiber as etiology. *Environ. Res.* 38, 319–331.
- Constantopoulos, S.H., Langer, A.M., Saratzis, N.A., Nolan, R.P., 1987a. Regional findings in Metsovo lung. *Lancet* 2, 452–453.
- Constantopoulos, S.H., Malamou-Mitsi, V.D., Goudevenos, J.A., Papaathanasiou, M.P., Pavlidis, N.A., Papadimitriou, C.S., 1987b. High incidence of malignant pleural mesothelioma in neighboring villages of Northwestern Greece. *Respiration* 51, 266–271.
- Constantopoulos, S.H., Theodoropoulos, P., Daskalopoulos, G., Saratzis, N., Sideris, K., 1991. Metsovo Lung Outside Metsovo: endemic pleural calcifications in the ophiolite belts of Greece. *Chest* 99, 1158–1161.
- Firat, D., 1983. Cancer mortality in Turkey and in the world, 1980–1981. Turkish Association for Cancer Research and Control, Ankara.
- International Labour Office Guidelines for the use of ILO International Classification of Radiographs of Pneumoconioses. Revised edition 1980. International safety and health series 22, Geneva 1980.
- Galani, V., Constantopoulos, S.H., Manda-Stachouli, C., Frangou-Lazaridis, M., Mavridis, A., Vassiliou, M., Dalavanga, Y.A., 2002. Additional proteins in BAL fluid of Metsovoites environmentally exposure to asbestos. More evidence of “protection” against neoplasia? *Chest* 121, 273–278.
- Gardner, M.J., Saracci, R., 1989. Effects on health of non-occupational exposure to airborne mineral fibers. In: Bignon, J., Petro, J., Saracci, R. (Eds.), *Non occupational exposure to mineral fibers*, vol. 90. IARC, Scientific Publications, Lyon, pp. 375–397.
- Haine, E., Dalquen, P., Bohlig, H., Dabbert, A., Hinz, I., 1974. Catamnestic investigations of the origin of mesothelioma. *Int. Arch. Arbeitsmed.* 33, 15–37 (in German).
- Hillerdal, G., 1983. Malignant mesothelioma, 198: review of 4,710 published cases. *Br. J. Dis. Chest* 77, 321–328.
- Karakoca, Y., Emri, S., Cangir, A.K., Baris, Y.I., 1997. Environmental pleural plaques due to asbestos and fibrous zeolite exposure in Turkey. *Indoor Built Environ.* 6, 100–105.
- Luce, D., Bugel, I., Goldberg, P., Goldberg, M., Salmon, C., Billon-Galland, M.A., Nocolau, J., Quenel, P., Fevotte, J., Brochard, P., 2000. Environmental exposure to tremolite and respiratory cancer in New Caledonia: a case-control study. *Am. J. Epidemiol.* 151 (3), 259–265.
- MacDonald, J.C., 1985. Health implications of environmental exposure to asbestos. *Environ. Health Perspect.* 62, 319–328.
- McConnochie, K., Simonato, L., Mavrides, P., Christofides, P., Pooley, F.D., Wagner, J.C., 1987. Mesothelioma in Cyprus: the role of tremolite. *Thorax* 42, 342–347.
- McConnochie, K., Simonato, L., Mavrides, P., Christofides, P., Mitha, R., Griffiths, D.M., Wagner, J.C., 1989. Mesothelioma in Cyprus. In: Bignon, J., Peto, J., Saracci, R. (Eds.), *Non-occupational exposure to mineral fibres*, vol. 90. WHO, IARC Scientific Publications, pp. 411–419.
- Manda-Stachouli, C., Dalavanga, Y., Dascalopoulos, G., Leontaridi, C., Vassiliou, M., Constantopoulos, S.H., 2004. Decreasing prevalence of pleural calcifications among Metsovoites with non-occupational asbestos exposure. *Chest* 126, 617–621.
- Newhouse, M.L., Thompson, H., 1965. Mesothelioma of pleura and peritoneum following exposure to asbestos in the London area. *Br. J. Ind. Med.* 22, 261–269.
- Osman, E., Hasan, B., Meral, U., Mehmet, T., Nazan, B., Ayhan, O., Erhan, E., Oner, D., 2007. Recent discovery of an old disease: malignant pleural mesothelioma in a village in south-east Turkey. *Respirology* 12, 448–451.
- Peters, G.A., Peters, B.J., 1998. Pathology, Immunology and Gene Therapy, Volume 17 of the Sourcebook on Asbestos Diseases: Causation, Diagnosis, Therapy and Related Aspects. Lexis Law Publishing, USA.
- Price, B., Ware, A., 2004. Mesothelioma trends in the United States: an update based on Surveillance, Epidemiology, and End Results Program Data for 1973 through 2003. *Am. J. Epidemiol.* 159, 107–112.
- Rey, F., Boutin, C., Steinbauer, J., Viallat, J.R., Alessandrini, P., Jutisz, P., Di Giambattista, D., Billon-Galland, M.A., Hereng, P., Dumortier, P., De Vuyst, P., 1993. Environmental pleural plaques in an asbestos exposed population of Northeast Corsica. *Eur. Respir. J.* 6, 978–982.
- Rey, F., Boutin, C., Viallat, J.R., Steinbauer, J., Alessandrini, P., Jutisz, P., Di Giambattista, D., Billon-Galland, M.A., Hereng, P., Dumortier, P., De Vuyst, P., 1994. Environmental asbestotic pleural plaques in Northeast Corsica: correlation with airborne and pleural mineralogic analysis. *Environ. Health Perspect.* 102 (5), 251–264.
- Sakellariou, K., Malamou-Mitsi, V., Haritou, A., Koumpaniou, C., Stachouli, C., Dimoliatis, I.D., Constantopoulos, S.H., 1996. Malignant pleural mesothelioma from non-occupational asbestos exposure in Metsovo (North-West Greece): slow end of an epidemic? *Eur. Respir. J.* 9, 1206–1210.
- Selcuk, Z.T., Coplu, L., Emri, S., Kalyoncu, A.F., Sahin, A.A., Baris, Y.I., 1992. Malignant pleural mesothelioma due to environmental mineral fiber exposure in Turkey. *Chest* 102, 790–796.
- Sichletidis, L., Dascalopoulou, E., Tsarou, V., Pneumatikos, I., Chloros, D., Vamvalis, C., 1992. Five cases of pleural mesothelioma with endemic pleural calcifications in a rural area in Greece. *Med. Lav.* 83, 326–329.
- Sichletidis, L., Chloros, D., Chatzidimitriou, N., Tsiotsios, I., Spyrtatos, D., Patalas, D., 2006. Diachronic study of pleural plaques in a rural population with environmental exposure to asbestos. *Am. J. Ind. Med.* 49, 634–641.
- Viallat, J.R., Boutin, C., Steinbauer, J., Gaudichet, A., Dufour, G., 1991. Pleural effects of environmental asbestos pollution in Corsica. *Ann. N. Y. Acad.* 643, 438–446.
- Yazicoglu, S., Oktem, K., Ilcayto, R., Balci, K., Sayli, B.S., 1978. Association between malignant tumors of the lungs and pleural and asbestosis: a retrospective survey. *Chest* 73, 52–56.
- Yazicoglu, S., Ilcayto, R., Balci, K., Yorulmaz, B., 1980. Pleural calcification, pleural mesotheliomas and bronchial cancers caused by tremolite dust. *Thorax* 35, 564–569.

Investigation of exposures to commercial asbestos in northeastern Minnesota iron miners who developed mesothelioma

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Abstract

A 70% excess of mesothelioma, an asbestos-related cancer, has been reported among men in northeastern Minnesota, where iron mining has been the major industry. The Minnesota Department of Health has studied iron miners who developed mesothelioma to identify possible sources of asbestos exposure. A database of all Minnesota residents diagnosed with mesothelioma between 1988 and 1996 was linked to a database of approximately 72,000 current and former Minnesota iron-mining employees to identify cases who had ever worked in the mining industry. The job histories of the cases were examined to determine if any of their jobs could have involved exposure to commercial asbestos. Seventeen individuals diagnosed with mesothelioma in Minnesota between 1988 and 1996 were found to have worked in the iron mining industry. Of the 15 for whom adequate work histories were available, 14 had identifiable sources of exposure to commercial asbestos in jobs held both inside and outside of the mining industry. The time between employment in these asbestos-exposed occupations and the diagnosis of mesothelioma is consistent with the 20 or more year latency period that has been observed in other studies of this cancer.

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1. Introduction

There has long been concern about a possible link between the iron mining industry in northeastern Minnesota and the occurrence of cancers and respiratory diseases in that region. In 1973, amphibole fibers were found in the Duluth water supply and traced to tailings that had been disposed of in Lake Superior by the Reserve Mining Company. This finding prompted studies of the fibers (Langer et al., 1979), the effects of ingestion of the fibers (Hilding et al., 1981; Levy et al., 1976), and the morbidity and mortality of iron ore workers (Clark et al., 1980; Cooper et al., 1988, 1992; Higgins et al., 1983; Lawler et al., 1985), among other studies.

In 1997, the Minnesota Cancer Surveillance System (MCSS) reported that the rate of mesothelioma, a rare asbestos-related cancer, was 70% higher than the statewide average among men in northeastern Minnesota during the period 1988–1994 (standardized morbidity ratio = 1.72; 95% confidence interval = 1.22–2.35) (Breslow and Day, 1987; Minnesota Cancer Surveillance System, 1997). Subsequent data from MCSS showed a continuing excess in men in this region—at 81% for the 12-year period 1988–1999 (Minnesota Cancer Surveillance System, 2003). No excess has been found among females.

Mesothelioma is a cancer of the lining of the lung or abdomen. A past history of exposure to asbestos can be identified among most victims of this disease. Mesothelioma has not been associated with smoking. There are approximately 60 cases of mesothelioma per year in Minnesota. Due to a latency period of 20 or more years, it is

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often difficult to determine exactly when or where an individual diagnosed with mesothelioma may have been exposed to asbestos.

Mesothelioma is rapidly fatal; consequently, it is often not possible to obtain direct interviews with the subjects themselves. In addition, historical monitoring data are often not available. For this reason, many studies use past work histories and job titles as a surrogate for potential exposures.

It was not clear what sources of asbestos led to the elevated rate of this cancer among men in northeastern Minnesota. Exposures related to cancers that were diagnosed in the 1980s and early 1990s would have had to have taken place in the 1940s to the 1970s, or earlier. While an increased rate was observed in men, the rate in women was not elevated, pointing to the likelihood of an occupational exposure. It was known that between 1958 and 1974, the Conwed Corporation plant in Cloquet, Minnesota, also located in the northeast region of the state, used several types of asbestos as a raw material in the manufacturing of mineral board and ceiling tile (Bender et al., 1993; Williams, 1994). However, preliminary evidence indicated that it was unlikely that Conwed was the sole explanation for the elevated rate of mesothelioma (Minnesota Cancer Surveillance System, 1999). Because the iron mining industry has been a major employer in this region and because of the history of concern about the mineral fibers, concern remained that there may be some mining process that resulted in asbestos exposure.

In 1998, the Minnesota Department of Health (MDH) began a series of investigations to determine to what extent, if any, employment in the iron mining industry was associated with the excess of mesothelioma or other occupational respiratory diseases. To investigate the mesothelioma excess, record linkage was conducted to identify cases of mesothelioma that may have occurred among former iron miners. A case series study was then conducted to determine the extent to which mesothelioma in miners could be explained by exposures to commercial asbestos (commercially-available asbestos and asbestos-containing materials, such as insulation). Such exposures—known to be associated with mesothelioma risk in many other industries—would need to be identified and accounted for in assessing health risks to miners. If no commercial asbestos exposures could be identified, other exposures (e.g., taconite fibers) would have to be evaluated.

2. Methods

2.1. Minnesota Iron Miner cohort

The Minnesota Iron Miner cohort was assembled by the University of Minnesota, School of Public Health in the early 1980s, with the support of the Minnesota Iron Range Resources and Rehabilitation Board and the cooperation of the seven mining companies then in operation. The cohort consists of approximately 72,000 individuals who had worked in the iron mining industry in northeastern Minnesota between the 1930s and the early 1980s, including taconite workers and persons who had worked in

certain natural ore operations. (Reserves of natural ore were largely depleted by the 1970s. Taconite, a lower-grade iron ore, has been mined commercially in Minnesota since 1955.) In addition to demographic information, the cohort records contain the employment histories of these workers.

2.2. Identification of Minnesota iron miners who developed mesothelioma

MCSS records for all Minnesota residents diagnosed with mesothelioma between 1988 and 1996 (years of data available when the study began) were linked to the Minnesota Iron Miner cohort database, to identify cases who had ever been employed in the mining industry. Because former iron miners could have moved out of the seven counties of northeastern Minnesota, the iron miner database was linked to MCSS records for all Minnesota residents. The records were matched on first, middle and last name, date of birth, and social security number. The computerized matches were performed using a probabilistic record linkage program (Fellegi and Sunter, 1969).

2.3. Identification of mining and non-mining jobs held by miners who developed mesothelioma

Mining jobs held by workers who developed mesothelioma were identified using records from the Minnesota Iron Miner cohort. Non-mining jobs were identified using employment applications included in the iron miner records, workers compensation claim records, and newspaper death notices.

2.4. Identification of possible exposures in mining occupations

The first step in the qualitative assessment of possible exposures to commercial asbestos in the mining jobs involved interviewing people who had worked in these jobs. An advisory committee to MDH provided technical assistance in the development of a questionnaire that was used to ask workers about potential exposures to commercial asbestos in different mining jobs. Questions asked about materials handled and tasks that may have involved direct or indirect exposures to asbestos (Fletcher et al., 1993), referring to the work environment as it existed in the 1940s–1970s. This study did not include any assessments of exposure to taconite dust.

A list of job titles for each of the mining companies was developed consisting of jobs held by workers from that company, if any, who had been diagnosed with mesothelioma, plus other randomly-chosen jobs. The extra jobs were added so that the interviewees and those assessing the jobs could not assume that the job they were reporting on, or evaluating, had been held by a worker who developed mesothelioma.

More than 350 telephone interviews were conducted covering 122 different job titles from the seven different mining companies (two of which were no longer in operation at the time of the study). Ninety-six percent of the respondents had experience in the job they reported on, while the remaining 4% were coworkers and/or supervisors. An attempt was made to interview at least three persons per job title. The interviews were summarized by MDH's consulting certified industrial hygienist (CIH) who examined the interview responses and used them to assign an initial rating of exposure to commercial asbestos for each job.

An assessment panel for each company was convened to make the final exposure determinations. Each panel consisted of knowledgeable union and management representatives, plus a non-mining industrial hygienist or safety engineer. The panels used the initial ratings, the interview responses (with identifying information removed), available job descriptions from the relevant time period, and their own knowledge of the mining environment to estimate the potential for exposure to commercial asbestos in each of the jobs. The panels considered regular (everyday) and shutdown responsibilities separately. (Shutdowns are scheduled periods when regular processing at a mining operation stops so that equipment can be retooled or maintained. Workers may change jobs or even move to a different facility to perform shutdown duties.) The panels rated

the jobs as exposed (in terms of high likelihood/high intensity; high likelihood/low intensity; low likelihood/high intensity or low likelihood/low intensity), not exposed, or unknown exposure. When no interviews were available (i.e., no interviewees could be found), the panels made determinations using other information (e.g., job descriptions and their own knowledge). If no determination could be made, the potential for exposure was marked unknown.

2.5. Identification of possible exposures in non-mining occupations

Other studies of asbestos-exposed occupations were reviewed to determine whether a particular non-mining job could have involved exposure to commercial asbestos. In addition, the list of miners with mesothelioma was checked against a roster of former Conwed employees (Minnesota Department of Health, 1989), to see how many had also worked at that facility. Any Conwed job was considered as having potential commercial asbestos exposure. A final review of these jobs was provided by the CIH.

3. Results

3.1. Description of the case series

Of the 340 male Minnesota residents diagnosed with mesothelioma between 1988 and 1996, 17 were found to have worked in the iron mining industry. Two of the 17 also worked at Conwed. None of the 92 female Minnesotans diagnosed with mesothelioma between 1988 and 1996 were found in the iron miner cohort.

Fifteen of the 17 were diagnosed with pleural mesothelioma while two had peritoneal mesothelioma. The age at diagnosis ranged from 55 to 82. Fourteen were diagnosed while residing in northeastern Minnesota while three were diagnosed while living elsewhere in Minnesota. Since MCSS only collects cancer data for Minnesota residents, it is not known how many, if any, miners may have developed mesothelioma outside of Minnesota.

3.2. Occupational histories

The number of different iron mining jobs held by each of the 17 men varied, as did the length of their employment in the mining industry, ranging from 2 months to 40 years. With the addition of known non-mining jobs, the extent of the employment history documented for the 17 men ranged from 5 to 60 years. The years of their employment ranged from the 1930s through the 1980s. Complete job histories for the relevant exposure period were available for 10 of the 17 cases. For five cases, there were small gaps in job history information. Thus, for 15 cases, occupational histories were sufficiently complete to allow evaluation of potential exposures to commercial asbestos. A listing of occupations held by the cases is included in the MDH report (Minnesota Department of Health, 2003).

3.3. Exposures to commercial asbestos

Table 1 contains a summary of the panel exposure estimates for the 17 cases in terms of “probable” and “possible” likelihood of exposure. Probable was used when the

Table 1

Summary of estimated exposures to commercial asbestos 20 or more years prior to diagnosis for 17 iron-mining employees who developed mesothelioma

Likelihood of exposure to commercial asbestos	Total No.	Exposure in non-mining occupation(s)	Exposure in mining occupation(s)	Exposure in both mining and non-mining occupations
Probable	11	3 ^a	4	4
Possible	3	1	0	2
None identified	1	—	—	—
Unknown due to incomplete job histories	2	—	—	—

^a Includes two individuals who also had non-mining occupations with possible exposure.

panel exposure estimate was: high likelihood/high intensity; high likelihood/low intensity or low likelihood/high intensity. Possible was used when panel exposure estimate was low likelihood/low intensity.

Fourteen of the 15 miners who developed mesothelioma had potential exposures to commercial asbestos: 11 had job(s) with probable exposure to commercial asbestos and another 3 had job(s) with possible exposure to commercial asbestos. One of the 15 had no apparent occupational exposures to commercial asbestos based on the information that was available. For two of the 17, a potential source of exposure could not be determined because the jobs they held for significant portions of their job histories were unknown.

Potential exposures to commercial asbestos were found in both mining and non-mining occupations. Many of the asbestos-exposed occupations held by the cases, like plumbing, were common to both mining and non-mining industries. Examples of mining jobs identified as having potential exposures to commercial asbestos were carpenter, maintenance mechanic and plumber. Non-mining jobs having potential exposures included boiler operator, sheet metal worker and Conwed (Cloquet, Minnesota) worker. The exposure determinations for the mining jobs are company-specific. That is, the panels rated the jobs as they existed at certain companies in the time period of interest, so exposure ratings may not be true for the same job title at a different operation. The time between employment in these asbestos-exposed occupations and the diagnosis of mesothelioma in this study was consistent with the 20 or more year latency period that has been observed in other studies of this cancer.

Of the 14 cases who held occupations in which exposure was possible or probable, mining occupations were the only identified source for 4; non-mining occupations were the only identified source for 4; and both mining and non-mining occupations were identified for 6. As noted in Table 1, 2 cases who had a non-mining job with probable exposure and a mining job with possible exposure were categorized as “probable/non-mining”.

4. Discussion

This study identified 17 Minnesota iron miners who were diagnosed with mesothelioma between 1988 and 1996. While the mesothelioma risk among miners cannot be quantified in this study and is not solely attributable to exposures within the mining workplace, this finding is in sharp contrast to previously published death certificate-based studies of Minnesota iron ore miners that have not found mesotheliomas or excesses of other respiratory diseases (Cooper et al., 1988, 1992; Higgins et al., 1983; Lawler et al., 1985). This finding, along with the results of the exposure assessment, demonstrates that exposure to asbestos has occurred in the iron mining industry during previous decades. Because of the long latency of asbestos-related diseases, these risks will continue into the future even in the absence of ongoing exposures.

4.1. Limitations and strengths

Case series studies, such as this study, must be cautiously interpreted. While exposures among the cases are categorized and explicitly described, there is no control group for comparison, and thus exposures among non-cases can only be implicitly assumed based on historical data or other knowledge. However, where there is a very strong relationship between exposure and disease, useful insights may be obtained even in the absence of controls (Cummings and Weiss, 1998). As with analytic studies, other sources of bias should still be addressed.

The major limitation of this study was the assessment of previous commercial asbestos exposure. This assessment was based on job titles and occupational histories—not actual monitoring data—and utilized existing records. Due to statutory limitations, study protocols did not allow contact of next of kin to gain more information about the work histories and potential exposures of the 17 individuals diagnosed with mesothelioma who worked in the mining industry. Complete work histories were not found for 2 of the 17. For one, documentation only up to age 26 was available.

Complete information may or may not have been found regarding an individual's work outside of the mining industry. This depended on whether the prior work history was included in their employment records, or was available through other sources (e.g., death notices). In addition, nothing was known about any non-occupational asbestos exposures (e.g., hobbies, home environment, spouse's occupational exposures).

Quantitative exposure data on which to base the assignment of asbestos exposure were not available. Even with qualitative exposure estimates, assumptions were made that a particular job title in a particular year at a particular mine conferred a particular probability of exposure. In addition, nothing was known about possible use of personal protective equipment.

Despite these limitations, this study has several strengths. First, a major strength is this study's use of cancer registry data, rather than death certificates, to identify all mesothelioma cases in the state. MCSS data come from the pathology reports and clinical records confirming that a cancer has been diagnosed. Quality control studies confirm the completeness and accuracy of these data. In contrast, death certificate-based studies (prior to the change from the International Classification of Disease revision 9 to revision 10 in 1999) will likely miss many, if not most, cases of mesothelioma that are often coded to other causes of death (such as lung cancer) (Lilienfeld and Gunderson, 1986). Among the 17 cases of mesothelioma in this study, only one would have been detected by the cause-of-death codes used for mesothelioma on death certificates (despite the fact that most of the death certificates had some mention of mesothelioma on the death certificate itself).

A second strength is the study's use of the previously established Minnesota Iron Miner cohort. Because those diagnosed with mesothelioma or their next of kin could not be contacted for this study, it would have been much more difficult and much less accurate to determine whether persons diagnosed with mesothelioma had ever worked in the mining industry without the mining cohort information. Mining cohort data also provided most of the information about the job titles and dates of employment for the study subjects.

A third strength was the protocol that blinded the assessment of potential exposures to commercial asbestos. None of the participants in the study knew which job titles were associated with miners who later developed mesothelioma.

Finally, the involvement of a technical advisory group provided information that was vital to the satisfactory completion of this study. The collaboration between labor and industry in the development of the protocol for this study allowed current and former iron miners to be interviewed about exposures to commercial asbestos in their jobs, in a way that ensured the confidentiality of their responses. In addition, the use of assessment panels consisting of mining company, labor and other industrial hygiene/safety professionals brought the most knowledgeable people together to make the best assessments with the available information.

4.2. Health issues not addressed by this study

While the study findings establish that miners are at some risk of mesothelioma and that past exposure to commercial asbestos is a likely explanation, this study does not address other significant health questions. In particular, this study does not address the morbidity and mortality among iron miners from all types of cancer or respiratory diseases, nor does it attempt to address potential health risks from exposures to respirable mineral dusts from taconite ore and its processing (silica, taconite, cummingtonite-grunerite, cleavage fragments, etc.). Other types of epidemiologic studies, such as a mortality follow-up study

(in which death rates and causes of death among miners would be compared to that for the overall population) or a medical screening of iron miners (which could look at lung abnormalities), would be required to address these questions.

5. Conclusion

Our findings demonstrate an unquantified risk of mesothelioma among former Minnesota iron miners and suggest that commercial asbestos exposure (inside and outside of the mining industry) is the likely cause of mesothelioma in this case series. However, at least one miner had no identifiable source of exposure to commercial asbestos and other causes cannot be ruled out.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- Bender, A.P., Williams, A.N., Parker, D.L., 1993. Experiences of a state-sponsored notification and screening program for asbestos workers. *Am. J. Ind. Med.* 23, 161–169.
- Breslow, N.E., Day, N.E., 1987. Statistical methods in cancer research. Volume II—the design and analysis of cohort studies. IARC Sci. Publ. 82, 1–406.
- Clark, T.C., Harrington, V.A., Asta, J., Morgan, W.K., Sargent, E.N., 1980. Respiratory effects of exposure to dust in taconite mining and processing. *Am. Rev. Respir. Dis.* 121, 959–966.
- 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.
- 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.
- Cummings, P., Weiss, N., 1998. Case series and exposure series: the role of studies without controls in providing information about the etiology of injury or disease. *Inj. Prev.* 4, 54–57.
- Fellegi, I., Sunter, A., 1969. A theory for record linkage. *J. Am. Stat. Assoc.* 25, 172–178.
- Fletcher, A., Engholm, G., Englund, A., 1993. The risk of lung cancer from asbestos among Swedish construction workers: self-reported exposure and a job exposure matrix compared. *Int. J. Epidemiol.* 22 (Suppl. 2), S29–S35.
- 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.
- Hilding, A.C., Hilding, D.A., Larson, D.M., Aufderheide, A.C., 1981. Biological effects of ingested amosite asbestos, taconite tailings, diatomaceous earth and Lake Superior water in rats. *Arch. Environ. Health* 36, 298–303.
- Langer, A.M., Maggione, C.M., Nicholson, W.J., Rohl, A.N., Rubin, I.B., Selikoff, I.J., 1979. The contamination of Lake Superior with amphibole gangue minerals. *Ann. NY Acad. Sci.* 330, 549–572.
- Lawler, A.B., Mandel, J.S., Schuman, L.M., Lubin, J.H., 1985. A retrospective cohort mortality study of iron ore (hematite) miners in Minnesota. *J. Occup. Med.* 27, 507–517.
- Levy, B.S., Sigurdson, E., Mandel, J., Laudon, E., Pearson, J., 1976. Investigating possible effects of asbestos in city water: surveillance of gastrointestinal cancer incidence in Duluth, Minnesota. *Am. J. Epidemiol.* 103, 362–368.
- Lilienfeld, D.E., Gunderson, P.D., 1986. The “missing cases” of pleural malignant mesothelioma in Minnesota, 1979–81: preliminary report. *Public Health Rep.* 101, 395–399.
- Minnesota Cancer Surveillance System, 1997. Cancer rates and trends in Northeastern Minnesota. MCSS Epidemiology Report 97:1.
- Minnesota Cancer Surveillance System, 1999. Cancer incidence rates in Northeastern Minnesota. MCSS Epidemiology Report 99:2.
- Minnesota Cancer Surveillance System, 2003. Cancer incidence rates in Northeastern Minnesota with an emphasis on mesothelioma, MCSS Epidemiology Report 03:1.
- Minnesota Department of Health, 1989. Medical screening for asbestos-related lung disease among Conwed Corporation (Cloquet) workers and their spouses: preliminary report to the Minnesota Legislature.
- Minnesota Department of Health, 2003. Exposures to commercial asbestos in Northeastern Minnesota iron miners who developed mesothelioma. Minneapolis; November 7, 2003. Available online: <http://www.health.state.mn.us/divs/hpcd/cdee/occhealth/reports.html>.
- Williams, A.N., 1994. An epidemiologic study of radiographic abnormalities among asbestos ceiling tile workers and their spouses. University of Minnesota, Minneapolis.

Rapporteur's Report Session 4: Grunerite asbestos (amosite) and tremolite–ferroactinolite asbestos: Risk of environmental mesothelioma: John F. Gamble

Paper 1—South African experience with asbestos-related environmental mesothelioma: Is fiber type important?

Neil White, Gill Nelson, Jill Murray

The purpose of this review was to illustrate the importance of the type of asbestos in environmental mesothelioma. South Africa is a logical place to assess fiber type. The three major types of asbestos (crocidolite, amosite and chrysotile) were mined (all asbestos mining stopped in 2002) in South Africa. The association between asbestos and mesothelioma was discovered in South Africa. The occupational literature indicates high mesotheliomagenic potential for crocidolite, less for amosite and less still for chrysotile. Since South Africa has been a major source of crocidolite, relatively high rates of mesothelioma in the mining population is not surprising. High rates of mesothelioma due to environmental exposure is surprising, except perhaps when the authors' point out potential sources for community exposures (e.g., mine tailings used for road surfacing, golf courses, brick and plaster making; insulation in residential ceilings; children playing on fiber-rich waste rock).

The authors' reviewed four studies reporting on mesothelioma cases and their sources of exposure and fiber type. Overall 23% of the known cases were attributed to the environmental (not occupational) exposure and about 90% were due to crocidolite asbestos. The proportion of environmental mesothelioma is considerably higher than in Western Australia where crocidolite is also mined. There the overall rate of environmental mesothelioma is about 6% (and less than 1% from residence in a crocidolite mining area).

About 10% of cases were related to amosite or mixed fiber (amosite + crocidolite). Toxicity may be related in part to this difference in fiber type, but the size of the exposed populations is undoubtedly related as well. There were no cases attributed to chrysotile exposure. There are a few cases of mesothelioma among Canadian chrysotile miners where the chrysotile is contaminated with tremolite asbestos, which may be the active agent. In South Africa it is not clear whether the lack of mesothelioma cases caused

by chrysotile is due to no contamination by tremolite asbestos and/or the small size of the exposed population.

The first two papers present two contradictory interpretations regarding the risk of asbestos-related environmental disease among Libby, Montana residents.

Paper 2—Exposure to airborne amphibole structures and health risks: Libby, Montana

Bertram Price

EPA and ASTDR and news reports suggest the residents of Libby are at substantial and imminent risk of asbestos-related disease. This paper reviews these claims and concludes that Libby residents in the absence of occupational exposure are not at increased risk of lung cancer, mesothelioma, asbestosis or pleural abnormalities.

Occupational health risks are associated with the vermiculite deposit in Libby, Montana. Libby vermiculite is a mixture of cleavage fragment and asbestiform minerals. The high proportion of long, thin asbestiform fibers (for example over 70% longer than 10 μm , about 10% longer than 20 μm) is consistent with labeling the mixture as "Libby Asbestos" (LA).

Exposure–response analyses from the two occupational cohort studies suggest a doubling of lung cancer risk occurs somewhere between cumulative exposures of 130–400 fibers/mL years. The EPA risk model predicts a doubling of risk at about 100 fibers/mL years. Cumulative exposures of residents are several orders of magnitude below these occupational exposures. Results of an ATSDR study indicated statistically significant risks for Libby males but not females. Price suggests the female results are the better estimate of risk for Libby residents. The male estimate is biased upward because of smoking and mine employment. If these confounders were accounted for he contends there would not be significant lung cancer excess for Libby residents.

Proportional mortality ratios (PMR) for mesothelioma ranged from 1.2% to 4.2% in the two occupational cohorts, which is 6–21 times greater than the 0.2% for the US popula-

tion. There were no exposure-response analyses for mesothelioma, but Price suggests the minimum cumulative exposure is probably about 4.3 fibers/mL years for the 14 mesothelioma cases in the two occupational cohort studies. This cumulative exposure is about 100 times greater than the EPA estimate for the highest cumulative exposure of about 0.04 fibers/mL years for the highest exposure of a Libby resident. The EPA risk assessment estimates about a 0.01% risk of mesothelioma for the highest exposed Libby resident. On the basis of these estimates, Price suggests the risk of mesothelioma is negligible for a Libby resident.

An ATSDR mortality study suggested asbestosis mortality among Libby residents was increased 40–80 times expected depending on the referent population. Price suggests this estimate is misleading because 11 of the 12 deaths were mine workers and the 12th death was a woman having household contact to a mine worker with 20-years tenure. The suggested threshold for asbestosis is 25–100 fibers/mL $\times$ years, which is about 60–240 times the worst ambient exposure. Therefore, Price contends the correct interpretation is that Libby residents are not at increased risk of asbestosis.

Finally, ATSDR conducted a screening study looking at radiographic abnormalities including asbestosis and pleural thickening/plaques. Price suggests it is a false implication that residence in Libby significantly increases risk of asbestos-related pleural disease. The basis for this assertion is in large part related to diagnosis misclassification and that the most relevant group is the one without occupational and domestic exposures. Misreading of the X-rays for pleural abnormalities is likely for several reasons. There was a lack of control films and B-readers did not read the films blind. The B-readers were concerned that pleural abnormalities may actually be fat about 30% of the time and pleural abnormalities may be biased upward by perhaps 20% because of obesity. Finally, the prevalence of pleural abnormalities in this group may not actually be increased as it is “near the internal background rate.” Further explanation of this latter point would be helpful as it is not clear what the true internal background rate is.

Paper 3—Environmental mesothelioma associated with fibrous tremolite asbestos: Lessons from the experiences of Turkey, Greece, Corsica, New Caledonia and Cyprus
Stavros H. Constantopoulos

Constantopoulos reviews the occurrence of mesothelioma due to non-occupational domestic exposure to asbestiform minerals. This exposure is unrelated to occupation but is from domestic use of asbestos with exposure coming from the processing of asbestos for use as white-wash and/or continuous dust from the walls of the home. Locations and characteristics included the following:

Cappadokia, Turkey. This is the first known incident of exclusively environmentally caused mesothelioma, with half the population dying of mesothelioma at early ages

of 35–55. The population lived in caves built in volcanic rock containing erionite (a fibrous zeolite). Most villagers now live in modern houses so the epidemic may begin to decline because of the reduction in exposure. There was also a high incidence of pleural plaques, but it appears those with plaques had a reduced incidence of mesothelioma compared to those without plaques.

A recent genetic study (Dogan et al., 2006) suggests both erionite exposure and a genetic predisposition are producing the mesothelioma epidemic in Cappadokia. In three villages mesothelioma occurs in certain houses but not in others, which led to the hypothesis that a unique, more carcinogenic erionite was present in certain houses. However, analysis indicated erionite had the same X-ray diffraction pattern and crystal structure in villages and homes irrespective of the occurrence of mesothelioma. Pedigree studies indicated mesothelioma was prevalent in certain families but not in others. When high-risk mesothelioma family members married into families with no history of it, mesothelioma appeared in the descendants. However, genetically predisposed family members do not seem to develop mesothelioma when born and raised outside the mesothelioma villages.

These new data suggest erionite exposure and predisposition may be necessary for the occurrence of mesothelioma related to environmental exposure to erionite.

Cyprus. The iron rich form of tremolite asbestos called actinolite has been described in the Akapnov Forest area of Cyprus but not in the chrysotile mine in Troodos (Ross and Nolan 2003). Mesothelioma was diagnosed in an elderly woman from a nearby village. But she was a non-miner and it was tremolite asbestos fibers in the lung, not chrysotile. On further investigation 12 additional cases of mesothelioma were discovered among miners, wives of miners and non-miners in villages away from the mine. Tremolite–actinolite asbestos was considered the attributable cause in all cases. The source of tremolite–asbestos has been shown to be present outside the chrysotile mine and it was found in domestic and outdoor dust samples.

Corsica. In northeast Corsica there was a chrysotile mine operating till 1965. Chrysotile miners had a relatively low prevalence ($\sim$ 4%) of pleural plaques. However, 41% of a sample of residents in a nearby village had pleural plaques. Surrounding the chrysotile mine were zones where there were surface deposits of (tremolite?) asbestos. Since the village was in this asbestos zone, environmental exposure from the surface deposits was considered the cause of pleural plaques.

New Caledonia. A high incidence of mesothelioma and lung cancer among women living in New Caledonia was associated with non-occupational environmental exposure to tremolite asbestos contained in whitewash applied to walls of the home. Pleural plaques were not mentioned.

It is interesting that in Cappadokia pleural plaques seem to be a protective factor against mesothelioma. In Cyprus, Corsica and New Caledonia tremolite asbestos from local outcroppings seemed to be the causative agent for

1. Mesothelioma (with no mention of pleural plaques) in Cyprus.
2. Pleural plaques (with no mention of mesothelioma) in Corsica.
3. Mesothelioma and lung cancer (with no mention of pleural plaques) in New Caledonia.

Are these data contradictory or are these differences in response due to differences in exposure, susceptibility, physico-chemical properties of the fiber or some combination of these factors or some factor we have yet to discover?

Reference

- Dogan, A.U., Baris, Y.I., Dogan, M., Emri, S., Steele, I., Elmishad, A.G., Carbone, M., 2006. Genetic predisposition to fiber carcinogenesis causes a mesothelioma epidemic in Turkey. *Cancer Res.* 66, 5063–5068.
- Ross, M., Nolan, R.P., 2003. History of asbestos discovery and use and asbestos-related disease in context with the occurrence of asbestos within ophiolite complexes. *Geol. Soc. Am.* 373, 447–476 (special issue).

Paper 4—Investigation of exposure to commercial asbestos in Northeastern Minnesota iron miners who developed mesothelioma

Wendy M. Brunner, Allan N. Williams, Alan P. Bender

Northeastern Minnesota has a 70% excess of mesothelioma. Since there is no excess among women it seems likely the source of exposure is occupational. Assuming a latency of 20 years the relevant exposures would have been prior to about 1970. Potential sources of exposures that might cause mesothelioma included a manufacturing plant using several types of asbestos as a raw material. Another potential source was iron mining where about 72,000 individuals

had worked between the 1930s and early 1980s. Taconite, a lower grade iron ore containing nonasbestiform amphiboles had been mined since 1955. There have been several mortality studies of iron ore miners, but no cases of mesothelioma were identified. Major limitations of these studies was that latency was short for mesothelioma and the death certificate was the source for identifying cause of death.

The purpose of the Brunner et al. study was to mesothelioma among iron ore workers to identify possible sources of asbestos exposure as part of the mining experience. They used the Minnesota Cancer Surveillance System (MCSS) to identify mesothelioma cases from 1988 to 1996. Use of the MCSS is a strength of this study as many mesothelioma cases will be missed if death certificates alone had been used. Of the 340 male cases of mesothelioma, 5% had worked in the iron mining industry. For the fifteen cases with sufficient work histories, 14 were identified as having worked in jobs with possible or probable asbestos exposure. Exposure to commercial asbestos (only in mining jobs) was identified for four miners in such jobs as carpenter, maintenance mechanic and plumber.

Brenner et al. conclude that commercial asbestos exposure is a likely cause of mesothelioma among iron miners in this series and that there are jobs within the mining industry where asbestos exposure occurs. They appropriately indicate that case series studies must be cautiously interpreted. Since asbestos is strongly associated with mesothelioma (in fact is often a marker of asbestos exposure), their extensive (and blinded) assessment of exposures makes their conclusions reasonable. The inability to find a source of commercial asbestos exposure in at least one miner suggested other causes besides asbestos cannot be ruled out. Because one miner without identifiable asbestos exposure is too few individuals to do further analysis, they were unable to further evaluate taconite as a possible cause of mesothelioma.

Risk of gastrointestinal cancers from inhalation and ingestion of asbestos

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Abstract

This paper summarizes the weight of epidemiological evidence to evaluate the hypothesis that asbestos exposure is causally associated with increased risk of gastrointestinal (GI) cancers as suggested by Selikoff in an early study of insulation workers. This review looks at populations that develop GI cancers, namely stomach, colorectal, colon and rectal. Guidelines for assessing causality are strength of association, biological gradient and consistency of the associations. Exposure–response (E–R) was evaluated using three methods to estimate exposure. Rate Ratios (RRs) for lung cancer and percent of mesothelioma are used as surrogate measures of asbestos exposure for all the cohorts of exposed workers. Quantitative or semi-quantitative estimates of cumulative exposure to asbestos were also used to assess E–R trends and were compared to E–R trends for lung cancer and mesothelioma in individual studies. Surrogate measures are important since there are few individual studies that have assessed E–R. None of the various methods to estimate asbestos exposure yielded consistent E–R trends and the strength of the associations were consistently weak or non-existent for the four types of GI cancers. The epidemiological evidence detracts from the hypothesis that occupational asbestos exposure increases the risk of stomach, colorectal, colon, and rectal cancer. Findings are briefly summarized below.

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Keywords: Asbestos; Colon cancer; Colorectal cancer; Gastrointestinal cancers; Ingestion; Lung cancer; Mesothelioma; Rectal cancer; Review; Stomach cancer

1. Introduction

Selikoff et al. (1979, 1980) reported that among 632 building trades insulation workers with “light, intermittent exposure to asbestos” there was a 3-fold increased risk of GI cancers. Based on the 29 cancer cases, they concluded that the “data suggest that there may perhaps be an etiological relationship between industrial asbestos exposure and carcinoma of the gastrointestinal tract”. With 20 more years follow-up GI cancers still showed the 3-fold excess. Lung cancer showed a 7-fold increased risk at both time periods, while the occurrence of mesothelioma increased from 7% of total cancers to 18% during the follow-up.

20 or more years follow- up	Obs/Exp = SMR (1942–1963) Selikoff et al. (1964)	Obs/Exp = SMR (1942–1977) Selikoff et al. (1979)
Lung cancer	42/6 = 7.0	93/13.3 = 7.0
Mesothelioma (<i>N</i> cases/ total cancers)	7/95 = 7.4%	38/210 = 18.1%
Stomach	12/4.3 = 2.79	19/5.4 = 3.5
colorectal	17/5.2 = 3.27	23/8.3 = 2.8

Since then there have been a large number of mortality studies of asbestos workers and several reviews examining the associations of asbestos exposure and GI cancers. The conclusions are somewhat varied and range from a clear causal association to a lack of evidence to support

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the causal criteria or the presence of biased associations (Miller, 1978; Levine, 1985; Doll and Peto, 1985; Neugut and Wylie, 1987; Edelman, 1988; Frumkin and Berlin, 1991; Arbmman et al., 1993; Homa et al., 1994; Gamble, 1994; Weiss, 1995; Goodman et al., 1999). The preponderance of the conclusions has been about colorectal cancer. But combining colon and rectal cancers might hide an association as suggested by Arbmman et al. (1993). There have been fewer studies of stomach cancer, although in the follow-up study of the insulation cohort of Selikoff et al. (1979), stomach cancer showed an increased SMR and colorectal cancer a decreased SMR.

The purpose of this review is to evaluate the association between asbestos exposure and risk of stomach, colon and rectal cancers separately. The weight of the evidence from epidemiological studies will be graphically displayed so the causal criteria of strong association, exposure–response trends, and consistency can be evaluated. Known risk factors for these GI cancers will be briefly summarized to help identify potential confounders.

2. Methods

2.1. Study populations

A search of Toxline and Medline was conducted to identify cohort or case–control studies of asbestos-exposed workers where mortality or incidences of stomach, colon, rectal or colorectal cancers were analyzed. The references from individual studies and reviews were also searched for additional studies not obtained in the literature search. Cohorts or case control studies nested within asbestos-exposed cohorts will be the primary study populations included to be more certain of asbestos exposure. Only the latest updates of relevant studies were included in the tabulations.

2.2. Causal criteria

The weight of the evidence to assess the validity of the hypothesis that asbestos exposure causes stomach, colon or rectal cancer will be based on three causal criteria. These are strength of association, biological gradient, and consistency. None of these criteria alone or a single study alone can completely refute or confirm a causal relationship. The weight of the evidence refers to the pattern from the existing studies as to whether or not there is a convincing case for the hypothesis of a causal relationship.

- *Strength of association* refers to how much the risk ratios are above no risk, or the null value of one. A risk ratio greater than about 1.5–2 is less likely to be caused by bias or other factors and more likely to be due to asbestos. In external comparisons the strength of association is the standardized mortality ratio (SMR) or incidence ratio (SIR), which compares the cause-specific mortality or incidence of asbestos-exposed workers with an external comparison group, adjusted for age, race, and gender and cannot account for possible effects of confounding exposures such as smoking or diet for example. Consistently weak associations are considered to detract from a causal association.
- *Biological gradient* refers to the presence of a dose–response (or exposure–response, E–R) trend for cancer risk to increase with increasing exposure to asbestos. Since the comparison group is generally fellow workers this internal analysis is less likely to be confounded by lifestyle risk factors. Also, this analysis gets higher weight because it is based on individual estimates of exposure rather than surrogates. The consistent lack of an E–R trend is considered to detract from the hypothesis of a causal association.

- *Consistency* is the repeated observation of an association in different populations under different circumstances. If most of the associations are weak or null and there are no apparent E–R gradients, then the weight of the evidence is suggestive that there is unlikely to be a causal association. Moderate or strong associations at higher exposures suggest that asbestos may cause GI cancer at those levels of exposure.

2.3. Exposure surrogates

Relatively few studies of GI cancers have assessed E–R. Therefore, average risk of lung cancer and mesothelioma are exposure surrogates that have been utilized to crudely assess biological gradient of asbestos and GI cancer. A useful surrogate should satisfy two criteria. One, the surrogate must show an exposure–response relationship. Second, the surrogate exposure measure is increasingly informative when the health outcome is specific for asbestos and is not confounded by other uncontrolled exposures.

Risk of both lung cancer and mesothelioma increase as asbestos exposure increases, albeit with different slopes, and are therefore a useful surrogate measure of exposure. Many studies have shown that the risk of lung cancer increases with increasing exposure to asbestos (Dupre et al., 1984), although there is some heterogeneity in the slope of the exposure–response curve and there may be a threshold below which no increased risk may be observed (Goodman et al., 1999; Brown et al., 1994). Brown et al. (1994) shows that where there are estimates of exposure the threshold for increased risk of lung cancer is somewhere in the range of 25–100 f/cc. He also notes that several studies show no increased risk although asbestos exposure was not negligible as evidenced by the occurrence of mesothelioma, pleural changes, and some asbestosis. Mesothelioma is related to duration of exposure up to ~30 years, with few observed deaths for exposure less than about 3 months (Liddell, 1993). Dupre et al. (1984) consider it unlikely that mesothelioma cases may have been caused by insignificant doses of asbestos. They suggest all the evidence supports the idea that mesothelioma is dose-related, but that only a few cases are expected to occur after brief or low exposures. Using percent mesothelioma as a proxy estimate for asbestos exposure, Goodman et al. (1999) showed that lung cancer SMRs increased in an exposure–response fashion with increasing percentages of mesothelioma deaths. Counts of long fibers in the lung of mesothelioma cases indicate that as the number of fibers increases the risk does also, so that at the histological level there is a biological gradient (Tuomi et al., 1991; Becklake and Case, 1994). These data also suggest that amphiboles may be more toxic than serpentines.

Asbestosis is caused by asbestos exposure in an exposure-related manner. However, the diagnosis is based on clinical examination of X-ray findings of fibrosis plus a history of exposure. Many of the studies do not report asbestos as a cause of death and non-malignant causes of respiratory mortality often include non-asbestos related causes so that the role of asbestos cannot be readily assessed.

Mesothelioma is a more appropriate indicator of asbestosis than lung cancer in that there is greater specificity and no confounding from smoking. Potential drawbacks of using lung cancer as an exposure surrogate are a lesser degree of specificity and potential confounding effect from cigarette smoke. Lung cancer is also caused by other occupational exposures (e.g. radon), but these exposures are unlikely to be present in these studies.

Asbestos exposure is a more or less specific cause of mesothelioma that is independent of smoking. In most cases the SMR for mesothelioma is not estimated, and only the number of cases is reported. In this review the number of mesotheliomas divided by the total number of cancer expressed as a percent is used as the measure of risk and asbestos exposure. Total cancer is used instead of total deaths because the latter is not available for incidence studies of cancer.

In summary, the reasoning behind this assessment of biological gradient is as follows:

- Asbestos exposure causes lung cancer and mesothelioma and the risks are dependent on the level of exposure.
- The greater the risk of lung cancer and mesothelioma the greater the asbestos exposure in the cohort of workers.
- Therefore, using SMRs for GI cancers from individual studies and stratifying by risk of lung cancer and mesothelioma provides crude estimates of E–R for asbestos exposure and GI cancer. Mesothelioma risk is considered the better indicator since asbestos exposure is the best known/most common cause of mesothelioma; smoking does not appear to increase the risk of mesothelioma, so the mesothelioma risk is relatively unconfounded by smoking or other factors. On the other hand, a major cause of lung cancer is smoking, so the lung cancer SMR might be over-estimated (biased) because of higher smoking among asbestos-exposed workers than among the comparison group.

2.4. Occupation and fiber type as exposure surrogates

Fiber type further complicates the issue of using a proxy measure of asbestos exposure. Most of the studies involve exposure to several fiber types, although often there is a predominant type. Amphiboles appear to pose the greater risk for mesothelioma, perhaps less so than for lung cancer, and mixed fiber types a greater risk for lung cancer (Dupre et al., 1984). But if asbestos causes any of the GI cancers it is not clear which fiber-type might show the strongest association. Assessment by fiber type is made difficult by the fact that the use of different types is often not well defined and because several types are often used at varying time intervals. Also risk of GI cancer has not been assessed by intensity of exposure within the occupational groups. Analysis by fiber type will not be assessed in this review.

2.5. Ranking the usefulness of asbestos exposure estimates

The rank order of biological gradients is weighted as:

1. *Individual-level E–R*: Internal comparisons are considered the most important because there is less potential confounding, and cumulative exposure is directly related to individual asbestos exposure of each GI cancer case. Quantitative exposure estimates (e.g. f/cc-years or mppcf-years) are considered superior to qualitative estimates such as high Vs low exposure categories. E–R trends for lung cancer and mesothelioma are graphically displayed when available. These graphs provide some measure of reliability of the individual estimates of cumulative asbestos exposure and also provide a comparison between asbestos-attributable mortality (lung cancer, mesothelioma) and GI cancer where attribution is being assessed. If there is a causal association of asbestos exposure and GI cancers, the E–R should to some respect mirror the lung cancer/mesothelioma E–R trends.
2. *Surrogate E–R (mesothelioma)*: External comparisons of studies stratified by mesothelioma risk is of moderate weight because mesothelioma is a specific result of asbestos exposure and is not confounded by smoking and less confounded by lifestyle. Thus, mesothelioma compared to lung cancer is considered the better proxy for evaluating asbestos/GI cancer exposure-response trends and more weight will be given to these findings in assess causality.
3. *Surrogate E–R (lung cancer)*: External comparisons of studies stratified by risk of lung cancer are given lesser weight because smoking is a primary cause of lung cancer and potentially confounds risk.

Similar results from lung cancer and mesothelioma analyses increase the likelihood of a correct interpretation, but a greater weight will be given to the mesothelioma results. Contradictory evidence reduces the weight of evidence.

3. Results

Results are presented individually for stomach cancer, colorectal cancer (CRC), colon and rectal cancer. The pri-

mary results are E–R trends presented in reverse order of importance: one figure each for surrogate E–R gradients (risk of lung cancer and mesothelioma) followed by variable numbers of graphs displaying E–R trends for individual studies.

Table 1 is a summary of the results from the 44 studies of asbestos-exposed workers included in this review. In Tables 2 and 3 the data from Table 1 are rearranged by type of GI cancer in order of increasing exposure (estimated by risk of lung cancer and mesothelioma, respectively) and are the bases of the visual representation of E–R using surrogate exposures.

3.1. Stomach cancer

Overall there are 37 cohorts with 791 stomach cancer cases enumerated with an overall risk ratio (RR) of 1.01 (0.94–1.08). Eighteen of the studies had RRs of 1.0 or less. There were two small studies that reported no excess risk but did not report the number of cases (Tulchinsky et al., 1999; Szeszenia-Dabrowska et al., 1998). About a third of the cases were from two studies. The largest was the last follow-up of the cohort of Canadian chrysotile miners and millers with 158 cases and an SMR of 1.26 (1.07–1.48) (Liddell et al., 1997). The other was a population-based survey of Norwegian men with 100 cases and qualitative asbestos exposure based on questionnaires (Waage et al., 1993). The stomach cancer SMR was 0.81 (0.66–0.99). The idea was to assess the risk of asbestos-related disease, but incidence of both lung cancer (SIR = 0.99) and mesothelioma (0.65%) were low, suggesting asbestos exposure was also low.

3.2. Surrogate E–R

Fig. 1 shows there is no apparent association for the risk of stomach cancer to increase as risk of lung cancer increases. The point estimates for stomach cancer tended towards 1.0 in cohorts when the excess lung cancer risk was less than 4-fold and tended to be somewhat elevated when lung cancer RRs were 4-fold or greater. The only significant association was a 4-fold increased risk of stomach cancer (5 cases) when lung cancer risk was increased 6-fold among Chinese workers with very high exposures to Chinese Chrysotile (Pang et al., 1997). Exposures in the 1950s ranged from about 2.5 to 415 mg/m³ and from about 0.7 to 35 mg/m³ in the 1960s. All the other risks of stomach cancer were 2-fold or less in individual studies. Combined RRs for stomach cancer stratified by lung cancer categories showed suggestive trend with a significant deficit (0.80) when lung cancer SMRs were <1.0 that increased monotonically to a significant 1.43-fold excess in the studies with lung cancer SMRs >3.0 (Table 2).

There was no apparent visual association between stomach cancer risk and the incidence of mesothelioma as shown in both individual study results (Fig. 2) and from

Table 1

Summary of studies of asbestos-exposed workers showing risks of lung cancer, mesothelioma, and GI cancers

Study	Exposure	% Meso	Lung Cancer	Colon	Colorectal	Rectum	Stomach	Comments
Selkoff et al. (1979)	17800 U.S./Canada Insulation workers; follow-up 1967-76;	> 20 yrs latency 101/845 = 11.95%	> 20 yrs latency 397/93.7 = 4.24 (3.84-4.68)		> 20 yrs latency 54/39 = 1.38 (1.05-1.82)		> 20 yrs latency 18/12.7 = 1.42 (0.84-2.24)	Ch, Am Includes cohort of 632 NY/NJ insulation workers in original 1964 Selkoff study.
Selkoff et al (1980)	582 male amosite factory workers, 1941-1954 with >20-yrs latency; follow-up 1961-1977	4/103 = 3.9%	52/10.1 = 5.15 (3.88-6.81) 0		11/5.2 = 2.12 (1.06-3.79)		4/2 = 2.0 (0.54-5.12)	Factory workers in NJ plant making amosite products for shipyards and other industrial facilities, many with short-term exposures; plant closed in 1954
Thomas et al. (1982); update of Elwood et al (1964)	1970 asbestos cement factory workers > 6 mos 1936-1977; 1977 follow-up;	2/58 = 3.41% 1935-6: Cr use: 2/22=9.1%	> 15 yrs latency 24/25.8 = 0.93(0.60-1.39) 1935-6: Cr use: 7/9.2=0.76 (0.31-1.57)		> 15 yrs latency GI 14/14.1 = 0.99(0.54-1.67) 1935-6: Cr use: 6/5=1.20 (0.44-2.92)			>15 y latency GI tract cancers Cr 1935-6; Ch use after 1936; 50% worked < 2 yrs, 75% < 4 yrs; wet process and low asbestos levels
Berry and Newhouse (1983)	13460 workers making friction material, employed 1941 +, follow-up to 1980; 10-yr latency	> 10 yrs latency 10/419=2.4% <10 y: 1/56=1.8% > 10 yrs 9/184=4.9%	> 10 yrs latency 159/150.8=1.05 < 10 y: 23/22=1.05 >10y: 60/49.6=1.21 CC by f/ml-yrs OR (n cases) <10 : 1.0 (50) 10-49: 0.79 (37) 50-99: 0.86 (13) 100-356: 0.88 (5)		GI Cancer: > 10yrs latency: combined men+women 123/134.6=0.91 (0.76-1.09) SMR = 23/18.1 = 1.27(0.81-1.91) SMR = 33/41.5 = 0.80(0.55-1.11) Case-control by f/ml-yrs: matched on DOH, DOB, survival time; same controls for lung and GI cancers: <10 f/ml-yrs: 1.0 (36/36) 10-49: 1.18 (40/33.9) 50-99: 0.83 (9/10.8) 100-356: 0.24 (1/4.2)			Ch used almost exclusively except: Cr 1929-33; 1939-44 used in well-defined areas and minority exposed; all mesos had Cr exposure; No excesses or E-R for lung or GI cancers associated with Ch, but exposures low (< 100 f-yrs/ml)
McDonald et al (1984)	3641 > 1 mos 1938-58 in Conn. Textile plant; follow-up to 1978	> 20-yr latency 0/202=0%	20-yr latency 73/49.0 = 1.49(1.18-1.88)		> 20-yr latency Digestive Cancers: 59/51.75 = 1.14 (0.88-1.48)			Ch
Acheson et al. (1984)	5969 Insulation manufacture; 1945-78; 1980 follow-up	5/109 = 4.6% (4 = mesos counted in lung cancer deaths) 0/24=0 (other)	Asbestos exposed: 61/29.1 = 2.10(1.62-2.71) Other (not asbestos) 10/9.4=1.06	Asbestos exposed: 6/4.4 = 1.37(0.50-2.97) Other (not asbestos) 2/1.4=1.42 (0.17-5.2)	-----	Asbestos exposed: 4/3.2 = 1.24 (0.34-3.2) Other(not exposed) 0/1.1=0	Asbestos exposed: 7/7.5 = 0.94 (0.37-1.92) Other: 4/2.5=1.59 (0.44-4.1)	20-40% Am + intermittent Ch, Cr
Ohlson et al. (1984)	3442 Railroad maintenance; > 3 wks 1939-80	5/144 = 3.5% latencies = 30-57 yrs	> 20 yrs latency 27/25.7 = 1.05(0.69-1.53) Cum Exposure score Low: 2/7.5=0.27 (0.003-0.96) Mod: 2/3.7=0.53 (0.07-1.95) High: 6/4.5=1.34 (0.49-2.91) Very hi: 17/10= 1.62 (0.99-2.72)		> 20 yrs latency 15/20.9 = 0.72(0.40-1.18)		> 20 yr latency 30/51.1 = 0.59 (0.40-0.84) Cum Exposure Low: 3/10.2=0.29 (0.01-0.86) Mod: 6/6.2=0.96 (0.36-2.11) Hi: 7/10.1= 0.69 (0.28-1.43) Very hi: 14/24.6 =0.57 (0.31-0.96)	>20 y latency Ch, Cr, Am Cum exposure = Σ(intensity x yrs worked)
Finkelstein (1984)	535 asbestos cement > 1-yr before 1960; follow-up to 1978	> 20-yr latency 8/44=18.2%	> 20-yr latency 21/4.1=5.12 ()		> 20-yr latency GI = 8/2.8= 2.86 (1.23-5.63)			Ch, Cr in production workers >1 mos asbestos exposure < 1962; All cause SMR = 1.81
Ohlson and Hogstedt (1985)	1176 Swedish asbestos cement workers; >3 mos 1943-76; follow-up to 1982;	0 / 44 = 0	0 latency=1/9=1.23 > 20 yrs latency SMR = 6/4.3 = 1.40 <2 yr tenure = 3/1.3 = 2.31		GI cancer: no latency = 1/5.9=0.17(0.004-0.94) > 20-yr latency SMR = 3/5.1 = 0.59 (0.12-1.72) < 2 y tenure SMR = 3/1.5=2.0(0.41-5.84)			<1970: dust ~2 f/ml, 10 mg/m3 dust; 1970s: ~ 1 f/ml, ~ 5 mg/m3 ; Ch mostly; <1% Am 149-51, Cr 1962;
Peto et al. (1985)	Textile factory Cohort I	> 10-yr latency 2/23 = 8.7%	> 10-yr latency 13/1.58 = 8.23(4.38-14.1)		> 10-yr latency 2/0.98 = 2.04(0.25-7.4)		> 10-yr latency 2/1.02 = 1.96 (0.24-7.08)	>10 y latency Men >20 y before 1933 Mainly Ch, 5% Cr
	Cohort II	0/19 = 0	4/1.90 = 2.11(0.57-5.4)		4/2.02 = 1.98(0.54-5.1)		2/1.08 = 1.85 (0.22-6.69)	>10 y latency Women >10 yrs employment
	Cohort III	10/184 = 5.4%	93/64.6 = 1.44(1.17-1.77)		13/16.7 = 0.78(0.41-1.33)		18/16.7 = 1.08 (0.64-1.70)	>20 y latency hired after 1933 Men
Seidman et al. (1986)	820 men Amosite asbestos factory 1941-5	>5 yrs latency 6/197=3.05%	102/20.5=4.97(4.08-6.1) >5 yr latency: f/ml-yrs <6: 14/5.31=2.64* 6-12: 12/2.89=4.15* -25: 15/3.39=4.42* -50: 12/2.78=4.32* -100: 17/2.38=7.14* -150: 9/1.49=6.04* -250: 12/1.32=9.09* 250+: 11/0.94=11.7*		SMR for colorectal cancer: 22/11.9 = 1.85 (1.16-2.79) Total GI cancer SMR = 32/19.74=1.62(1.12-2.29) >5 yr latency: f/ml-yrs for GI cancer: O/E= SMR <6: 8/4.83 = 1.66 (0.71-3.26) 6-12: 2/3.05= 0.66 (0.08-2.37) -25: 9/3.29 = 2.74 (1.25-5.2) -50: 1 / 2.48 = 0.40 (0.01-2.25) -100: 7/2.30 = 3.04 (1.22-6.27) -150: 2/ 1.43 = 1.40 (0.17-5.05) -250: 1/1.35 = 0.74 (0.02-4.13) 250+: 2/1.02 = 1.96 (0.24-7.08)		9/5.78 = 1.56 (0.71-2.96)	>5 y latency Am
Hodgson and Jones (1986)	31,150 UK asbestos workers; 1981 follow-up;	>10 y latency: worked < 1969 34/196= 11.95%	>10 y latency: worked < 1969 SMR: 152/112.1 = 1.36 (1.15-1.59) Bv yrs worked: <10: (40) 0.92 >10: (145) 1.41 only after 1969 1/1.0=0.96		>10 y latency: worked < 1969 SMR: 5/15.4 = 0.33 (0.11-0.76) Bv yrs worked: <10: (1) 0.40 >10: (5) 0.45 only after 1969 0/2		>10 y latency: worked < 1969 SMR: 9/12 = 0.75 (0.34-1.42) Bv yrs worked: <10: (1) 0.52 >10: (9) 0.82 only after 1969 0/1	>10 y latency Mixed asbestos; Only considered those working before 1969, when exposures higher and longer latency

(continued on next page)

Table 1 (continued)

Study	Exposure	% Meso	Lung Cancer	Colon	Colorectal	Rectum	Stomach	Comments
Gardner et al. (1986)	2167 UK chrysotile cement factory; employment + follow-up 1941-83;	1/121 = 0.83%	41/42.2 = 0.97 (0.70-1.32)	6/9.2 = 0.65 (0.24-1.42)	-----	5/6.2 = 0.81 (0.26-1.88)	15/13.7 = 1.09 (0.61-1.81)	Ch, small amounts Am 1980-2; 1970+ mean levels <1 f/ml, most <0.5 f/ml; higher exposures <1968
Hughes et al. (1987)	6931 Chrysotile asbestos cement plant > 1 mo before 1970; follow-up 1982 or age 80. Assumed 1.4 f/ml = 1 mppcf	> 20-yr latency 4/353 = 1.1% Plant 1: 1/127=0.8% Plant 2: 3/226=1.3%	> 20-yr latency—lung cancer 155/115.5 = 1.34 (1.14-1.58) Colon f/ml-vrs Plant 2(>3 m) < 8.4 20/18.9=1.06 (0.65-1.63) 8.4-33.6 19/14.5=1.31 (0.79-2.04) 35-68.6 12/6=2.00 (1.03-3.5) 70-138.6 10/5.5=1.81 (0.87-3.35) >140 12/5.2=2.31 (1.19-4.04) f/ml-vrs Plant 1(>6 m) < 8.4 3/2.9=1.04 (0.21-3.02) 8.4-33.6 9/8=1.12 (0.52-2.14) 35-68.6 2/3.7=0.54 (0.07-1.95) 70-138.6 3/3.8=0.79 (0.16-2.31) >140 5/4.1=1.22 (0.40-2.84)	> 20-yr latency—colorectal cancer 21/23.3 = 0.90 (0.56-1.38) Plant 2 > 3 mos 2/3.9=0.51 (0.06-1.85) 8.4-33.6 1/2.8=0.36 (0.01-1.44) 35-68.6 0/1.2 = 0 70-138.6 3/1.1=2.73 (0.56-7.96) >140 0/1.0 = 0	-----	-----	> 20-yr latency 22/19.5 = 1.13 (0.71-1.70) Plant 2 (>3 mos) <8.4 3/3.2=0.93 (0.19-2.74) -33.6 4/2.3=1.74 (0.47-4.45) -68.6 1/0.8=1.25 (0.03-6.96) -138.6 0/0.8 = 0 >140 1/0.7=1.43 (0.04-7.96)	>20 yr latency Ch = primary asbestos in Plant 1 and 2 Plant 1 = small amount Am and Cr from early 1960s; Plant 2 = Cr used continuously since 1946
Enterline et al. (1987)	1074 Asbestos workers retired 1941-67; follow-up 1980;	8/208 = 3.8%	77/28.44 = 2.71 (2.15-3.40)	14/14.24 = 0.98 (0.54-1.65)	-----	9/5.66 = 1.59 (0.73-3.02)	20/11.09 = 1.80 (1.10-2.78)	88% mortality; production and maintenance workers of US asbestos products plant; Ch, Am, Cr
Amandus and Wheeler (1987); same mine as McDonald et al (1986)	575 Vermiculite miners and millers hired <1970 for >1 yr, follow-up 1970-81.	2/38 = 5.3%	SMR = 20/9 = 2.23 (1.36-3.45) <50 6/4=1.51 -99 2/1.4=1.46 -399 2/1.9=1.06 400+ 10/1.7=5.76	Digestive-Stomach(colorectal): SMR=4/6.5=0.62 (0.17-1.58) Digestive (150-159): SMR=6/8.1=0.74 (0.27-1.62) <50 F-yrs: 2/3.8=0.53 (0.06-1.9) 50-99 F-yrs: 2/1.2 = 1.67 (0.20-6.02) 100-399 F-yrs: 0/1.7 = 0 400+ F-yrs: 2/1.6 = 1.25 (0.15-4.51)	-----	-----	SMR = 2/1.6 = 1.24 (0.15-4.49)	Tremolite-actinolite asbestos, > 1 year
Armstrong et al (1988)	6505 miner/millers 1943-66; follow-up to 1981	32/207=15.5%	91/34.5=2.64 (2.15-3.24)	14/12.3=1.14 (0.67-1.92)	-----	-----	17/8.95 = 1.90 (1.18-3.06)	Cr; Only 73% follow-up of men
Tola et al. (1988)	608 pipefitters among Finnish shipyard workers >1 yr 1945-60; 1981 follow-up	0/48 = 0%	SIR = 23/15.0 = 1.54 (0.97-2.3)	SIR = 1/3.5 = 0.29 (0.01-1.59)	-----	-----	SIR = 2/6.1=0.33 (0.04-1.18)	No latency; asbestos used for insulation from ~1955-1975 and spraying common; exposure not high
Raffn et al. (1989)	7028 asbestos cement factory; all employed 1928-1984; follow-up incidence 1943-1984	13/580 = 2.24% SIR, pleural meso = 10/1.83 = 5.46 (2.62-10.05); >15 yr latency: 5 yr tenure: SIR = 13.6 (5.84-26.72) (n=8) SIR for mediastinum = 3/0.60 = 5.00 (1.01-14.61) Total meso SIR = 13/2.43 = 5.35	SIR = 162/89.8 = 1.80 (1.54-2.10) >15 yr latency <5 yr tenure: 45/25.82 = 1.74 (1.27-2.33) >5 yr tenure: 59/31.13 = 1.90 (1.44-2.45)	SIR = 32/30.16 = 1.06 (0.73-1.50) Raffn et al (1996); follow-up to 1990; Men only; > 15 yrs latency: SIR = 44/33.72=1.30 (0.95-1.75)	-----	SIR = 35/27.77 = 1.26 (0.88-1.75) Raffn et al (1996); follow-up to 1990; Men only; > 15 yrs latency: SIR = 35/27.44=1.28 (0.89-1.77)	SIR = 43/30.09 = 1.43 (1.03-1.93) >15 yr latency <5 yr tenure: 13/7.36=1.77 (0.94-3.02) >5 yr tenure: 15/11.83 = 1.27 (0.70-2.07)	Ch 1928-1946; Amosite 1946+; Cr 1952+; 1948: 50-800 f/ml; 1973: 41% > 2 f/ml
Melkild et al. (1989)	Norwegian shipyard	2/232 = 0.86%	>10-yr latency 50/29.2 = 1.71 (1.27-2.26)	>10-yr latency 7/13.4 = 0.52 (0.21-1.08)	-----	>10-yr latency 16/11.4 = 1.40 (0.80-2.28)	>10-yr latency 13/19.1 = 0.68 (0.36-1.16)	>10 yr latency Ch
Piolatto et al. (1990)	1058 Italian chrysotile miners >1 yr 1946-1987; follow-up 1946 to 1988;	2/82 = 2.4% SMR: 2/0.3=6.7 > 20-yr tenure: 2/0.2 = 10	SMR= 22/19.9 = 1.11 (0.69-1.67) By tenure: <10: 10/8.5 = 1.2 10-20: 4/3.8=1.1 >20: 8/7.6=1.1	Intestinal cancers = 6/6.6 = 0.91 (0.33-1.98) By tenure: <10: 3/2.9=1.0 10-20: 0/1.3 >20: 3/2.3 = 1.3	-----	-----	SMR = 12/12.7 = 0.94 (0.49-1.65) By tenure: <10: 4/5.8=0.7 10-20: 5/2.8=1.8 >20: 3/4=0.75	Ch; no fibrous amphiboles found in bulk samples; 0.2-0.5% fibrous silicate (balangeroite) with 0.2-1.5 µ diameters were found;
Albin et al. (1990)	1929 Swedish asbestos cement workers; >3 mos 1907-77; follow-up 1958-86	> 20-yr latency 13/164 = 7.9% f-vrs/ml 0 1.0 <15 1.9 (0.2-21) -39 21.2 (2.5-178) >40 23 (2.4-212)	> 20-yr latency 35 Obs RR = 1.8 (0.90-3.7) f-vrs/ml: RR 0 1.0 <15 1.8 (0.8-3.9) 15-39 1.9 (0.7-5.3) >40 1.9 (5-7.1)	> 20-yr latency 26 Obs; RR = 1.5 (0.7-3.0) f-vrs/ml: RR 0 1.0 <15 1.3 (0.5-2.9) 15-39 1.1 (0.3-3.9) >40 3.4 (1.2-9.5) p=0.04 for trend	-----	-----	> 20-yr latency 23 obs RR=1.0 (0.5-2.0) f-vrs/ml: RR (n=0.9) 0 1.0 <15 0.8 (0.3-1.8) 15-39 1.6 (0.6-4.4) >40 1.7 (0.2-3.3)	> 95% Ch, Cr, Am; 1233 industrial workers and non case referents used for comparison to estimate RR
Hilt et al. (1991)	287 asbestos exposed production & maintenance workers in HNO ₃ plant; follow-up incidence 1953-88	> 20-yr latency 6/52 = 11.5% Exposure Heavy: 3/26 = 11.5% Light: 3/28 = 10.7%	> 20-yr latency 19/4.59 = 3.88 Exposure Heavy: 6.47 (3.24-11.59) (11/1.7) Light: 1.75 (0.70-3.6) (7/4.0)	> 20-yr latency 3/3.0 = 1.0 (0.21-2.92) Exposure Heavy: 2.85 (0.57-8.36) (3/1.1) Light: 2/2.4 = 0.85 (0.08-3.05)	-----	0 cases	> 20-yr latency 5/4.3 = 1.16 Exposure Heavy: 1.66 (0.33-4.86) (3/1.8) Light: 0.59 (0.06-2.12) (2/3.4)	> 20-year latency Cr in early years, amphiboles + Ch from 1940s on.
Sanden et al (1992)	3893 Swedish shipyard workers; follow-up 7-15 yrs after exposure ceased; follow-up 1978-87	>20-yr latency + heavy exposure 8/70 = 11.4% SIR=14.3 (6.2-28)	>20-yr latency + heavy exposure 11/10.2=1.08 (0.54-1.9)	>20-yr latency + heavy exposure 9/8.2=1.10 (0.50-2.1)	-----	-----	>20-yr latency + heavy exposure 2/4 = 0.50 (0.06-1.8)	Ch
Cheng and Kong (1992)	Chinese chrysotile products workers, 1972-87; > 1-yr exposure before 1972	0/44 = 0%	21/6.67 = 3.15 (1.95-4.82)	0 cases	-----	0 cases	7/6.35 = 1.10 (0.44-2.27)	Ch in textiles, friction materials, asbestos cement

Table 1 (continued)

Study	Exposure	% Meso	Lung Cancer	Colon	Colorectal	Rectum	Stomach	Comments
McDonald et al. (1993); last update = Liddell et al. (1997)	11,000 Canadian chrysotile miners and millers born 1891-1920; >1 month 1904-1992, follow-up 1992; mppcf-yr exposure accumulated to age 55; deaths 1950-1992 after age 55	E-R = mppcf-yr 7 5/67=1.12 64/50.4=1.27 61/59.2=1.03 60/45.4=1.32 61/42.1=1.45 67/52.8=1.27 35/31.8=1.10 1.21 (1.10-1.33) 1.46 (0.98-2.16) 1.84 (1.49-2.28) 2.97 (2.18-3.96) Total % meso = 38/1900 = 2.0%	SMRs by mppcf-yr 7 5/67=1.12 64/50.4=1.27 61/59.2=1.03 60/45.4=1.32 61/42.1=1.45 67/52.8=1.27 35/31.8=1.10 1.21 (1.10-1.33) 1.46 (0.98-2.16) 1.84 (1.49-2.28) 2.97 (2.18-3.96) 587/431.6 = 1.36 Smoking NS: 33/60 = 0.55 ExS: 49/68.1 = 0.72 <20: 87/60.8 = 1.43 >20: 240/94.1 = 2.55 SIR = 246/248.2 = 0.99 (0.87-1.12)	Other Abdominal Cancers (150; 152-159) SMRs by mppcf-yr 51/59.3=0.86 (0.65-1.14) 39/42.8=0.91 (0.65-1.25) 49/46.7=1.05 (0.78-1.39) 31/34.4=0.90 (0.61-1.28) 38/31.7=1.20 (0.85-1.64) 31/39.2=0.79 (0.54-1.12) 21/24.7=0.85 (0.53-1.30) 260/279.6=0.93 (0.82-1.05) 11/15.06=0.73 (0.56-1.31) 33/36.7=0.90 (0.62-1.18) 15/13.4 = 1.12 (0.63-1.85) 319/343 = 0.93 (0.83-1.04) Smoking NS: 42/47.7 = 0.88 ExS: 42/45.6 = 0.92 <20: 36/40 = 0.90 >20: 51/58.6 = 0.87 SIR = 157/161.56 = 0.97 (0.83-1.14)	Colorectal SMRs by mppcf-yr 32/22.7=1.41 (0.97-1.99) 22/15.9=1.38 (0.87-2.09) 15/16.9=0.89 (0.50-1.46) 13/12.1=1.07 (0.57-1.84) 13/11.2=1.16 (0.62-1.98) 16/13.9=1.15 (0.66-1.86) 7/8.8=0.80 (0.32-1.64) 118/101.7=1.16 (0.96-1.39) 7/5.4=1.29 (0.52-2.67) 16/13.2=1.21 (0.69-1.96) 17/5.3=3.21 (1.87-5.13) 158/125.4=1.26 (1.07-1.48) Smoking NS: 13/14=0.93 ExS: 6/13=0.46 <20: 20/11.5 = 1.74 >20: 31/16.4 = 1.89	Rectum Stomach SMRs by mppcf-yr 32/22.7=1.41 (0.97-1.99) 22/15.9=1.38 (0.87-2.09) 15/16.9=0.89 (0.50-1.46) 13/12.1=1.07 (0.57-1.84) 13/11.2=1.16 (0.62-1.98) 16/13.9=1.15 (0.66-1.86) 7/8.8=0.80 (0.32-1.64) 118/101.7=1.16 (0.96-1.39) 7/5.4=1.29 (0.52-2.67) 16/13.2=1.21 (0.69-1.96) 17/5.3=3.21 (1.87-5.13) 158/125.4=1.26 (1.07-1.48) Smoking NS: 13/14=0.93 ExS: 6/13=0.46 <20: 20/11.5 = 1.74 >20: 31/16.4 = 1.89	Stomach SMRs by mppcf-yr 32/22.7=1.41 (0.97-1.99) 22/15.9=1.38 (0.87-2.09) 15/16.9=0.89 (0.50-1.46) 13/12.1=1.07 (0.57-1.84) 13/11.2=1.16 (0.62-1.98) 16/13.9=1.15 (0.66-1.86) 7/8.8=0.80 (0.32-1.64) 118/101.7=1.16 (0.96-1.39) 7/5.4=1.29 (0.52-2.67) 16/13.2=1.21 (0.69-1.96) 17/5.3=3.21 (1.87-5.13) 158/125.4=1.26 (1.07-1.48) Smoking NS: 13/14=0.93 ExS: 6/13=0.46 <20: 20/11.5 = 1.74 >20: 31/16.4 = 1.89	Ch Little tendency for inc SMRs below 300 mppcf-yr. Stomach Ca: Hi SMRs at <10 mppcf-y probably due to SES, and hi SMR of 3.2 due to excess <12 deaths; apparent smoking effect. Other Abdominal Cancers no apparent trends Lung Cancer: not trend < 300 mppcf-yr, and excess probably due to smoking; About 20% of excess above 300 mppcf-yr due to smoking;
Waage et al. (1993)	21319 Norwegian males 40+ years in 1982 population-based survey; 8-yr follow-up;	11/1695=0.65%	SIR = 246/248.2 = 0.99 (0.87-1.12)	SIR = 157/161.56 = 0.97 (0.83-1.14)	-----	SIR = 120/110.18 = 1.09 (0.90-1.31)	SIR = 100/123.25 = 0.81 (0.66-0.99)	Incidence; no lag; type of asbestos not reported; asbestos by questionnaire
Botta et al. (1991)	2608 men and 759 females working at Italian asbestos cement plant 1950-1980; follow-up 1964-1986	No latency M: 28/275 = 10.2% F: 15/79 = 19%	SMR M: 110/40.6 = 2.71 (2.23-3.27) F: 7/1.7 = 3.96 (1.59-8.16)	SMR: Males: 11/16.9 = 0.65 (0.32-1.16) Females: 7/3.9 = 1.80 (0.72-3.70)	-----	-----	M: 17/20.9=0.81 (0.47-1.30) F: 4/2.9 = 1.36 (0.37-3.48)	Plant active 1907-1980 producing asbestos-cement products e.g. sheets, chimney pipes, pipes; limited data on asbestos type, but includes Cr and Ch
Dement et al. (1994), Brown et al. (1994) add 15 y follow-up to Dement et al. (1983); same cohort as McDonald et al. (1983)	3002 chrysotile textile workers; > 1 mos 1940-1975, follow-up vital status to 1991;	2/283 = 0.7% Total: 2/283 = 0.71% WM: 2/137 = 1.5% BM: 0/48 = 0% WF: 0/98 = 0%	Total: 126/99.2 = 1.97 (1.69-2.28) WM: 74/32.17 = 2.30 (1.88-2.79) BM: 14/17.9 = 0.78 (0.47-1.22) WF: 38/38/13.8 = 2.75 (2.06-3.61)	Digestive and peritoneum (150,152-9) excluding stomach Total: 44/51.6 = 0.85 (0.62-1.14) WM: 20/19.8 = 1.01 (0.62-1.56) BM: 12/12.95 = 0.93 (0.48-1.62) WF: 12/19 = 0.63 (0.33-1.11)	-----	-----	Total: 9/10 = 0.90 (0.47-1.56) WM: 3/3.9 = 0.77 (0.21-2.0) BM: 6/3.75 = 1.60 (0.69-3.15) WF: 0/2.38	White male and females; black males Ch
Rosler et al. (1994)	616 German female asbestos workers exposed 3 yrs, > 9 yrs latency, 1977-88	13/32 = 40.6%	SPMR = 5/1.5 = 3.39 (1.10-7.90)	-----	SPMR = 3/3.1 = 0.96 (0.20-2.81)	-----	SPMR = 0/1.6 = 0 (0-2.31)	SPMR = standardized proportional mortality rate; Ch, perhaps some Cr
Giaroli et al. (1994)	3341 Italian cement workers; all workers employed at 10 factories 1952-1973 to 1987; follow-up June, 1989.	5/103 = 4.85% 5 more cases occurred at end of follow-up and not counted	33/26.5 = 1.24 (0.91-1.66) > 20-yr latency respiratory cancer: 20/9.63 = 2.08 SIR = 236/274 = 0.86 (0.75-0.97) >15 y latency: 230/268.1 = 0.86	Digestive tract + Peritoneum = 27/30.2 = 0.89 (0.59-1.31)	-----	-----	-----	Inadequate latency; 10-20% asbestos (50-95% Ch, 5-50% Cr); up to 44 f/cc <1975, < 1 f/cc in recent years;
Nokso-Koivisto et al. (1994)	8391 Finnish locomotive drivers 1953-1990; follow-up 1953-1991;	8/915 = 0.87% SIR = 4.05 (1.75-7.97)	SIR = 236/274 = 0.86 (0.75-0.97) >15 y latency: 230/268.1 = 0.86	SIR = 36/37 = 0.98 (0.69-1.36)	-----	29/34 = 0.85 (0.57-1.22)	86/112 = 0.77 (0.61-0.94)	Incidence; mainly An + Ch; Potential confounding exposure to combustion diesel, coal + lubricating oils, creosote, coal;
Mourman et al. (1994)	736 Male Finnish anthophyllite miners >3 mos exposure 1953-91. 167 Female miners >3 mos 1953-67; follow-up 1991	Total Male: 4/137 = 2.9% Exposure Hi: 4/91=4.4% Mod: 0/46=0 Total Female: 0/23=0% Exposure Hi: 0/16=0% Mod: 0/7=0%	Total Male: 76/26.4 = 2.88 (2.27-3.60) Exposure Hi: 3.15 (2.37-4.09) Mod: 2.35 (1.45-3.58) Total Female: 1/0.45 = 2.22 (0.06-12.4) Exposure Hi: 3.58 (0.09-20) Mod: 0/0.17=0 (0-21)	----- Total Female: 3/0.87=3.45 (0.71-10) Exposure Hi: 3.66 (0.44-13) Mod: 3.14 (0.08-3.14)	----- Total Female: 3/0.87=3.45 (0.71-10) Exposure Hi: 3.66 (0.44-13) Mod: 3.14 (0.08-3.14)	----- Total Female: 1/0.66=1.52 (0.04-8.44) Exposure Hi: 2.39 (0.06-13) (1) Mod: 0 (0-15.2)/	Total Male: 13/9.2 = 1.42 (0.76-2.43) Exposure Hi: 1.24 (0.50-2.56) (7) Mod: 1.71 (0.63-3.7) (6) Total Female: 1/1.49=0.67 (0.02-3.7) Exposure Hi: 0 (0-3.81) Mod: 1.89 (0.05-10.5) (1)	(≥ 3 months tenure, incidence, Amosite
Demers et al. (1994)	261 colon and rectal incident cases 1984-1991 in construction (jobs in insulation, sheetmetal, boilermakers, pipefitters, plumbers; 183 controls not in construction from random dialing	OR: Unexposed: 1.0 Exposed: 14.4 (5-41.4) Duration: <20 y: 3.7 (0.7-20.5) >20 y: 29.2 (8.4-101) Latency: <40 y: 12.4 (3.2-47.9) >40 y: 16.5 (4.4-62.3) Adj age, packyr	----- Adj age, packyr	OR: Unexposed: 1.0 Exposed: 0.4 (0.2-0.9) Duration: <20 y: 0.4 (0.1-1.2) >20 y: 0.4 (0.1-1.3) Latency: <40 y: 0.3 (0.1-1.2) >40 y: 0.5 (0.2-12.3) Adj age, packyr	OR: Unexposed: 1.0 Exposed: 0.5 (0.3-1) Duration: <20 y: 0.6 (0.3-1.5) >20 y: 0.4 (0.1-1.2) Latency: <40 y: 0.4 (0.1-1.3) >40 y: 0.6 (0.2-1.4) Adj age, packyr	----- Adj age, packyr	----- Adj age, packyr	Exposure based on occupational titles; no information on potential confounders (e.g. diet, physical activity, family history); high physical activity may have resulted in reduced risks;
Tsai et al. (1996)	1821 maintenance workers in refinery and petrochemical plant >1 yr in 1948; follow-up 1989;	5/166 = 3.01%	58/73.8 = 0.79 (0.60-1.02)	13/14.7 = 0.88 (0.47-1.52)	-----	2/3.0 = 0.66 (0.08-2.40)	4/6.8 = 0.59 (0.16-1.50)	> 20-yr latency; potential exposure jobs = insulator, pipefitter, boilermaker, electrician, welder, carpenter, laborer;

(continued on next page)

Table 1 (continued)

Study	Exposure	% Meso	Lung Cancer	Colon	Colorectal	Rectum	Stomach	Comments
Imbernon et al. (1996)	French workers in electric and gas industries exposed to asbestos	12/548 = 2.2%	Any exposure = 1.4(1.1–1.9) 310 cases fiber-yrs Adj OR 0 1.0 1.1 0.8(0.5–1.6) 3.6 0.6(0.3–1.1) 8.1 1.9(1.8–3.1) 33.8 1.4(0.8–2.6)	OR = 0.75(0.4–1.3) Adj for SES; 110 cases, 436 matched controls; “No association” between exposure to asbestos and colon cancer.	-----	-----	-----	Case-control study; total cancers include only pleural, lung, larynx, colon No exposure-response trend of colon cancer and asbestos exposure
Pang et al. (1997)	160 male + 370 female workers in Chinese asbestos plant with >1 yr by 1972; follow-up 1994	0/22 = 0%	9/1.47 = 6.12 (2.8–11.6) Men = 3/0.59 = 5.08 All smokers Female = 6/0.88 = 6.82 All nonsmokers 17–42 yrs latency; All > 15 yrs tenure All cases had highest level of exposure	Not reported	-----	Not reported	5/1.14 = 4.40 (1.42–10.2) Men = 5/0.64 = 7.9 Female = 0/0.5 = 0 Latencies = 18–26 yrs; 15–25 yrs exposure	Ch only; mfg brake shoes, textiles, rope; primarily Chinese Ch; very high exposures: 1950–60s: 2.5–415 mg/m ³ ; 1970–80s: 0.7–35.3 mg/m ³ ; 1990s: 0.5–16.7 mg/m ³ 78% males smoked; all females = nonsmokers;
Levin et al. (1998)	1130 former workers at Tyler, TX asbestos insulation pipe manufacture plant, 1954–1972;	10-yr latency 6/78 = 7.7% SMR: pleural meso = 4/0.1 = 28.8 (7.85–73.8)	10-yr latency SMR: 35/12.6 = 2.77(1.93–3.85)	10-yr latency SMR: 6/2.9 = 2.07(0.76–4.51)	-----	10-yr latency SMR: 0/0.7 = 0	10-yr latency SMR: 0/1.1 = 0	Possible incomplete ascertainment of cohort; 90% Amosite in insulation; Surveys 1967, 1970, 1971 with avg f/ml from 15.9–91.4; plant closed 1972 because of high exposures
Szeszenia-Dabrowska et al. (1998)	1526 workers at Polish asbestos cement plant; >3 mos 1959–1985; follow-up 1996;	14/95 = 14.7% Male SMR = 12/0.1 = 81.35 (35.3–127.4) Female SMR = 2/0 = 203 (24.4–733) 2 cases with 11 and 12 years latency;	SMR = 32/29.8 = 1.07(0.74–1.51)	SMR = 7/2.5 = 2.8(1.12–5.8)	-----	No significant excess	No significant excess	males + females; Cr used since beginning of plant 1959 till 1985; about 15% wt of processed asbestos; Ch also used; Dry processing so high dust levels, 30–40 f/ml in pipe cutting/grinding areas; 7–14 f/ml at fiber treatment / beater floor; also community exposure.
Tulchinsky et al. (1999) Follow-up of Djerassi et al. (1979) Tulchinsky et al. (1992)	3057 males Israeli asbestos cement plant; 1953–1992	21/153 = 13.7% SIR 1978–92 = 28/20.7 = 1.35(0.85–1.85) 21/0.37 = 56.8 (32–81)	SIR 1978–92 = 28/20.7 = 1.35(0.85–1.85)	SIR 1978–92 = 19/24.1 = 0.79(0.43–1.15)			No excess risk	90% Ch, 10% Cr; very high exposures in early yrs (could not see hands at arms length); lung cancer low in Israeli males; Short latencies (2 of mesos 11 and 12 yrs)
Battista et al. (1999)	734 Italian railway carriage construction and repair workers employed 1945–1969; follow-up 1970–1997.	5/99 = 5.1%; SMR = 5/0.38 = 13.3 (5.2–27.9) 2 meso cases alive and not counted in SMR	SMR = 26/21 = 1.24 (0.87–1.72) No excess respiratory cancer until latency > 20 years.	Intestine + Rectum = 6/6.45 = 0.93(0.41–1.84)			SMR = 13/9.95 = 1.31 (0.77–2.08)	Asbestos use began in 1940's, using Ch as insulating agent; Cr use began in 1950's as sprayed mixtures on internal surface of railway carriages
Weiderpass et al. (2003)	All Finnish women workers b 1906–1945; SIR of GI cancers correlated with job-related exposures at 0, low and med/hi levels	-----	-----	SIR: Lo: 1.14 (0.95–1.38) Hi: 0.87 (0.56–1.34) P=0.60	-----	SIR: Lo: 0.96 (0.71–1.30) Hi: 0.86 (0.50–1.49) P=0.57	SIR: Lo: 1.06 (0.83–1.35) Hi: 1.24 (0.85–1.79) P=0.25	Exposures based on job titles, so exposures and cancer risk were not linked with individual women but averaged over each job title; some false positives because of multiple comparisons.
Koskinen et al. (2003)	23285 men with >10 yrs in construction (<1980) or >1 yr in shipyard (<1976) or >1 yr in asbestos (<1981) product industry in 1990–2 follow-up to 1999	19/1392 = 0.93% (M) 0/55 = 0% (F)	SIR = 302 / 264.9 = 1.14 (1.01–1.26) F SIR = 7/2.9 = 2.39 (0.96–4.92)	SIR = 67 / 67 = 1.00 (0.77–1.26) (M) F SIR = 3 / 3.57 = 0.84 (0.17–2.45)	-----	SIR = 60 / 57.1 = 1.05 (0.80–1.34) (M) F SIR = 1 / 2.17 = 0.01–2.56)	SIR = 82 / 71.3 = 1.15 (0.92–1.43) (M) F SIR = 2 / 2.44 = 0.82 (0.10–2.96)	Screening program with worker primarily from construction; type asbestos not reported or known; average exposure relatively low; screening program in Finland; incidence

Colon + rectum column = colorectal cancer unless otherwise noted.

% mesothelioma = n mesotheliomas/total cancers exposed as percent

Rate ratios (usually SMRs) and 95% confidence interval for lung, colon and colorectal cancers with observed deaths/expected deaths

Ch = Chrysotile asbestos; Am = Amosite asbestos; An = Anthophyllite asbestos

combined results when stratified by mesothelioma exposure group where there were overall deficits in the highest and lowest mesothelioma exposure categories (Table 3).

3.3. Individual-level E–R

There are seven cohorts that have assessed individual-level E–R of stomach cancer with some estimate of asbestos exposure (Figs. 3–6). There is a consistent lack of significant excess stomach cancer risk but general increases in risk of lung cancer and mesothelioma. The largest and most important study of chrysotile miners/millers is sug-

gestive of a threshold for stomach cancer, lung cancer and mesothelioma.

Four studies have qualitative estimates of cumulative exposure with categorical categories (e.g. high, moderate) (Acheson et al., 1984; Meurman et al., 1994; Hilt et al., 1991; Weiderpass et al., 2003) (Fig. 3). For two of the studies with qualitative exposure estimates (Acheson et al., 1984; Meurman et al., 1994) the risk of stomach cancer decreased with increasing exposure while the risk of lung cancer and mesothelioma increased. Hilt et al. (1991) reported that the SMRs for stomach cancer went from a deficit (0.59) to a 66% increase while the increased

Table 2
Summary of risk of GI cancers stratified by risk of lung cancer

Lung cancer SMRs	Colon cancer SMRs	Colorectal cancer	Rectal cancer	Stomach cancer	Reference
<i>SMRs > 3.0 strong association with lung cancer</i>					
13/1.58 = 8.23	—	2/0.98 = 2.04 (0.25–7.4)	—	2/1.02 = 1.96 (0.24–7.08)	Peto et al. (1985) Cohort I
9/1.47 = 6.12	—	—	—	5/1.14 = 4.40 (1.42–10.2)	Pang et al. (1997)
52/10.1 = 5.15	—	11/5.2 = 2.12 (1.06–3.79)	—	4/2 = 2 (0.54–5.2)	Selikoff et al. (1980)
102/20.5 = 4.97	—	22/11.9 = 1.85 (1.16–2.79)	—	9/5.78 = 1.56 (0.71–2.96)	Seidman et al. (1986)
397/93.7 = 4.24	—	39/28.3 = 1.38 (1.05–1.82)	—	18/12.7 = 1.42 (0.84–2.24)	Selikoff et al. (1979)
7/1.7 = 3.96	—	7/2.9 = 1.80 (0.72–3.70)	—	4/2.9 = 1.38 (0.38–3.48)	Botta et al. (1991) (F)
19/4.9 = 3.88	3/3 = 1.0 (0.21–2.92)	—	—	5/4.3 = 1.16 (0.38–2.71)	Hilt et al. (1991)
5/1.5 = 3.39	—	3/3.1 = 0.96 (0.20–2.81)	—	0/1.6 = 0 (0.0–2.31)	Rosler et al. (1994) (PMR)
21/6.67 = 3.15	—	—	—	7/6.35 = 1.10 (0.44–2.27)	Cheng and Kong (1992) Ch
Subtotal	3/3 = 1.0 (0.21–2.92)	84/52.4 = 1.60 (1.29–2.0)	—	54/37.8 = 1.43 (1.08–1.88)	
<i>SMRs 2–3 moderately strong association with lung cancer</i>					
76/26.4 = 2.88	—	3/5.45 = 0.55 (0.11–1.6)	—	13/9.15 = 1.42 (0.76–2.43)	Meurman et al. (1994) (M)
35/12.6 = 2.77	6/2.9 = 2.07 (0.76–4.51)	—	0/0.7 = 0	0/1.1 = 0	Levin et al. (1998)
77/28.44 = 2.71	14/14.24 = 0.98 (0.54–1.65)	—	9/5.66 = 1.59 (0.73–3.02)	20/11.09 = 1.80 (1.10–2.78)	Enterline et al. (1987)
110/40.6 = 2.71	—	11/16.9 = 0.65 (0.32–1.16)	—	17/20.9 = 0.81 (0.47–1.30)	Botta et al. (1991) (M)
91/34.5 = 2.64	—	14/12.3 = 1.14 (0.67–1.92)	—	17/8.95 = 1.90 (1.18–3.06)	Armstrong et al. (1988)
7/2.9 = 2.39	3/3.57 = 0.84 (0.17–2.45)	—	1/2.17 = 0.46 (0.01–2.56)	2/2.44 = 0.82 (0.10–2.96)	Koskinen et al. (2003) (F) (SIR)
20/9.0 = 2.23	—	4/6.5 = 0.62 (0.17–1.58) digestive (stomach)	—	2/1.6 = 1.24 (0.15–4.49)	Amandus and Wheeler (1987)
1/0.45 = 2.22	3/0.87 = 3.45 (0.71–10)	—	1/0.66 = 1.52 (0.04–8.4)	1/1.49 = 0.67 (0.02–3.7)	Meurman et al. (1994) (F)
4/1.9 = 2.11	—	4/2.02 = 1.98 (0.54–5.1)	—	2/1.08 = 1.85 (0.22–6.7)	Peto et al. II (1985)
61/29.1 = 2.10	6/4.4 = 1.37 (0.50–2.97)	—	4/3.2 = 1.24 (0.34–3.2)	7/7.5 = 0.94 (0.37–1.92)	Acheson et al. (1984)
Subtotal	32/25.98 = 1.23 (0.84–1.74)	36/43.2 = 0.83 (0.58–1.15)	15/12.39 = 1.21 (0.68–2.0)	81/65.3 = 1.24 (0.99–1.55)	
<i>SMRs 1–2 weak association with lung cancer</i>					
126/99.2 = 1.97	—	44/51.6 = 0.85 (0.62–1.14)	—	9/10 = 0.90 (0.47–1.56)	Dement et al. (1994)
35/19.4 = 1.80	—	26/17.3 = 1.5 (0.7–3)	—	23/23 = 1.0 (0.5–2.0)	Albin et al. (1990) (RR)
162/89.8 = 1.80	32/30.16 = 1.06 (0.73–1.50)	—	35/27.8 = 1.26 (0.88–1.75)	43/30.09 = 1.43 (1.03–1.93)	Raffin et al. (1989)
50/29.2 = 1.71	7/13.4 = 0.52 (0.21–1.08)	—	16/11.4 = 1.40 (0.80–2.28)	13/19.1 = 0.68 (0.36–1.16)	Melkild et al. (1989)
23/15.0 = 1.54	—	1/3.5 = 0.29 (0.01–1.59)	—	2/6 = 0.33 (0.04–1.18)	Tola et al. (1988)
93/64.6 = 1.44	—	13/16.7 = 0.78 (0.41–1.33)	—	18/16.7 = 1.08 (0.64–1.70)	Peto et al. (1985) (III)
6/4.3 = 1.40	GI = 3/5.1 = 0.59 (0.12–1.72)	—	—	—	Ohlson and Hogstedt (1985) 20-years latency
587/431.6 = 1.36	—	319/343 = 0.93 (0.83–1.04)	—	158/125.4 = 1.26 (1.07–1.48)	Liddell et al. (1997)

(continued on next page)

Table 2 (continued)

Lung cancer SMRs	Colon cancer SMRs	Colorectal cancer	Rectal cancer	Stomach cancer	Reference
152/112.1 = 1.36	5/15.4 = 0.33 (0.11–0.76)	—	9/12 = 0.75 (0.34–1.42)	24/24.9 = 0.96 (0.62–1.44)	Hodgson and Jones (1986)
28/20.71 = 1.35	—	19/24.1 = 0.79 (0.43–1.15)	—	No excess risk	Tulchinsky et al. (1999)
155/115.5 = 1.34	—	21/23.3 = 0.90 (0.56–1.38)	—	22/19.5 = 1.13 (0.71–1.70)	Hughes et al. (1987)
26/21 = 1.24	—	6/6.45 = 0.93 (0.41–1.84) intestine + rectum	—	13/9.95 = 1.31 (0.70–2.23)	Battista et al. (1999)
302/264.9 = 1.14	67/67 = 1.0 (.77–1.26)	—	60/57.1 = 1.05 (0.80–1.34)	82/71.3 = 1.15 (0.92–1.43)	Koskinen et al. (2003) (M) (SIR)
22/19.9 = 1.11	—	6/6.6 = 0.91 (0.33–1.98)	—	12/12.7 = 0.94 (0.49–1.65)	Piolatto et al. (1990)
302/264.9 = 1.14	67/67 = 1.0 (.77–1.26)	—	60/57.1 = 1.05 (0.80–1.34)	82/71.3 = 1.15 (0.92–1.43)	Koskinen et al. (2003) (M) (SIR)
11/10.2 = 1.08	—	9/8.2 = 1.10 (0.50–2.1)	—	2/4 = 0.50 (0.06–1.8)	Sanden et al. (1992)
32/29.8 = 1.07	7/2.5 = 2.8 (1.12–5.8)	—	No significant excess	No significant excess	Szeszenia-Dabrowska et al. (1998)
27/25.7 = 1.05	—	15/20.9 = 0.72 (0.40–1.18)	—	30/51.1 = 0.59 (0.40–0.84)	Ohlson et al. (1984) >20 y latency
159/150.8 = 1.05	GI = 123/134.6 = 0.91 (0.76–1.09)	—	—	—	Berry and Newhouse (1983)
Subtotal	118/128.46 = 0.92 (0.76–1.10)	479/521.65 = 0.92 (0.84–1.01)	120/108.3 = 1.11 (0.92–1.33)	451/423.74 = 1.06 (0.97–1.17)	
<i>SMRs <1.0 no association</i>					
246/248.2 = 0.99	157/161.6 = 0.97 (0.83–1.14)	—	120/110.2 = 1.09 (0.90–1.31)	100/123.25 = 0.81 (0.66–0.99)	Waage et al. (1993)
41/42.2 = 0.97	6/9.2 = 0.65 (0.24–1.42)	—	5/6.2 = 0.81 (0.26–1.88)	15/13.7 = 1.09 (0.61–1.81)	Gardner et al. (1986)
24/25.8 = 0.93	GI 14/14.1 = 0.99 (0.54–1.67)	—	—	—	Thomas et al. (1982) 10-years latency
236/274 = 0.86	36/37 = 0.98 (0.69–1.36)	—	29/34 = 0.85 (0.57–1.22)	86/112 = 0.77 (0.61–0.94)	Nokso-Koivisto and Pukkala (1994)
58/73.8 = 0.79	13/14.7 = 0.88 (0.47–1.52)	—	2/3.0 = 0.66 (0.08–2.40)	4/6.8 = 0.59 (0.16–1.50)	Tsai et al. (1996)
Subtotal	212/222.5 = 0.95 (0.83–1.09)	—	156/153.4 = 1.02 (0.87–1.19)	205/255.75 = 0.80 (0.70–0.92)	
Total	365/379.9 = 0.96 (0.87–1.07)	599/617.25 = 0.97 (0.89–1.05)	291/274.09 = 1.06 (0.94–1.19)	791/782.58 = 1.01 (0.94–1.08)	

risks for both lung cancer and mesothelioma increased substantially. Weiderpass et al. (2003) correlated SIRs of stomach cancer by exposure for Finnish women born between 1906 and 1945. There was no apparent association ($p = 0.25$) with SIRs of 1.06 (0.83–1.35) and 1.24 (0.85–1.76) by low and high exposures, respectively. Risk of lung cancer and mesothelioma were not assessed in this study (Fig. 3).

Ohlson et al. (1984) studied railroad maintenance workers and used semi-quantitative exposure estimates and four exposure categories (Fig. 4). Among workers with 20 or more years latency there was a deficit of stomach cancer mortality both overall (SMR = 0.59; 95% confidence intervals 0.40–0.84) and for each exposure category and therefore no E–R trend. There was no overall excess of lung cancer (SMR = 1.05; 0.69–1.53), but there was a monotonic trend for risk of lung cancer to increase with increas-

ing estimates of cumulative exposure. Among workers with more than 30-years tenure the lung cancer SMR was elevated to 1.54 (0.94–2.32) while the stomach cancer SMR was significantly less than 1.0 (SMR = 0.56; 0.33–0.89). There were 5 cases of mesothelioma, which was 3.5% of the cancer deaths (Fig. 4).

The other two studies use quantitative estimates of cumulative exposure (Hughes et al., 1987; Liddell et al., 1997) (Figs. 5 and 6). Hughes et al. (1987) evaluated E–R for stomach and lung cancers by cumulative exposures in workers in asbestos cement plant 2 (Fig. 5). There was no apparent E–R trend for stomach cancer, but there were only 9 cases, with only 2 cases total in the 3 highest exposure categories (1 in 36 mppcf-years, 0 in 71 mppcf-years and 1 in 164 mppcf-years). As a result confidence limits are quite wide. Lung cancer showed a significant positive trend to increase with asbestos exposure. There were eight

Table 3

Summary of risk of GI cancers stratified by percent mesothelioma (% of cancers)

Percent mesothelioma	Colon cancer SMRs	Colorectal cancer
<i>>10% Mesothelioma (very high)</i>		
13/32 = 40.6%	—	3/3.1 = 0.96 (0.20–2.8)
15/79 = 19%	—	7/3.9 = 1.80 (0.72–3.70)
8/44 = 18.2%	GI = 8/2.8 = 2.86 (1.23–5.63)	14/12.3 = 1.14 (0.67–1.92)
32/207 = 15.5%	7/2.5 = 2.8 (1.12–5.8)	—
14/95 = 14.7%	—	19/24.1 = 0.79 (0.43–1.15)
21/153 = 13.7%	—	54/39 = 1.38 (1.05–1.82)
101/845 = 11.95%	—	—
34/196 = 11.95%	5/15.4 = 0.33 (0.11–0.76)	—
6/52 = 11.5%	3/3 = 1.0 (0.21–2.92)	—
8/70 = 11.4%	—	9/8.2 = 1.10 (0.50–2.1)
28/275 = 10.2%	—	11/16.9 = 0.65 (0.32–1.16)
Subtotal	15/20.9 = 0.72 (0.40–1.18)	117/107.5 = 1.09 (0.90–1.31)
<i>>5–10% Mesothelioma (high)</i>		
2/22 = 9.1%	GI = 6/5 = 1.20 (0.44–2.62)	—
2/23 = 8.7%	—	2/0.98 = 2.04 (0.25–7.4)
13/164 = 7.9%	—	26/17.3 = 1.5 (0.7–3.0)
6/78 = 7.7%	6/2.9 = 2.07 (0.76–4.51)	—
10/184 = 5.4%	—	13/16.7 = 0.78 (0.41–1.33)
2/38 = 5.3%	4/6.5 = 0.62 (0.17–1.58) digestive minus stomach	—
5/99 = 5.1%	—	Intestine + rectum 6/6.45 = 0.93 (0.41–1.84)
5/103 = 4.9%	Digestive tract + peritoneum = 27/30.2 = 0.89 (0.59–1.3)	—
Subtotal	6/2.9 = 2.07 (0.76–4.51)	51/47.9 = 1.06 (0.80–1.41)
<i>>1–5% Mesothelioma (moderate)</i>		
9/184 = 4.9%	GI = 132/134.6 = 0.98 (0.82–1.17)	—
5/109 = 4.6%	6/4.4 = 1.37 (0.50–2.97) unexp = 2/1.4 = 1.43 (0.17–5.2)	—
4/103 = 3.9%	—	11/5.2 = 2.12 (1.06–3.79)
8/208 = 3.8%	14/14.24 = 0.98 (0.54–1.65)	—
5/144 = 3.5%	—	15/20.9 = 0.72 (0.40–1.18)
2/58 = 3.41%	14/14.1 = 0.99 (0.54–1.67)	—
6/197 = 3.05%	—	22/11.9 = 1.85 (1.16–2.79)
5/166 = 3.01%	13/14.7 = 0.88 (0.47–1.52)	—
4/137 = 2.9%	—	3/5.45 = 0.55 (0.11–1.60)
2/82 = 2.4%	—	6/6.6 = 0.91 (0.33–1.98) = intestinal cancers

Rectal	Stomach	Reference
—	0/1.6 = 0 (0.0–2.31)	Rosler et al. (1994) (PMR)
—	4/2.9 = 1.36 (0.37–3.48)	Botta et al. (1991) (F) Finkelstein (1984)
No significant excess	17/8.95 = 1.90 (1.18–3.06) No significant excess	Armstrong et al. (1988) Szeszenia-Dabrowska et al. (1998)
—	No excess risk	Tulchinsky et al. (1999) (>20-years latency)
—	18/12.7 = 1.42 (0.84–2.24)	Selikoff et al. (1979)
9/12 = 0.75 (0.34–1.42)	24/24.9 = 0.96 (0.62–1.44)	Hodgson and Jones (1986)
—	5/4.3 = 1.16 (0.38–2.71)	Hilt et al. (1991)
—	2/4 = 0.50 (0.06–1.8)	Sanden et al. (1992)
—	17/20.9 = 0.81 (0.47–1.30)	Botta et al. (1991) (M)
9/12 = 0.75 (0.34–1.42)	87/80.25 = 1.08 (0.87–1.34)	
—		Thomas et al. (1982)
—	2/1.02 = 1.96 (0.24–7.08)	Peto et al. (1985) (I)
—	23/23 = 1.0 (0.5–2.0)	Albin et al. (1990)
0/0.7 = 0%	0/1.1 = 0%	Levin et al. (1998)
—	18/16.7 = 1.08 (0.64–1.70)	Peto et al. (1985) (III)
—	2/1.6 = 1.24 (0.15–4.49)	Amandus and Wheeler (1987)
—	13/9.95 = 1.31 (0.77–2.08)	Battista et al. (1999)
		Giaroli et al. (1994)
0/0.7 = 0	58/53.37 = 1.09 (0.83–1.42)	
		Berry and Newhouse (1983)
4/3.2 = 1.24 (0.34–3.2)	7/7.5 = 0.94 (0.37–1.92) unexp =	Acheson et al. (1984)
unexp = 0/1 = 0	4/2.5 = 1.59 (0.44–4.1)	
—	4/2 = 2 (0.54–5.2)	Selikoff et al. (1980)
9/5.66 = 1.59 (0.73–3.02)	20/11.09 = 1.80 (1.10–2.28)	Enterline et al. (1987)
—	30/51.1 = 0.59 (0.40–0.84)	Ohlson and Hogstedt (1985)
—		Thomas et al. (1982)
—	9/5.78 = 1.56 (0.71–2.96)	Seidman et al. (1986)
2/3 = 0.66 (0.08–2.4)	4/6.8 = 0.59 (0.16–1.50)	Tsai et al. (1996)
—	13/9.15 = 1.42 (0.76–2.43)	Meurman et al. (1994)
—	12/12.7 = 0.94 (0.49–1.65)	Piolatto et al. (1990)

(continued on next page)

Table 3 (continued)

Percent mesothelioma	Colon cancer SMRs	Colorectal cancer	Rectal	Stomach	Reference
13/580 = 2.2%	32/30.16 = 1.06 (0.73–1.5)	—	35/27.8 = 1.26 (0.88–1.75)	43/30.1 = 1.43 (1.03–1.93)	Raffin et al. (1989)
38/1900 = 2.0%	—	319/343 = 0.93 (0.83–1.04)	—	158/125 = 1.26 (1.08–1.48)	Liddell et al. (1997)
19/1392 = 1.4%	67/67 = 1.0 (.77–1.26)	—	60/57.1 = 1.05 (0.80–1.34)	82/71.3 = 1.15 (0.92–1.43)	Koskinen et al. (2003) (M) (SIR)
4/353 = 1.1%	—	21/23.3 = 0.90 (0.56–1.38)	—	22/19.5 = 1.13 (0.71–1.7)	Hughes et al. (1987)
Subtotal	132/130.5 = 1.01 (0.85–1.20)	397/416.35 = 0.95 (0.86–1.05)	110/96.76 = 1.14 (0.94–1.38)	404/352.02 = 1.15 (1.04–1.27)	
<1% Mesothelioma (low)					
8/915 = 0.87%	36/37 = 0.98 (0.69–1.36)	—	29/34 = 0.85 (0.57–1.22)	86/112 = 0.77 (0.61–0.94)	Nokso-Koivisto and Pukkala (1994)
2/232 = 0.86%	7/13.4 = 0.52 (0.21–1.08)	—	16/11.4 = 1.40 (0.80–2.28)	13/19.1 = 0.68 (0.36–1.16)	Melkild et al. (1989)
1/121 = 0.83%	6/9.2 = 0.65 (0.24–1.42)	—	5/6.2 = 0.81 (0.26–1.88)	15/13.7 = 1.09 (0.61–1.81)	Gardner et al. (1986)
2/283 = 0.70%	—	Intestine, colon, rectum = 44/51.6 = 0.85 (0.62–1.14)	—	9/10 = 0.90 (0.47–1.56)	Dement et al. (1994)
11/1695 = 0.65%	157/161.56 = 0.97 (0.83–1.14)	—	120/110.2 = 1.09 (0.90–1.31)	100/123.25 = 0.81 (0.66–0.99)	Waage et al. (1993)
0/202 = 0%	Digestive cancers = 59/51.75 = 1.14 (0.88–1.48)	—	—	—	McDonald et al. (1984)
0/55 = 0%	3/3.57 = 0.84 (0.17–2.45)	—	1/2.17 = 0.46 (0.01–2.56)	2/2.44 = 0.82 (0.10–2.96)	Koskinen et al. (2003) (F) (SIR)
0/48 = 0%	—	1/3.5 = 0.29 (0.01–1.59)	—	2/6.1 = 0.33 (0.04–1.18)	Tola et al. (1988)
0/23 = 0%	3/0.87 = 3.45 (0.71–10)	—	1/0.66 = 1.52 (0.04–8.44)	1/1.49–0.67 (0.02–3.7)	Meurman et al., 1994 (F)
0/22 = 0%	—	—	—	5/1.14 = 4.40 (1.42–10.2)	Pang et al. (1997)
0/19 = 0%	—	4/2.02 = 1.98 (0.54–5.1)	—	2/1.08 = 1.85 (0.22–6.69)	Peto et al. (1985) (II)
0/44 = 0%	GI = 1/5.9 = 0.17 (0.004–0.94) = no latency	—	—	—	Ohlson and Hogstedt (1985)
Subtotal	212/225.6 = 0.94 (0.82–1.08)	49/57.1 = 0.86 (0.63–1.13)	172/164.6 = 1.04 (0.90–1.22)	242/296.65 = 0.82 (0.72–0.93)	
Total	365/379.9 = 0.96 (0.87–1.07)	569/583.4 = 0.98 (0.90–1.06)	291/274.06 = 1.06 (0.94–1.19)	791/782.29 = 1.01 (0.94–1.08)	

Percent mesothelioma = n mesothelioma/total cancers.

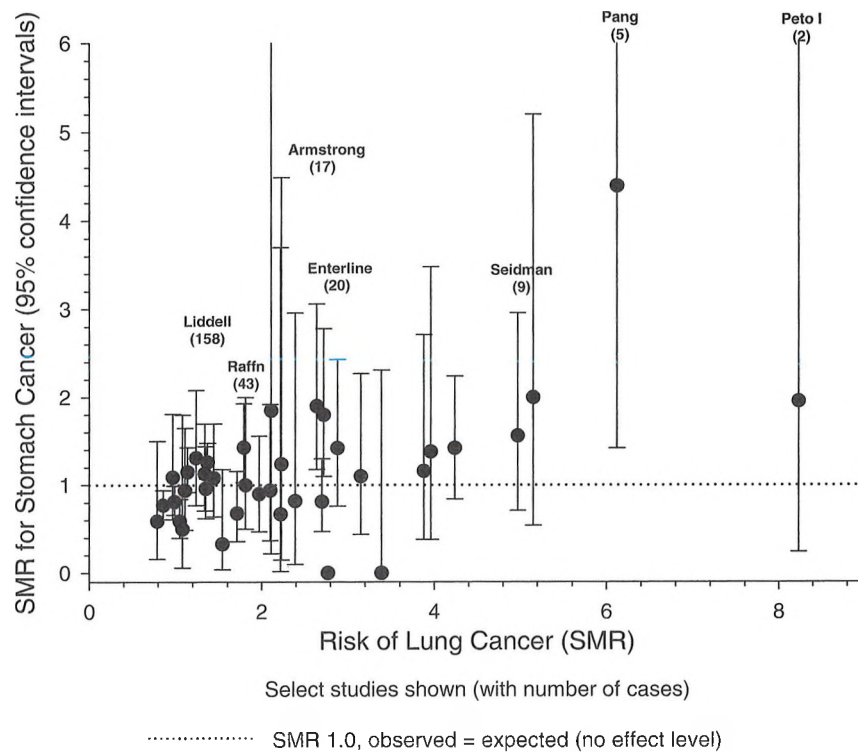


Fig. 1. Risk of stomach cancer stratified by risk of lung cancer in cohorts of asbestos-exposed workers.

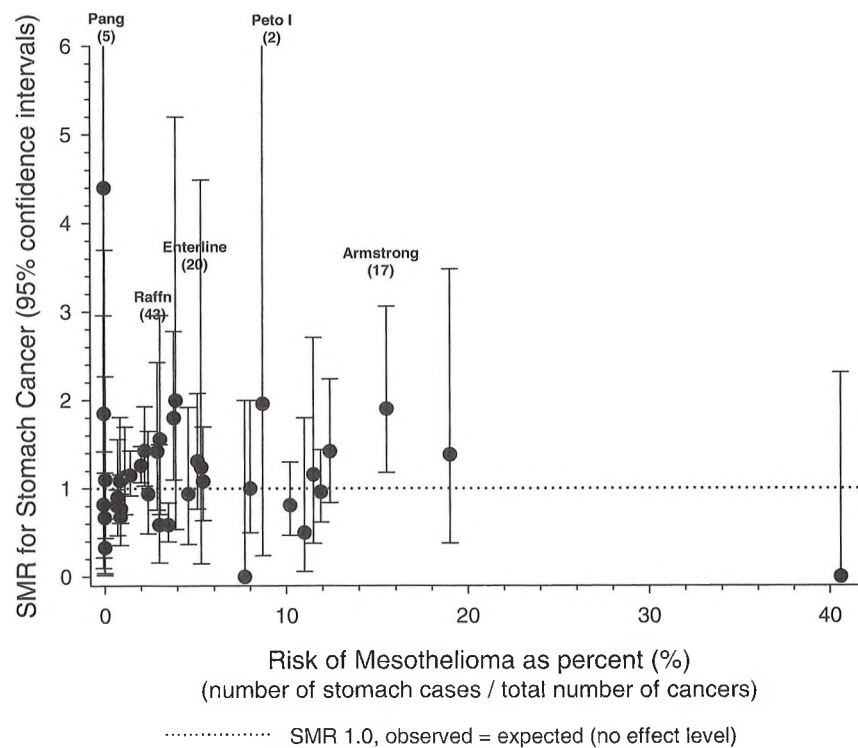


Fig. 2. Risk of stomach cancer stratified by risk of mesothelioma in cohorts of asbestos-exposed workers.

mesotheliomas (3.5%) that were largely attributed to crocidolite exposure. Exposure was to both crocidolite and chrysotile in the pipe area, and chrysotile only in the rest of the plant.

Liddell et al. (1997) is the largest study with evaluation of E–R for stomach cancer, lung cancer and mesothelioma by mppcf-years until age 55 in Canadian chrysotile miners/millers (Fig. 6). There appeared to be thresholds for stom-

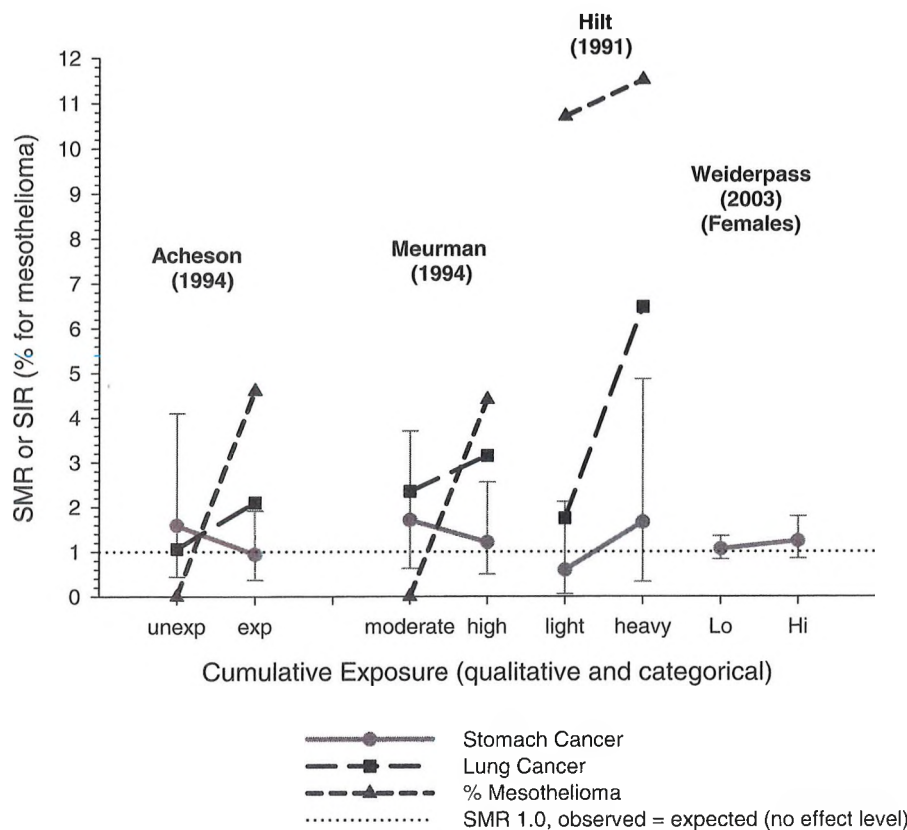


Fig. 3. Exposure-response for stomach cancer, lung cancer and mesothelioma by exposure categories.

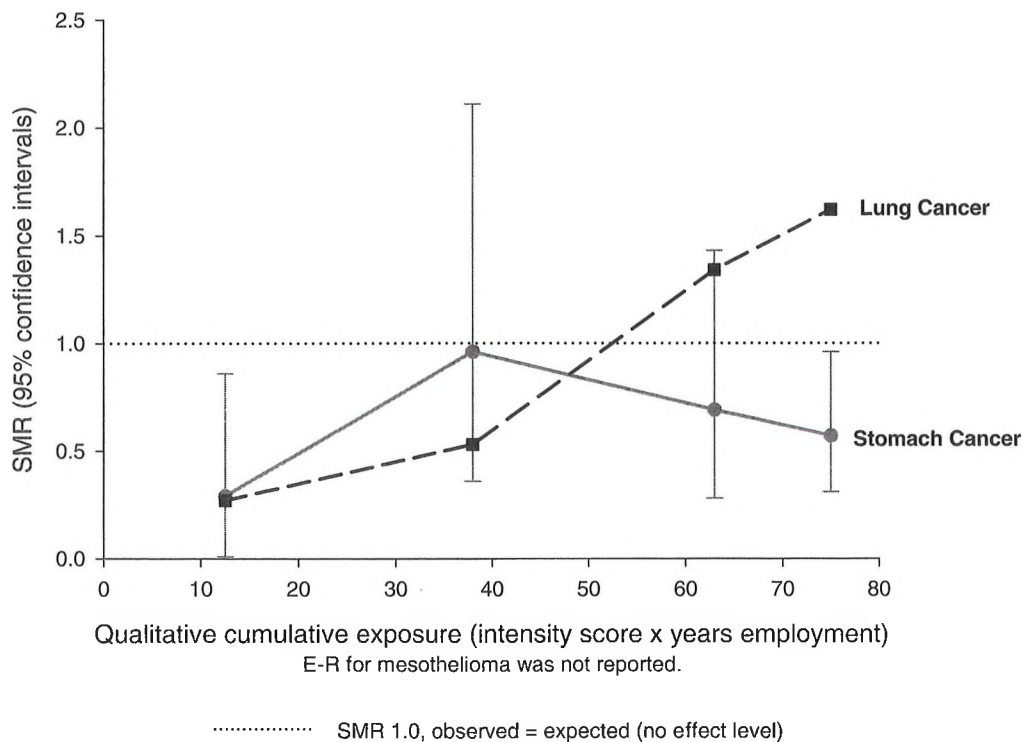


Fig. 4. Exposure-response for stomach cancer and lung cancer among Swedish railroad maintenance workers with >20-years latency exposed to chrysotile, crocidolite and amosite, Ohlson et al. (1984).

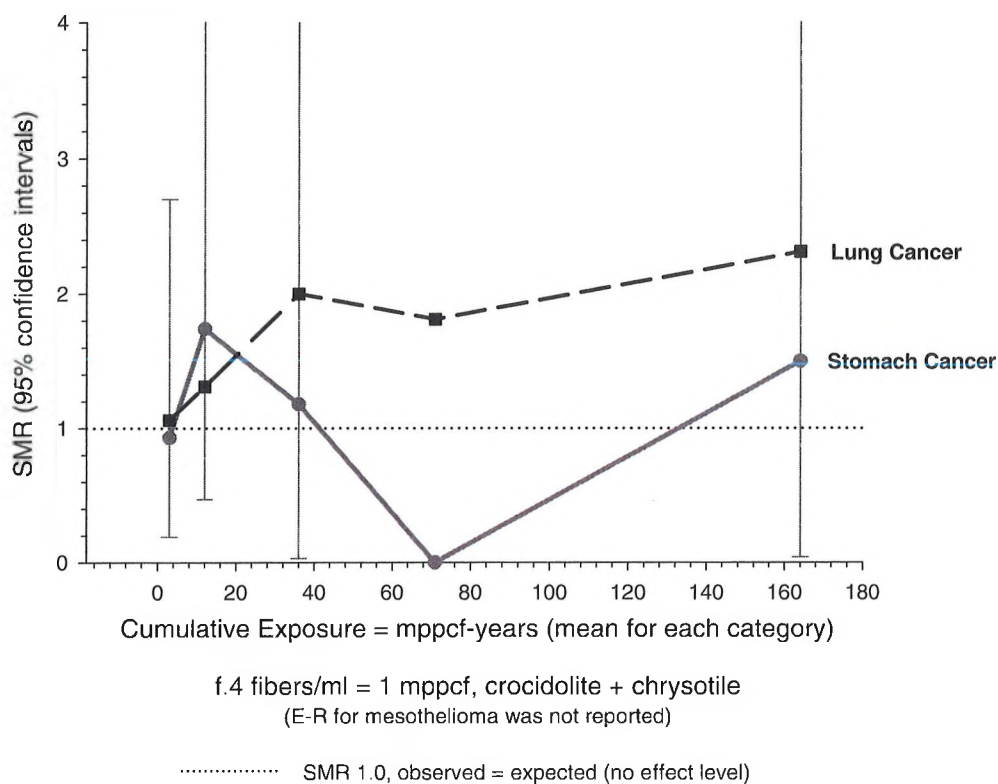


Fig. 5. Exposure–response for stomach cancer and lung cancer by million particles per cubic foot-years (mppcf-years) among asbestos cement workers in plant 2 (>20-years latency and >3-months employment), Hughes et al. (1987).

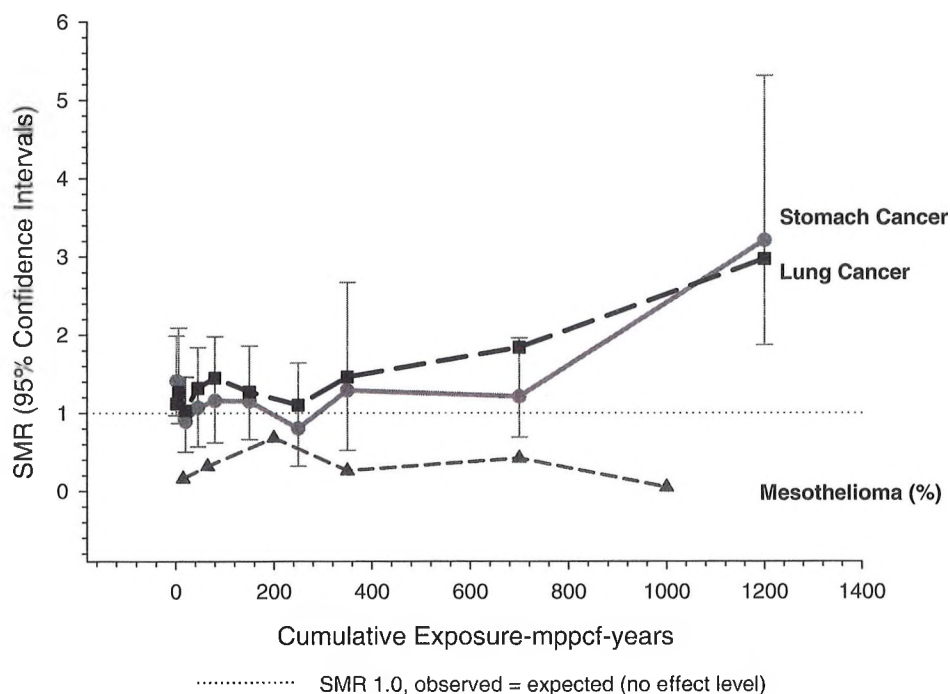


Fig. 6. Exposure–response for stomach cancer, lung cancer and mesothelioma by million particles per cubic foot-years (mppcf-years) among Canadian chrysotile miners/millers, Liddell et al. (1997).

ach cancer and lung cancer, with no apparent E–R trends below about 300 mppcf-years for lung cancer (587 cases) and about 700 mppcf-years for stomach cancer. There were

no trends for 38 cases of mesothelioma. The overall SMRs for lung cancer and stomach cancer were 1.36 (1.25–1.48) and 1.26 (1.07–1.48), respectively, with 2% mesothelioma.

3.4. Colorectal cancer (CRC)

There are 22 studies that estimated risk of colorectal risk with 599 cases and an overall SMR of 0.97 (0.89–1.05). Thirteen of the studies had SMRs <1.0, many with a small number of cases. The largest study was the Canadian chrysotile cohort with 319 cases and a nonsignificant SMR of 0.93 (0.83–1.04) (Liddell et al., 1997). The only significant findings were elevated SMRs of 2.12 (1.06–3.8), 1.85 (1.16–2.79) and 1.38 (1.05–1.82) for Seidman et al. (1986) with an SMR of 1.85 for CRC and Selikoff et al. (1979) with 11, 22 and 39 cases, respectively.

3.5. Surrogate E–R

There was a tendency for CRC risk ratios to be elevated when lung cancer risk ratios >4 (Fig. 7). Combined risk ratios showed deficits for colorectal cancers when lung cancer SMRs are below 3 and a significantly elevated SMR of 1.60 (1.29–2.0) above lung cancer risk ratios of 3 (Table 2).

There were no apparent E–R trends for colorectal SMRs to increase as % mesothelioma increased (Fig. 8).

3.6. Individual-level E–R

Six studies assessed E–R relationships. Amandus and Wheeler (1987) studied 575 miners/millers of vermiculite contaminated with tremolite asbestos. There were 4 cases of colorectal cancer with an SMR of 0.62 (0.17–1.58). E–R was assessed for digestive cancer (ICD 150–159) but esti-

mates were too unstable to evaluate trends given that there were only 6 cases.

There were two studies with semi-quantitative exposure categories. Meurman et al. (1994) reported no CRC risk associated with moderate or high exposure among male anthophyllite miners, but risks increased for both lung cancer and mesothelioma with increased exposure. Demers et al. (1994) found deficits in ORs for colorectal cancer stratified by duration and latency and the CRC risk ratio for exposed construction workers was slightly less than the unexposed controls. Lung cancer was not assessed but risk ratio for mesothelioma incidence was 14 times greater than among the unexposed adjusted for age and packyears (Table 1).

The three remaining studies used quantitative estimates of cumulative asbestos exposure. Hughes et al. (1987) assessed E–R for the 6 CRC cases with >3-months tenure and >20-years latency in Plant 2 of an asbestos cement plant using mostly chrysotile but some crocidolite in one of the 4 buildings in Plant 2. The gradient was irregular; 2 exposure categories had no cases and the penultimate category had 3 cases and a nonsignificant SMR of 2.7. Lung cancer showed an obvious gradient as SMRs were increased 2-fold in the three highest exposure categories above about 36 mppcf-years. The number of CRC cases is small so the trend is unstable (Fig. 9).

Liddell et al. (1997) found no E–R relationship of colorectal cancer with chrysotile asbestos measured as mppcf-years. The overall SMR was 0.93 (0.83–1.04) with 319 cases. Colorectal cancer is not related to exposure at any

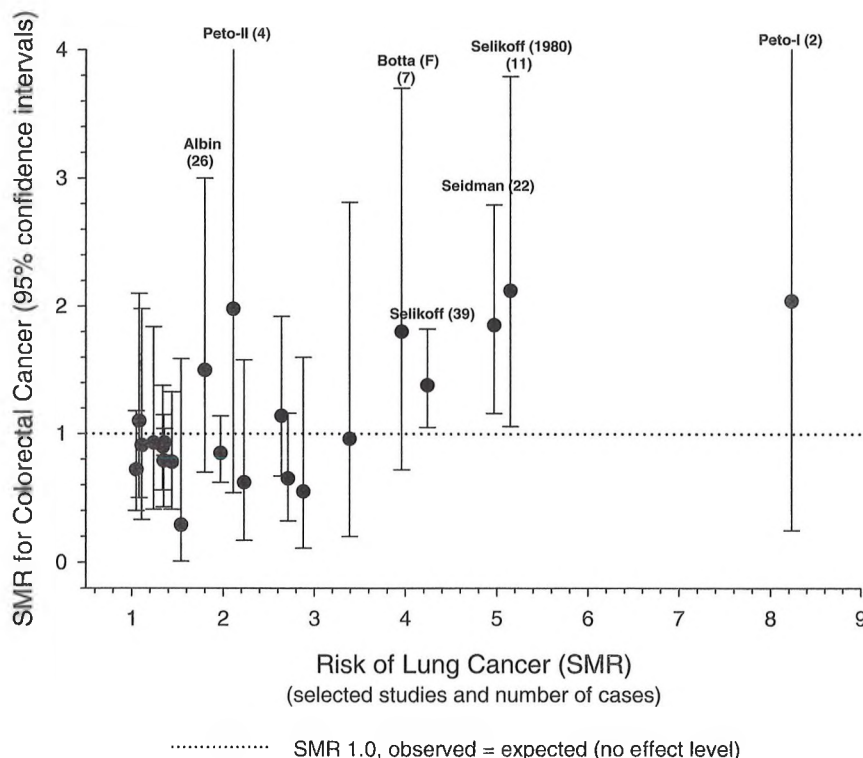


Fig. 7. Risk of colorectal cancer stratified by risk of lung cancer in cohorts of asbestos-exposed workers.

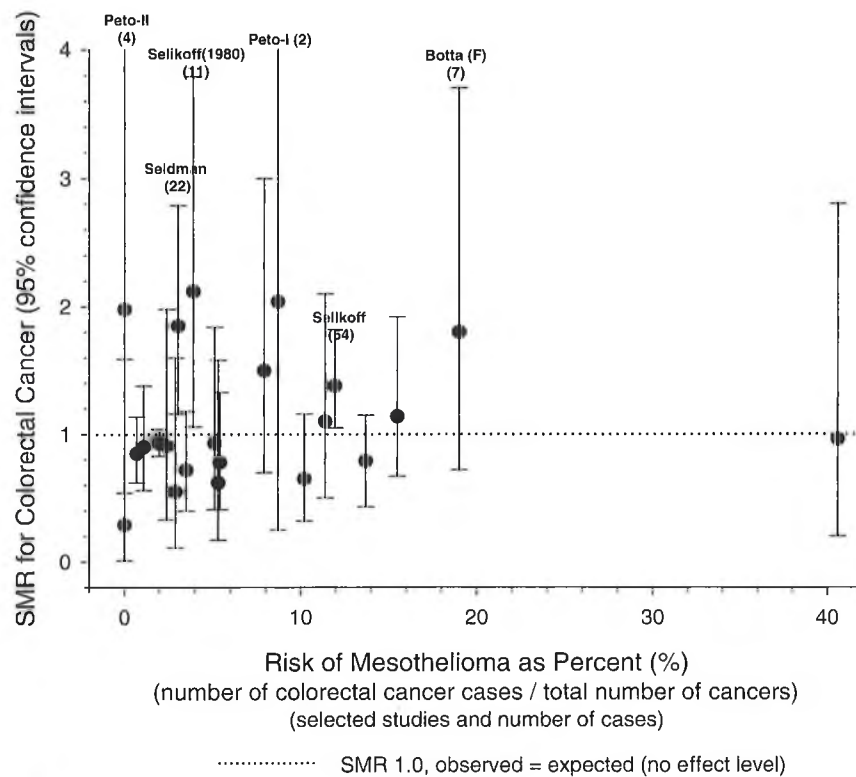


Fig. 8. Risk of colorectal cancer stratified by risk of mesothelioma in asbestos-exposed cohorts.

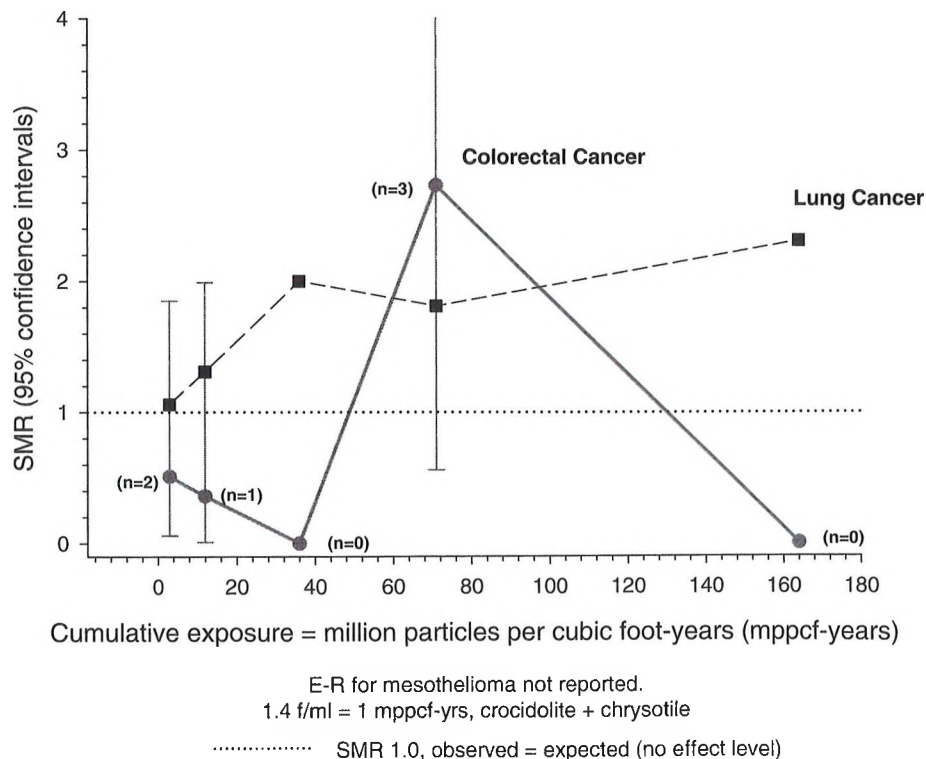


Fig. 9. Exposure-response of colorectal cancer and lung cancer among asbestos cement workers from Plant 2 with 20 or more years latency and more than 6 months employment by cumulative exposure (mppcf-years) to chrysotile, Hughes et al. (1987).

concentration in this study. Lung cancer mortality clearly became significantly increased at about 350 mppcf-years. This study of Canadian miners and millers provides the largest group of colorectal cases (Fig. 10).

Seidman et al. (1986) studied 820 men employed during WW II for relatively short time periods to high concentrations of amosite. There were 22 cases of colorectal cancer with an SMR of 1.85 (1.16–2.79). However, the risk of colorectal was not associated with exposure as the highest and significant SMRs were in the lower exposure groups. Lung cancer risks were clearly associated with increasing exposure as SMRs were elevated beginning with a 2.5-fold excess in the lowest exposure category and increasing to a 12-fold excess in the highest exposure category of 250+ f/ml-years (Fig. 11).

Albin et al. (1990) studied 1929 Swedish asbestos cement workers employed >3 months between 1907 and 1977 with 20 or more years latency and vital status follow-up from 1958 to 1988. Exposure was primarily to chrysotile, with <5% crocidolite and amosite. Relative risks were estimated using industrial workers and non-cases as comparison groups. There were 23 cases of colorectal cancer and 35 of lung cancer with overall RRs of 1.0 (0.5–2.0) and 1.8 (0.9–3.7), respectively. Thirteen (7.9%) of the cancer cases were mesotheliomas. There was a strong trend for mesothelioma to increase with increasing exposure, while the RR for lung cancer is about 2-fold at all exposure categories above the non-exposed comparison group. The E–R trend for colorectal cancer risk is significant ($p = 0.04$) but is

essentially flat with the risk increased significantly at about 40+ f/ml-years in the highest exposure category (Fig. 12).

3.7. Colon cancer

Overall there were 16 cohorts with 365 colon cancer cases and an SMR of 0.96 (0.87–1.07). Most of the studies had relatively few colon cancer cases. The largest number of cases was 157 from Waage et al. (1993) and 70 cases from Koskinen et al. (2003).

3.8. Surrogate E–R

There were no consistent trends for colon cancer to increase as lung cancer SMRs or percent mesothelioma increased. There were two significant findings. One was an excess SMR for colon cancer of 2.8 (1.12–5.8) with 7 cases (Szeszenia-Dabrowska et al., 1998).

3.9. Individual-level E–R

There are six studies that evaluated risk of colon cancer by qualitative estimates of exposure to asbestos (Fig. 15). There were no E–R evaluations using quantitative estimates of asbestos exposure.

Acheson et al. (1984) found a 2-fold excess lung cancer among exposed factory workers and no excess among unexposed. There was no effect on colon cancer as exposed and unexposed cases had the same SMRs for colon cancer

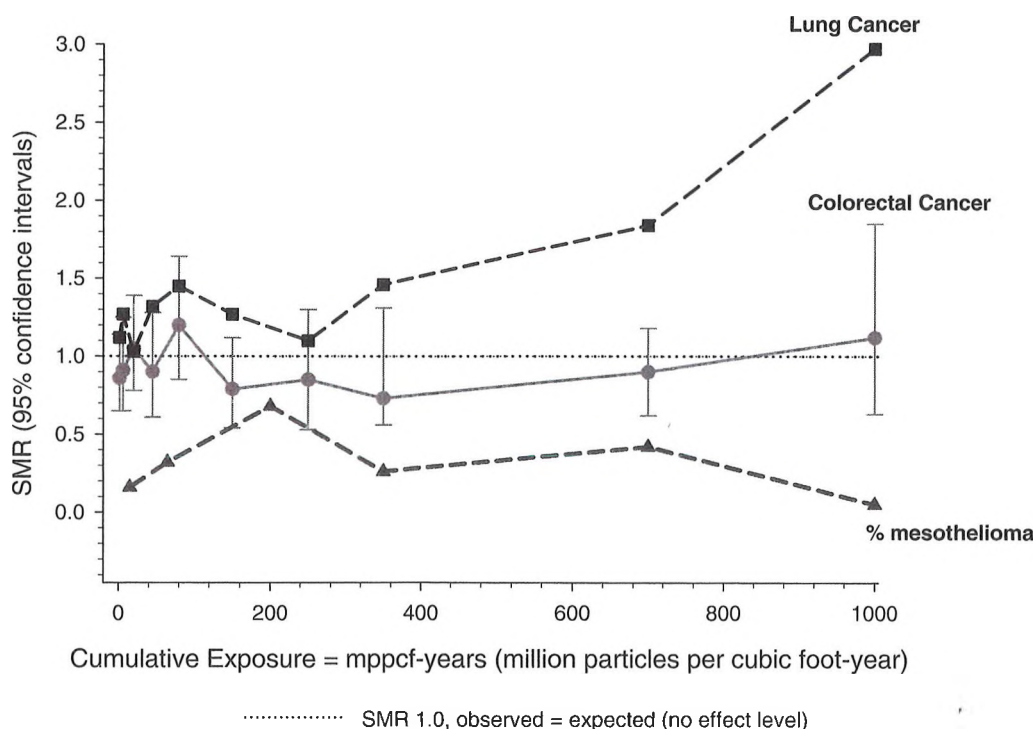


Fig. 10. Exposure–response of colorectal cancer and lung cancer among chrysotile miners/millers with >1 month, 1904–1992 by mppcf-years cumulative exposure accumulated to age 55, 1950–1992, Liddell et al. (1997).

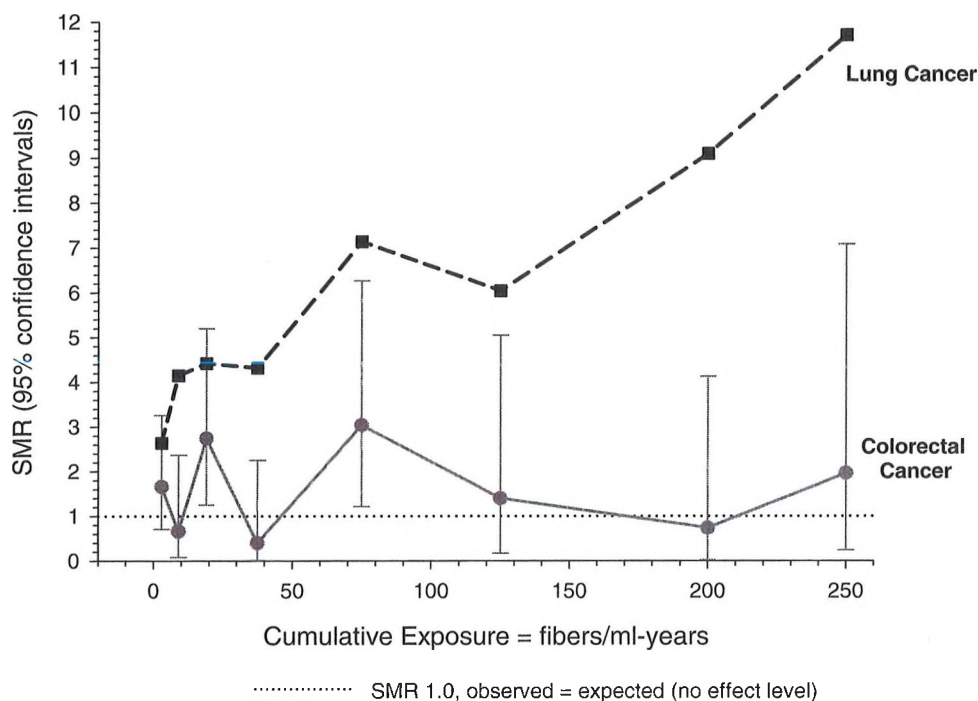


Fig. 11. Exposure-response of colorectal cancer and lung cancer among 820 amosite asbestos factory workers employed 1941–1945 with >5-years latency Seidman et al. (1986).

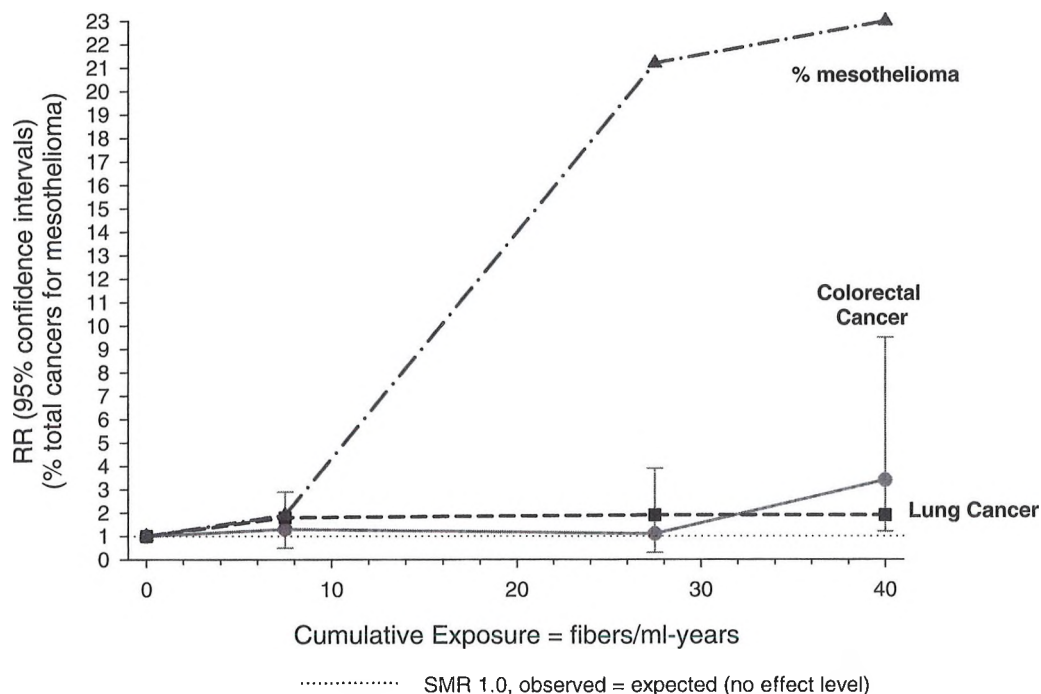


Fig. 12. Exposure-response of colorectal cancer, lung cancer and mesothelioma among Swedish asbestos cement workers with 3 months or more employment between 1907 and 1977 and >20-years latency (>95% chrysotile + crocidolite, amosite), Albin et al. (1990).

while risks of lung cancer and mesothelioma were increased in the asbestos-exposed group.

Hilt et al. (1991) found a strong relationship of lung cancer and mesothelioma incidence among heavy exposed maintenance workers compared to light exposed. Colon

cancer showed a less steep slope than lung cancer and a more steep slope than mesothelioma, but the colon cancer SIR was below the null for the light exposed cases and a nonsignificant 3-fold excess among heavy exposed cases.

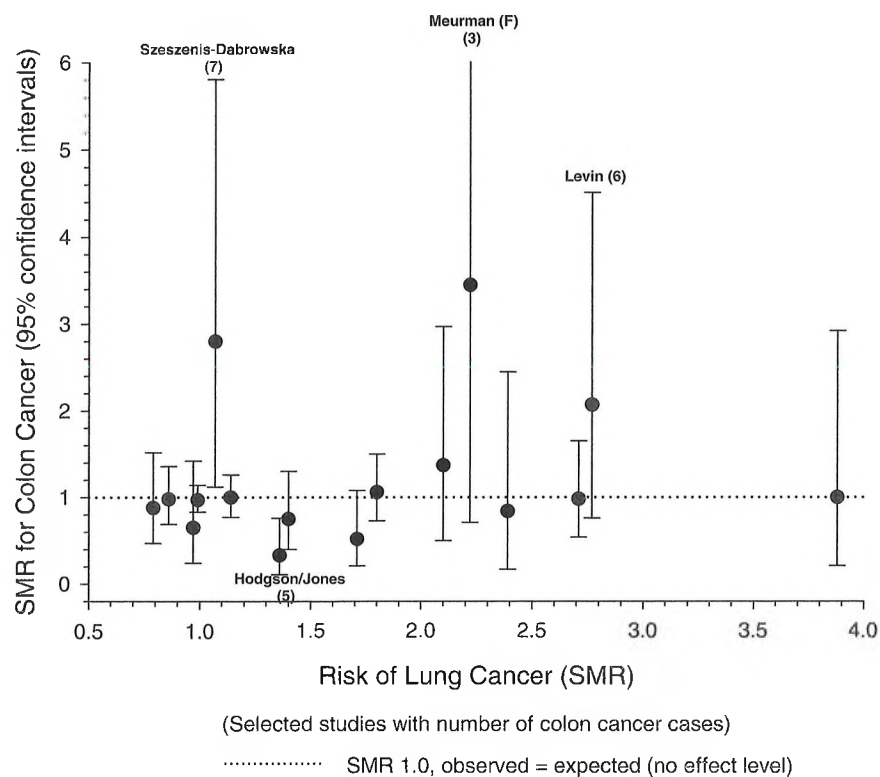


Fig. 13. Risk of colon cancer stratified by risk of lung cancer in asbestos-exposed cohorts.

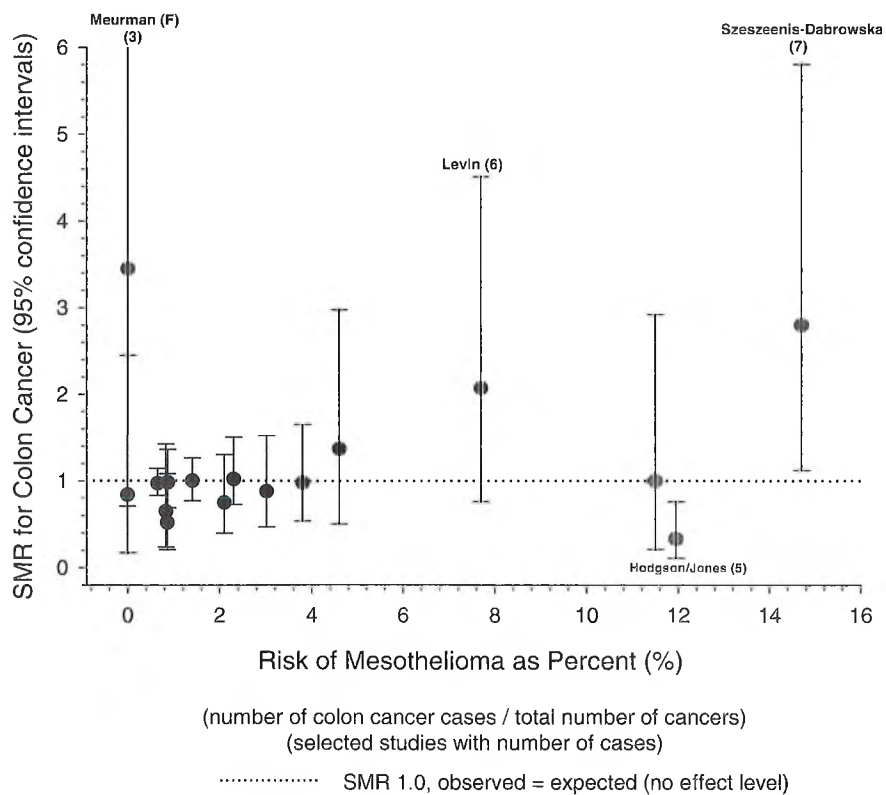


Fig. 14. Risk of colon cancer stratified by risk of mesothelioma in asbestos-exposed cohorts.

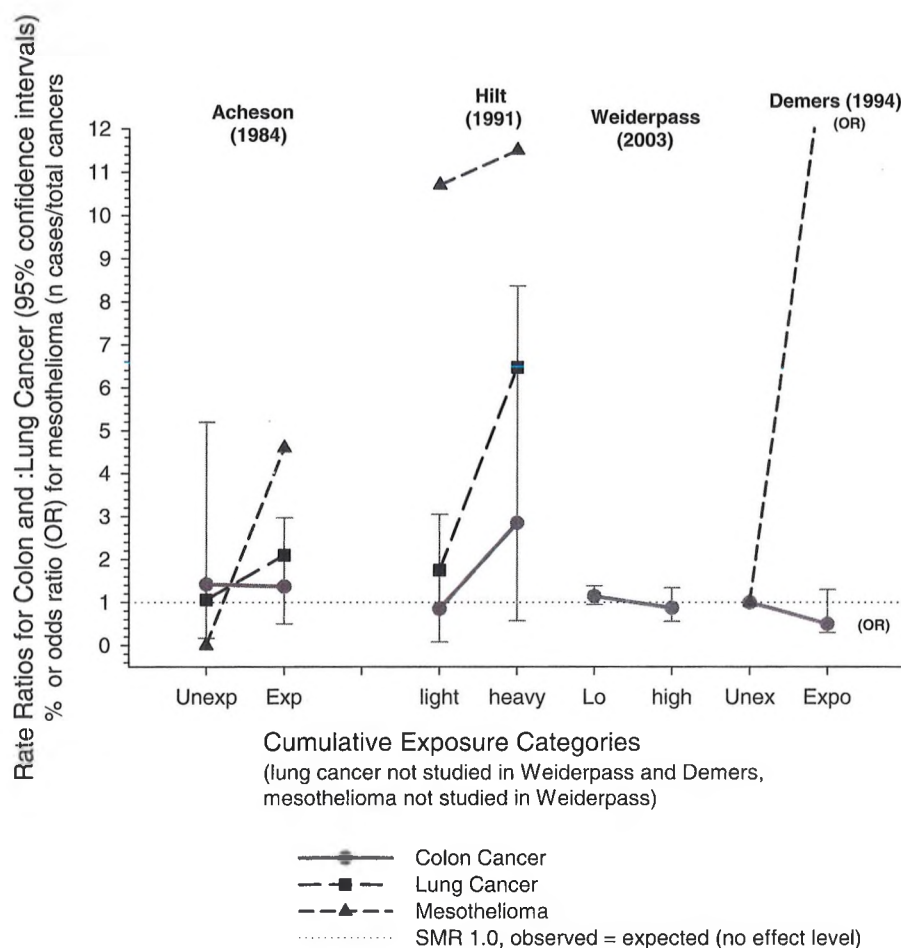


Fig. 15. Exposure-response for colon cancer by Qualitative Exposure Categories Acheson et al. (1984): UK factory workers (amosite + crocidolite + intermittent chrysotile) Hilt et al. (1991): Norwegian maintenance workers (crocidolite + chrysotile) Weiderpass et al. (2003): Finnish women workers Demers et al. (1994), asbestos-exposed constructions workers.

Meurman et al. (1994) reported nonsignificant 3- to 4-fold excess of colon cancer among women anthophyllite miners but the results are not included in Fig. 15 because the numbers are too small with only 23 total cancer cases, 1 lung cancer case and 3 colon cancer cases.

Weiderpass et al. (2003) found no association ($p = 0.60$) but an inverse trend between low and high asbestos-exposed Finnish women with SIRs of 1.14 (0.95–1.38) and 0.87 (0.56–1.34) for low and high exposures, respectively.

Demers et al. (1994) found no increased incidence of colon cancer among construction workers stratified by either duration or latency. There was a significant 14-fold excess risk of mesothelioma that increased from an OR of 3.7 (0.7–20.5) to 29.2 (8.4–101) in the <20- and >20-year latency groups.

Imbernon et al. (1996) investigated the risk of colon cancer among French workers exposed to asbestos in the electric and gas industries. There were 110 cases of colon cancer and an overall OR of 0.75 (0.4–1.3) with “no association” after adjustments for SES. In this cohort there were 12 (2.2%)

cases of mesothelioma and 310 cases of lung cancer with an overall OR of 1.4 (1.1–1.9). There was a nonmonotonic E–R trend for lung cancer with OR of 1.9 and 1.4 in the last two exposure categories. The results are not included in Fig. 15, as the colon cancer data were not shown.

3.10. Rectal cancer

There were 15 cohorts reporting on rectal cancer for a total of 291 cases and an overall SMR of 1.06 (0.94–1.19). Five of the studies had SMRs above 1.2. Two studies reported 0 cases (Levin et al., 1998; Cheng and Kong, 1992) and one reported no significant excess without listing the number of cases (Szeszenia-Dabrowska et al., 1998). About half of the cases (120) were from the population survey of Waage et al.

3.11. Surrogate E–R

There are no significant excesses of rectal cancer and there is no apparent trend for the risk to increase as the risk

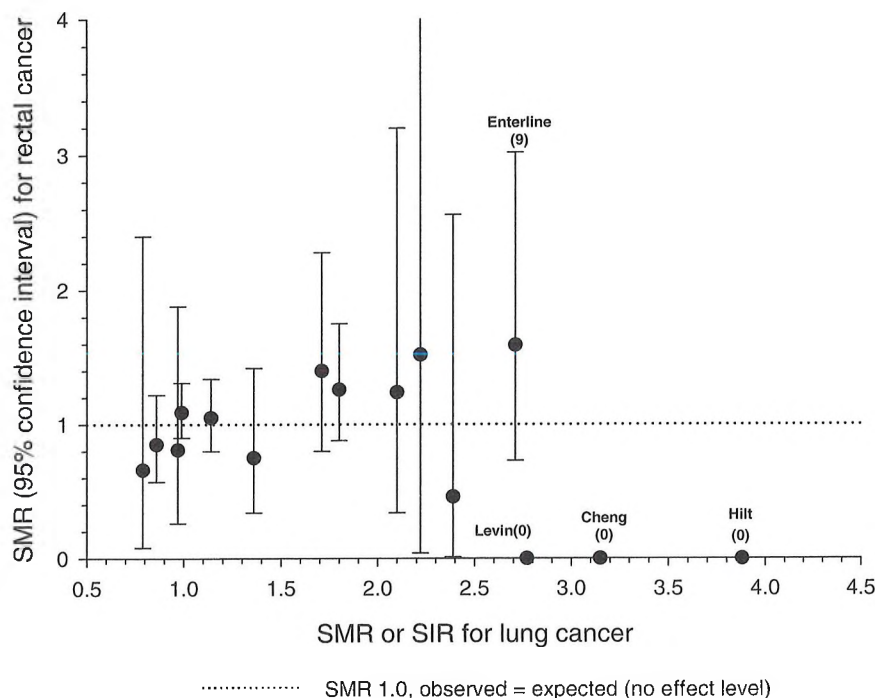


Fig. 16. Risk of rectal cancer stratified by risk of lung cancer in cohorts of asbestos-exposed workers.

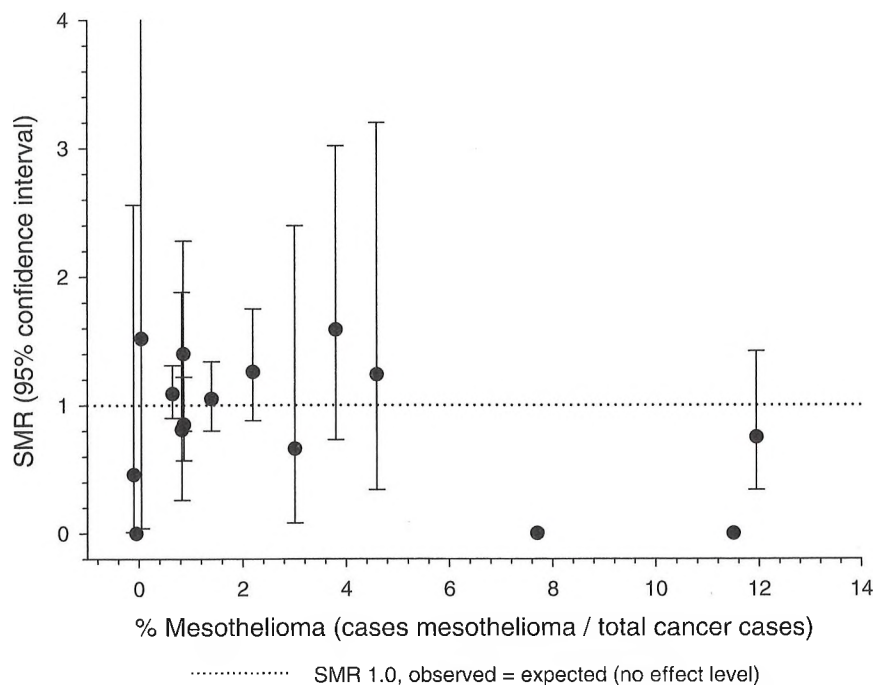


Fig. 17. Risk of rectal cancer stratified by risk of mesothelioma in cohorts of asbestos-exposed workers.

of lung cancer increases, although the five studies with rectal cancer SMRs >1.20 also had lung cancer SMRs >2.0 (Fig. 16).

There was no apparent trend for rectal cancer SMRs to increase as % mesothelioma increased (Fig. 17).

3.12. Individual-level E-R

There are three studies assessing rectal cancer with qualitative estimates of exposure (Fig. 18).

Acheson et al. (1984) found a nonsignificant 24% excess of rectal cancer (4 cases and 3.2 expected) among the asbes-

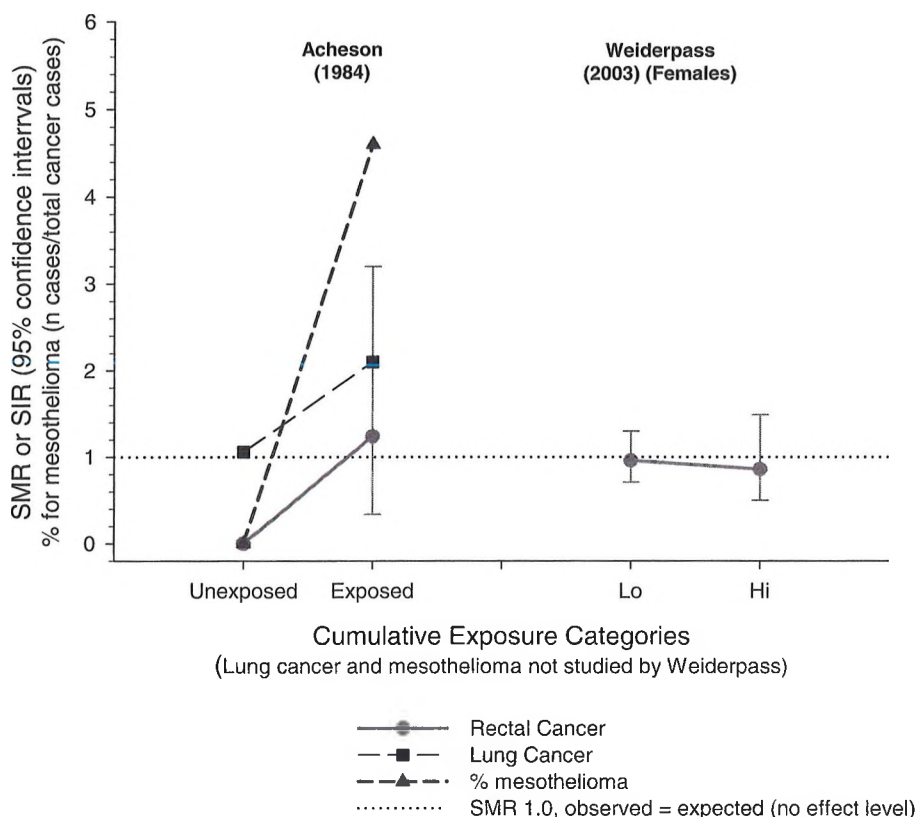


Fig. 18. Exposure–response for rectal cancer by Qualitative Exposure Categories, Acheson et al. (1984): UK factory workers (amosite + crocidolite + intermittent chrysotile), Weiderpass et al. (2003) Finnish women workers.

tos-exposed workers in insulation manufacture and 0 cases among non-exposed. Since there were only 1.1 expected the difference between exposed and unexposed is not significant. Among exposed workers there was a significant 2-fold excess of lung cancer and 4.6% of cancer cases were mesotheliomas.

Meurman et al. (1994) presented E–R trends for female anthophyllite miners, but there is only 1 case each of rectal cancer and lung cancer and 23 total cancer cases. Thus it is not possible to assess hazard from this study and the data are not included in Fig. 18.

Weiderpass et al. (2003) found no association of rectal cancer with asbestos exposure as SIRs were below expected for both low and high exposure categories: 0.96 (0.71–1.30) and 0.86 (0.50–1.49), respectively (Fig. 18).

3.13. Surrogate E–R

In 1955 mine-tailings or mill-waste from taconite ore began to be emptied into Lake Superior. In 1973 it was reported that 1–30 million amphibole fibers/liter were measured in Duluth, Minnesota tap water. Mean dimensions were 1.1 μm long and 0.18 μm wide and aspect ratio of 6.5 (Sigurdson, 1982). Although these particles have been referred to as asbestiform amphiboles (Levy et al., 1976), the dimensions are characteristic of cleavage fragments rather than asbestos. The taconite ore deposits contain

20–50% quartz and 10–36% magnetite with smaller amounts of other minerals including hematite, carbonates, amphiboles (mainly nonasbestiform minerals in the cumingtonite–grunerite series plus some actinolite and hornblende) greenalite, chamosite, minnesotaite, and stilpnomelane (Nolan et al., 1999).

The finding of what was thought to be asbestos resulted in several studies to evaluate possible risk. One set of studies assessed the risk of occupational exposure. Cohort studies of taconite miners from Reserve and Erie or Minntac taconite operations mining company were studied by Higgins et al. (1983) and Cooper et al. (1988, 1992), respectively. Fiber exposures by inhalation were low and there was no excess risk from lung cancer, mesothelioma or GI cancers.

A second set of studies were community ecological studies conducted to assess the possible hazard of high fiber content in drinking water for GI cancers. Carter and Taylor (1980) reported that amphibole fibers in tissue samples were much more common for people living in Duluth with 15 or more years oral intake compared to the people from control cities of Minneapolis and St. Paul, MN, and Houston, Texas. However, concentrations of chrysotile fibers were somewhat greater among the controls.

The first Duluth health-related study was by Masson et al. (1974) who compared mortality rates between 1950 and 1969 in Duluth with rates in Minneapolis and Minne-

sota. There were no consistent patterns of increased risk for persons of all ages or children. This study was followed by two additional studies of cancer incidence in Duluth (Levy et al., 1976; Sigurdson et al., 1981) that also suggested no consistent patterns of increased risk. Marsh (1983) reviewed these studies and suggested that basically all the methodological limitations associated with ingestion studies were present. Most notably these included ecologic study design, insufficient latency, low exposure, uncontrolled confounding and multiple comparison problems.

In 1974 amphibole fibers were discovered in municipal water supplies besides those in Duluth (Cook et al., 1974). This finding led to a number of ecological studies in other areas where the drinking water contained chrysotile in varying amounts. Marsh (1983) critically reviewed these individual studies identifying their limitations and summarizing his evaluation of the likelihood of an association with ingested asbestos. Relevant results from that summary are presented in Table 4.

These are all ecological studies where exposure was based on residence at a point in time in an area where the water supply contained fibers. Other weaknesses include too short latency (Duluth), no estimates of individual-level duration or exposure as migration, and multiple comparisons so some associations will be due to chance (Polissar et al., 1984; Marsh, 1983). In addition, the fibers may not always be asbestiform as is likely in Duluth.

Two additional studies use different study designs to address the question of risk of GI cancer by ingestion. Polissar et al. (1983, 1984) conducted a case control study in the Everett, Washington area to assess exposure-response

trends and to try and avoid some of the other problems associated with ecologic studies. The Sultan River has been the source of drinking water since 1918 and has among the highest concentrations of chrysotile (around 200 million fibers/liter) in the US for at least 60 years so latency is adequate. Stomach cancer among men was the only significant risk associated with 20 years, drinking the water. The risks of stomach, colon and rectal cancers were in the opposite directions for men and women, which is suggestive of no risk associated with the drinking water. There was no increased risk of lung cancer for either men or women (Fig. 19).

Anderson et al. (1993) studied 690 Norwegian male lighthouse keepers whose drinking water was from cisterns collecting rainwater coming off asbestos-cement tile roofs. Chrysotile fiber concentrations ranged from 1760 to 71,350 million fibers/liter. Among those with 20 or more years latency, incidence of stomach cancer was increased 2.4-fold expected. Incidence of intestinal and rectal cancers was not significantly elevated and there were no cases of mesothelioma. The cause of the stomach excess is not certain because of possible confounders such as diet (many of the lighthouse keepers were retired seamen). Exposure is not well defined, as it is not known when the tiles began to deteriorate and the size of the cohort is small.

4. Discussion

In general there are some findings of weak associations ($RR < 1.5$) at high surrogate exposures. Few studies evaluated individual-level E–R and in most instances there was a lack of E–R for the GI cancers while risk of lung cancer

Table 4

Summary of ecological studies of cancer risk in relation to contaminated drinking water (modified from Marsh, 1983)

	Mesothelioma	Lung cancer	Stomach	Colon	Rectum
<i>Duluth: amphiboles, 1,000,000–30,000,000 fibers/liter, 15–20 years maximum duration of exposure</i>					
Masson et al. (1974)	NS	+/0	+/+	0/0	+/+
Levy et al. (1976)	0/0	NS	+/0	–/–	0/0
Sigurdson et al. (1981)	0/0	0/0	0/0	0/0	0/0
<i>Connecticut: chrysotile, below limit of detection –700,000 fibers/liter, 23–44 maximum duration of exposure</i>					
Harrington et al. (1978)	NS	NS	0/0	0/0	0/0
Meigs et al. (1980)	NS	0/0	0/0	0/0	0/0
<i>Quebec: chrysotile, 1,100,000–1,300,000,000 fibers/liter; >50 years maximum duration of exposure</i>					
Wigle (1977)	NS	+/0	+/0	0/0	0/0
Toft et al. (1981)	NS	+/0	+/0	0/0	0/0
Graham (1981)#	+/+	+/0	+/+	+/+	–/+
<i>Bay Area, California: chrysotile, 25,000–36,000,000 fibers/liters; >40 years maximum exposure</i>					
Kanarek et al. (1980)	+/+	+/0	+/+	0/0	0/0
Conforti et al. (1981)	0/+	0/0	+/+	+/0	0/0
Tarter (1981)	NS	NS	NS	NS	0/0
<i>Utah: chrysotile, fiber counts not available; 20–30 years maximum exposure</i>					
Sadler et al. (1981)	0/0	NS	0/0	0/–	0/0
<i>Puget sound, Washington: chrysotile; 7,300,000–206,500,000 fibers/liter; >40 years maximum exposure</i>					
Severson (1979)	NS	NS	0/0	–/–	NS
Polissar et al. (1982)	0/0	0/0	0/0	0/0	0/0

Male/female: +, positive; –, negative; NS, not studied; #, not included in Marsh review, comparison of chrysotile mining counties (asbestos counties) with peripheral counties and other rural counties further away from asbestos counties.

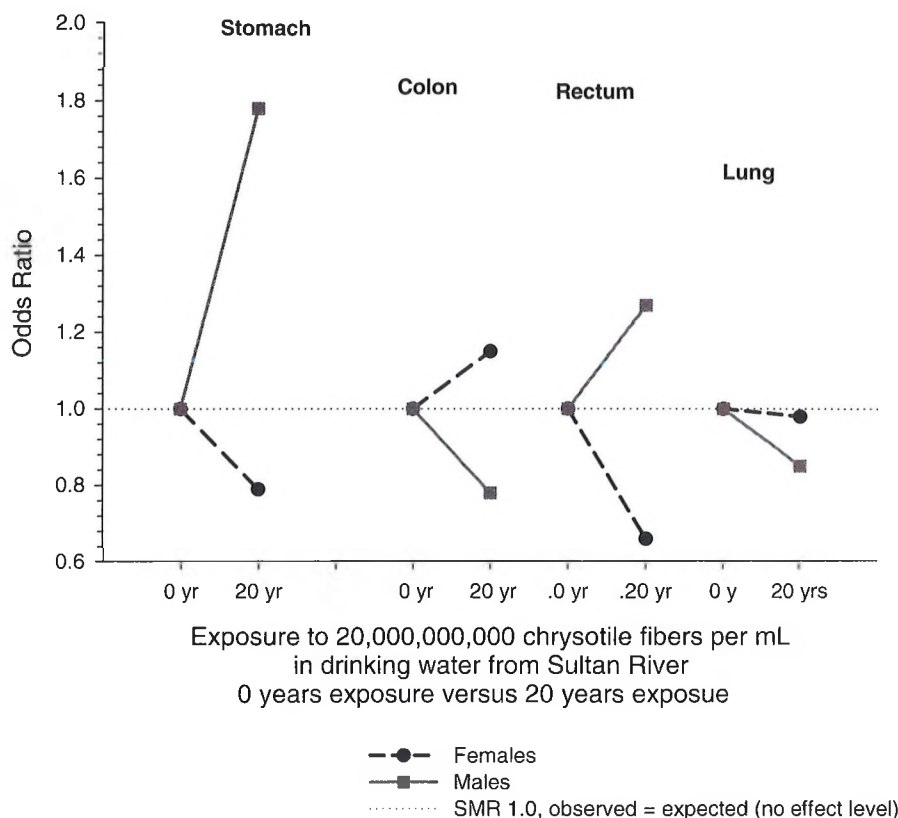


Fig. 19. Relative odds of stomach, colon, rectal and lung cancer (1977080) from chrysotile asbestos in drinking water, Everett area, Washington, Polissar et al. (1984).

and mesothelioma consistently increased as exposure increased. There was a consistent lack of surrogate E–R trends. These patterns detract from the hypothesis that asbestos exposure causes GI cancer. The ingestion data consistently show no association with GI cancers but the data are few and weak.

There are some exceptions to this general pattern.

- **Stomach cancer exceptions:** There is a 3-fold significantly increased risk of stomach cancer and lung cancer at cumulative exposures above 1000 mppcf-years among Canadian chrysotile miners/millers. This risk is consistent with the surrogate E–R trend where stomach cancer SMRs consistently increase when there are 4-fold increases in lung cancer (Figs. 1 and 6). In the chrysotile cohort 1000 mppcf-years is roughly equivalent to about 350 times the asbestos TLV of 0.1 f/ml (assuming that 1.4 f/ml is approximately equivalent to 1 mppcf and 40-years working lifetime). The excess among lighthouse keepers needs confirmation and demonstration of an E–R relationship. The weight of evidence suggests that at current exposure limits for asbestos there is no increased risk of stomach cancer.
- **Colorectal cancer exceptions:** Albin et al. (1990) reported a significant 3-fold increased CRC relative risk at about 40 f/ml-years that was higher than the 2-fold increased

risk for lung cancer. However, at about 7 f/ml-years and higher there was about a 2-fold increased lung cancer risk and mesothelioma showed a monotonic increase from 2% to 23% (Fig. 12). There is the suggestion of a trend for CRC risk to be increased about 2-fold when lung cancer risk is increased about 4-fold (Fig. 7). These increases are inconsistent with the pattern of no gradient at higher individual-level exposures (Seidman et al., 1986, Fig. 11; Liddell et al., 1997; Fig. 10). The weight of evidence suggests that at current exposure limits for asbestos there is no increased risk of colorectal cancer.

- **Colon cancer exceptions:** There are no obvious exceptions. The weight of evidence suggests that at current exposure limits for asbestos there is no increased risk of colon cancer. However there are only three studies with individual-level E–R analyses and they are qualitative.
- **Rectal cancer exceptions:** There are no obvious exceptions. The weight of evidence suggests that at current exposure limits for asbestos there is no increased risk of colon cancer. However there are only two studies with individual-level E–R analyses and they are qualitative.

The patterns of response by causal criteria that lead to conclusions of no causal associations are summarized below.

	Strength of association	Biological gradient (Exposure–response)			Consistency	Weight of evidence
		Lung	Mesothelioma	Internal		
Stomach cancer	Weak; overall RR = 1.01 ~50/50 split of neg./pos. studies	Possible trend: RR increased when lung cancer RR > 4; Sig. 43% increased risk when LC RR > 3	No trend	No trend except above threshold >700 mppcf-yrs	Lack of consistent findings below threshold	Lack of evidence of increased risk at or above current exposures
Colo-rectal cancer	Weak; overall RR < 1.0; more neg. than pos. studies	Possible trend when LC RR > 4	No trend	No trends in four adequate cohort studies	Lack of consistent positive associations except five cohorts LC RR > 3 (15% of 569 total cases)	Lack of evidence for increased risk except perhaps at high exposures >> current standards
Colon cancer	Weak; overall RR < 1.0 more neg. than pos. studies	No trend	No trend	No studies with quantitative E–R analysis	Lack of consistent positive associations	Lack of evidence for increased risk at any exposure levels
Rectal cancer	Weak; overall RR = 1.06, 50/50 split pos./neg. studies	No apparent trend, 5/6 pos SMRs when LC 1.5–2.6	No trend	No studies with quantitative E–R analysis, no apparent trends in two studies with qualitative exposures	Lack of consistent positive association	Lack of evidence for increased risk at any exposure level; fewer cases/study make it difficult to assess individual ER

Assessing the asbestos/GI cancer hypothesis is limited for several reasons. Primary emphasis in asbestos studies has been on lung cancer, which often has a sufficient number of cases for meaningful analysis of E–R trends. Focus has also been on mesothelioma, which is a rare tumor and specific for asbestos exposure. GI cancers have generally not been of primary interest and have at times been combined (i.e., as digestive cancers, colon + rectal into colorectal) without E–R analysis. Since there are relatively few internal E–R analyses of GI cancers, surrogate exposures and external comparison groups are an attempt to indirectly assess E–R gradients. The use of external comparisons can only be adjusted for age, sex and race, so an unknown amount of bias and confounding are inevitable in the risk estimates. This may be part of the reason for the somewhat heterogeneity of the SMRs. Some of these factors are mentioned in the discussion below for the individual GI cancers.

In addition, there is some bias/confounding in the surrogate exposure estimates. One is the effect of smoking on risk of lung cancer that cannot be accounted for in the external comparisons, and which undoubtedly varies between cohorts. So the risk ratios for lung cancer are not independent of the distribution of smoking in the exposed population. Also, amphiboles appear to pose a greater hazard for mesothelioma than serpentine asbestos (chrysotile), which could change the GI cancer/mesothelioma association in a fashion different than that for lung cancer.

Internal comparisons do not have these biases. A problem with individual level E–R data is that they comprise only a fraction of the total cases and so are related to the size of the study or the interests of the investigator. As a result the weight of the evidence regarding whether associations are causal should consider the consistency of the pattern of risks from all three estimates of exposure and for each kind of GI cancer independently. The following

discussion attempts to do this, including brief consideration of lifestyle risk factors that might further confound the risk estimates.

4.1. Stomach cancer

Stomach cancer was the leading cancer cause of death in 1930, but current rates have been reduced about 80%. Internationally stomach cancer is the second leading cause of death due to cancer and the seventh leading cause of death in the United States. Lower socioeconomic status (SES) and male gender are associated with a 2-fold increased risk compared to females and upper social class. Smoking and drinking show have inconsistent associations. SES and smoking are potential risk factors that cannot be controlled in the SMR analysis and in some instances could be confounders, as suggested by Liddell et al. (1997) in their study of chrysotile miners/millers. Other risk factors include nitrates and related compounds, salt, diets high in starch and low in fruits and vegetables and *Helicobacter pylori* bacteria (Nomura, 1996). Only age, gender and race can be adjusted for in the SMR analyses, so unless there are internal comparisons there is some potential for confounding from lifestyle risk factors and a potential cause for some of the heterogeneity in the SMRs.

The strength of association between stomach cancer and asbestos is consistently weak (<2) and about half of the studies show a deficit in the risk of stomach cancer. The one statistically significant excess is a study of Chinese chrysotile factory workers with five stomach cancer cases (all males) and a significant 7.9-fold excess, and a 4.4-fold excess when women are included (Pang et al., 1997). Past exposures were quite high as the high end of the estimated exposure ranges were 415 mg/m₃ in the 1950–1960s, 35 mg/m₃ in the 1970–1980s and 17 mg/m₃ in the 1990s. High exposures are consistent with the strong associations with lung cancer where risks were increased 5-fold among the

men (all smokers) and 7-fold among the women (all non-smokers); all cases were at the highest level of exposure. The higher risk of lung cancer among women but a higher risk of stomach cancer among men (there were no stomach cancer cases among women) is inconsistent with an asbestos etiology for the stomach cancer excess. The male/female ratio for occurrence of stomach cancer is about 1.5–2.5/1, which might explain some of the male excess. Smoking is a possible confounder and might also explain part of the increased risk among men but not women in this Chinese cohort.

There are no apparent E–R trends using risk of lung cancer and mesothelioma as surrogates of exposure (Figs. 1 and 2). The lack of E–R trends is also observed in individual studies using qualitative estimates of exposure and where lung cancer and mesothelioma generally increased significantly with increasing asbestos exposure (Figs. 3–5). The exception to this finding is from the cohort of Canadian chrysotile miners/millers where E–R trends for stomach and lung cancer were similar with no trend for risks to increase when cumulative exposures were below about 300 mppcf-years. The authors note that the increased SMRs for stomach cancer (~ 1.4) below 10 mppcf-years produced a negative E–R trend below 1000 mppcf-years (Fig. 6). They suggest the excess stomach cancer mortality is probably due to socioeconomic factors (an important risk factor). Smoking may also be a causal agent since smokers had about an 80% increased risk of stomach cancer while nonsmokers and exsmokers showed a deficit. Mesothelioma is not a good surrogate for exposure in this cohort as the E–R curve is flat (Fig. 6). And there is some question about chrysotile *per se* causing mesothelioma (Hodgson and Darnton, 2000).

In summary, the large amount of data obtained after the original finding of excess GI cancers among insulation workers by Selikoff et al. (1964) does not support the hypothesis that asbestos exposure causes stomach cancer at concentrations found in today's workplace or even higher. The data show a consistent pattern of weak associations with a high proportion of SMRs less than 1.0. There are no biological gradients using surrogate exposure estimates and a consistent lack of E–R in the few individual studies where a gradient was assessed. The study of chrysotile miners/millers shows a significant excess at the highest exposure group, some of which could be due to confounding (SES, smoking) or high dust.

4.2. Cancer of the large intestine

Cancer of the large intestine (colon + rectum or colorectal cancer) is often considered one disease, as was done in many of the asbestos cohorts. Colorectal cancer (CRC) is a common cause of death as it is the second most common cancer among women (after breast cancer) and third most common among men (after lung and prostate) (Schottenfeld and Winawer, 1996). About 70 male/female ratios of 1.3 and 1.7, respectively. Colorectal cancer is generally

not considered an occupational disease, although occurrence is affected by environmental factors.

Considering colorectal cancer as one disease may produce misleading and incorrect results because some risk factors for colon and rectal cancer are not quite the same in magnitude or in the nature of the risk. As a result the strength of the associations will be reduced or obscured by considering only colorectal cancer as an entity (Arbman et al., 1993). Since many of the cohort studies considered CRC rather than colon and rectum separately, results for all three are discussed, CRC and then colon and rectal cancers.

Some of the common and different risks are listed (Schottenfeld and Winawer, 1996).

- Higher incidence of colon cancer than rectal cancer among urban than rural residents and men than women;
- Inflammatory bowel disease increases risk CRC 4- to 20-fold;
- Suggestive protective effect for CRC with high fiber, fruits and vegetable diet and increased risk associated with high caloric/fat diet.

There are inconsistent or weak associations with alcohol and smoking, perhaps stronger for pipe smoking. However, the inconsistencies may be related to length of follow-up. If there is at least 20-years follow-up and adjusting for social class and physical activity, risk of both colon and rectal cancer risks are increased about 2-fold among heavy current smokers, about 1.35 among former smokers and pipe/cigar smokers. Risk of rectal cancer is also increased about 2-fold among users of chewing tobacco or snuff (Heineman et al., 1995).

4.3. Colorectal cancer (CRC)

The strength of association is consistently weak with positive SMRs always less than 2-fold and 60% of the associations are negative. There are no apparent biological gradients using either lung cancer or mesothelioma as surrogates of asbestos exposure (Figs. 7 and 8). The lack of E–R trends is generally consistent with the findings from the individual-level studies using cumulative exposure estimates (Figs. 9–12).

The E–R in Hughes et al. (1987) was irregular and equivocal because of the small number of cases and the small numbers of expected cases in each cell. The obvious gradient for lung cancer and 2-fold increased risks for lung cancer in the three highest exposure categories above about 36 mppcf-years increase credibility of the lack of CRC gradient (Fig. 9).

Liddell et al. (1997) showed a clear lack of biological gradient for CRC (actually negative correlation coefficients over the full range of exposure categories), while lung cancer SMRs were increased 3-fold in the highest exposure category. This is the largest and best-documented study of asbestos workers and with 319 cases the risk estimates

are stable. The relatively weak associations for lung cancer and mesothelioma are thought to be due to the relatively low concentrations of tremolite asbestos as a contaminant with predominant exposure to the less biopersistent chrysotile. Despite the high estimates of cumulative exposure, there is obviously no CRC gradient (Fig. 10).

The study of amosite-exposed workers by Seidman et al. (1986) showed no apparent biological gradient for CRC but a steep gradient for lung cancer going to 12-fold increased SMR at about 250 f/ml-years. SMRs for CRC were significantly increased about 3-fold in two of the eight exposure categories, but the increases were in the lower exposure categories. This group comprised cases with 5–40 years of latency, so some cases could have too short a latency period to have a work-related CRC cancer. This is unlikely to be a severe limitation given the steep gradient for lung cancer that requires a similar latency and the 3% incidence for mesothelioma, which has an even longer mean latency than CRC (Fig. 11).

E–R in Albin et al. (1990) is suggestive of a biological gradient between asbestos exposure and CRC mortality that is similar to the gradient for lung cancer but much less than that for mesothelioma. If a true association, the apparent threshold for CRC is around 40 fiber/ml-years. The steep gradient for mesothelioma is probably due to the presence of the amphiboles crocidolite and amosite. It is not clear why lung cancer risk remains constant at all exposure levels given the strong gradient for mesothelioma (Fig. 12).

Meurman et al. (1994) reported no CRC risk associated with exposure among male anthophyllite miners, but risks from both lung cancer and mesothelioma were associated with increased exposure. Demers et al. (1994) is a case–control study that showed a very strong association with mesothelioma, perhaps because the controls were from a different source population where one would expect few or no mesotheliomas. There was a deficit for colorectal cancer, which is consistent with no association (Table 1).

In summary, the weight of evidence suggests asbestos does not cause colorectal cancer because there is a consistent lack of associations in external comparisons and lack of E–R using surrogate exposures as well as individual-level assessments. When there are associations they are weak and not related to surrogates of exposure. Six individual studies are consistent with the surrogate exposure data in showing a lack of biological gradients.

4.4. Colon cancer

Colon cancer is among the most common cancers, and in the US is the second leading cause of cancer deaths. Dietary calcium and/or vitamin D (or sun exposure) are inversely related to the incidence of colon cancer (Holt, 1999). There is a protective effect of fiber-rich diets and vegetables and detrimental effect of fat, although it was not possible to discriminate between effects due to fiber and nonfiber effects due to vegetables (Trock et al., 1990; Reddy, 1995). Physical inactivity and obesity increase the risk of

colon cancer, and the risk associated with activity is attenuated if colon and rectal cancers are combined (Colditz et al., 1997; Ford, 1999). None of these risk factors can be adjusted for directly in the SMR analysis of risk.

The analysis of colon cancer provides similar relationships as was observed for colorectal cancer, but with somewhat less data and greater heterogeneity in the risk estimates. The strength of the association is consistently weak with over half of the overall SMRs being less than 1.0. Of the two statistically significant findings, one has a risk ratio significantly less than 1.0 (Hodgson and Jones, 1986) and the other a risk ratio significantly greater than 1.0 (Szeszenia-Dabrowska et al., 1998). Neither of these statistically significant findings is related to surrogate exposures as both have a high percentage of mesothelioma and low lung cancer. These figures also indicate a lack of E–R for all the studies using lung cancer and mesothelioma as surrogates for exposure (Figs. 13 and 14).

Three studies have qualitative E–R analyses and two compare exposed with unexposed; all involve amphibole exposures either wholly or partially (Fig. 15). In three of the studies there is either no difference in colon cancer risk between exposed and unexposed (Acheson et al., 1984) or a nonsignificant inverse trend (Weiderpass et al., 2003; Demers et al., 1994). There is a substantial increase in risk of mesothelioma as risk of colon cancer does not change (Acheson et al., 1984; Demers et al., 1994), and for the Acheson cohort a 2-fold increase in lung cancer as well. These three studies do not implicate asbestos as a risk factor for colon cancer.

In the remaining two studies the point estimates for risk of colon cancer are higher for the high-exposure groups compared to those with light or moderate exposure (Hilt et al., 1991; Meurman et al., 1994). Percent mesothelioma in Hilt et al. (1991) is quite high (11%) but does not change between light and heavy exposure, while the risk of lung cancer more than triples. Colon cancer is increased 3-fold in both moderate- and high-exposure categories among female anthophyllite miners (Meurman et al., 1994) are too small to define colon cancer risk despite the strong associations with both lung cancer and mesothelioma. There was a 3.5-fold increased SMR among three female colon cancer cases with 0.87 expected. There were three male cases of CRC but 5.45 expected for a deficit SMR of 0.55. The excess among the females is neither statistically significant nor consistent with the male incidence, so colon cancer are unlikely to be due to asbestos exposure for either sex unless there is a difference in gender susceptibility.

4.5. Rectal cancer

This category has the smallest number of cases and fewest studies because often rectal and colon cancer has been combined and because the number of cases is generally small. Eight of the 15 cohorts had deficits in the risk ratios. Three cohorts had zero observed cases of rectal cancer and

tended to be at the higher exposure categories. Associations were weak when present and there were no E–R trends for either lung cancer or mesothelioma as surrogate estimators of exposure. E–R analyses from the three individual studies are not inconsistent with the E–R using surrogate estimates of exposure. However, the individual level E–R analyses have only qualitative exposure categories. And two of the cohorts have relatively unstable numbers of cases.

In sum, because of consistently weak associations and lack of any apparent biological gradients, the available evidence does not support the hypothesis that asbestos exposure causes rectal cancer.

Conflict of Interest

The author was employed at Exxon Mobil Biomedical Science Inc in Annandale, NJ while writing the draft manuscript.

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References

- 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.
- Albin, M., Jakobsson, K., Attewell, R., Johansson, L., Welinder, H., 1990. Mortality and cancer morbidity in cohorts of asbestos cement workers and referents. *Br. J. Ind. Med.* 47, 602–610.
- Amandus, H.E., Wheeler, R., 1987. The morbidity and mortality of vermiculite miners and millers exposed to tremolite–actinolite. Part II. Mortality. *Am. J. Ind. Med.* 11, 15–26.
- Anderson, A. et al., 1993. Incidence of cancer among lighthouse keepers exposed to asbestos in drinking water. *Am. J. Epidemiol.* 138 (9), 682–687.
- Arbman, G., Axelson, O., Fredriksson, M., Nilsson, E., Sjodahl, R., 1993. Do occupational factors influence the risk of colon and rectal cancer in different ways? *Cancer* 72, 2543–2549.
- 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.
- Battista, G., Belli, S., Comba, P., Fiumalbi, C., Grignoli, M., Loi, F., Orsi, D., Paredes, I., 1999. *Occup. Med.* 49, 536–539.
- Becklake, M.R., Case, B.W., 1994. Fiber burden and asbestos-related lung disease: determinants of dose–response relationships. *Am. J. Respir. Crit. Care Med.* 150, 1488–1492.
- Berry, G., Newhouse, M.L., 1983. Mortality of workers manufacturing friction materials using asbestos. *Br. J. Ind. Med.* 40, 1–7.
- Botta, M., Magnani, C., Terracini, B., Bertolone, G.P., Castagneto, B., Cocito, V., DeGiovanni, D., Paglieri, P., 1991. Mortality from respiratory and digestive cancers among asbestos cement workers in Italy. *Cancer Detect. Prevent.* 15, 445–447.
- Brown, D.P., Dement, J.M., Okun, A., 1994. Mortality patterns among female and male chrysotile asbestos textile workers. *J. Occup. Med.* 36 (8), 882–888.
- Carter, R.E., Taylor, W.F., 1980. Identification of a particular amphibole asbestos fiber in tissues of persons exposed to a high oral intake of the mineral. *Environ. Res.* 21, 85–93.
- Cheng, W.N., Kong, J., 1992. A retrospective mortality cohort study of Chrysotile asbestos products workers in Tianjin 1972–1987. *Environ. Res.* 59, 271–278.
- Clemmesen, J., Hjalgrim-Jensen, S., 1981. Cancer incidence among 5686 asbestos-cement workers followed from 1943 through 1976. *Ecotoxicol. Environ. Safety* 5, 15–23.
- Colditz, G.A., Cannuscio, C.C., Frazier, A.L., 1997. Physical activity and reduced risk of colon cancer: implications for prevention. *Cancer Causes Control* 8, 649–667.
- Conforti, P.M., Kanarek, M.S., Jackson, P.M., Cooper, R.C., Murchio, J.C., 1981. Asbestos in drinking water and cancer in the San Francisco Bay Area: 1969–1974 incidence. *J. Chronic. Dis.* 34, 211–224.
- Cook, P.M., Glass, G.E., Tucker, J.H., 1974. Asbestiform amphibole minerals: detection and measurement of high concentrations in municipal water supplies. *Science* 185, 853–855.
- 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.
- 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.
- Dement, J.M., Harris, R.L., Symons, M.J., Shy, C.M., 1983. Exposures and mortality among chrysotile asbestos workers. Part II: Mortality. *Am. J. Ind. Med.* 4, 421–433.
- Dement, J.M., Brown, D.P., Okun, A., 1994. Follow-up study of chrysotile asbestos textile workers: cohort mortality and case-control analyses. *Am. J. Ind. Med.* 26, 431–447.
- Demers, R.Y., Burns, P.B., Swanson, G.M., 1994. Construction occupations, asbestos exposure, and cancer of the colon and rectum. *J. Occup. Med.* 36, 1027–1031.
- Djerassi, L., Kaufman, G., Bar-Nets, M., 1979. Malignant disease and environmental control in an asbestos cement plant Health Hazards of Asbestos Exposure. *Ann. N.Y. Acad. Sci.* 330, 243–254.
- Doll, R., Peto, J., 1985. Asbestos: Effects on Health of Exposure to Asbestos. Health and Safety Commission. Her Majesty's Stationery Office, London.
- Dupre, J.S., Mustard, J.F., Uffen, R.J., Dewees, D.N., Laskin, J.I., Kahn, L.B., 1984. In: Report of the Royal Commission on Matters of Health and Safety arising from the use of asbestos in Ontario, vols. 1–3. Queen's Printer for Ontario, Toronto.
- Edelman, D.A., 1988. Exposure to asbestos and the risk of gastrointestinal cancer: a reassessment. *Br. J. Ind. Med.* 45, 75–82.
- Elwood, P.C., Cochrane, A.L., Benjamin, I.T., Seys-Prosser, D., 1964. A follow-up study of workers from an asbestos factory. *Br. J. Ind. Med.* 21, 304–307.
- Enterline, P.E., Hartley, J., Henderson, V., 1987. Asbestos and cancer: a cohort followed up to death. *Br. J. Ind. Med.* 44, 396–401.
- Finkelstein, M.M., 1984. Mortality among employees of an Ontario asbestos-cement factory. *Am. Rev. Respir. Dis.* 129, 754–761.
- Ford, E.S., 1999. Body mass index and colon cancer in a National sample of adult US men and women. *Am. J. Epidemiol.* 150, 390–398.
- Frumkin, H., Berlin, J.A., 1991. Asbestos exposure and gastrointestinal cancer: a response., 409–411.
- Gamble, J.F., 1994. Asbestos and colon cancer: A weight-of-the-evidence review. *Environ. Health Perspectives* 102, 1038–1050.
- Gardner, M.J., Winter, P.D., Pannett, B., Powell, C.A., 1986. Follow up study of workers manufacturing chrysotile asbestos cement products. *Br. J. Ind. Med.* 43, 726–732.
- Giaroli, C., Belli, S., Bruno, C., Candela, S., Grignoli, M., et al., 1994. Mortality study of asbestos cement workers. *Int. Arch. Occup. Environ. Health* 66, 7–11.
- Goodman, M., Morgan, R.W., Ray, R., Malloy, C.D., Zhao, K., 1999. Cancer in asbestos-exposed occupational cohorts: a meta-analysis. *Cancer Causes Control* 10, 453–465.
- Graham, S., 1981. Methodological problems in ecologic studies of the asbestos–cancer relationship. *Environ. Res.* 25, 35–49.
- Harrington, J.M., Craun, G., Meigs, J.W., Landrigan, P.J., Flannery, J.T., Woodhull, R.S., 1978. An investigation of the use of asbestos

- cement pipe for public water supply and the incidence of gastrointestinal cancer in Connecticut, 1935–1973. *Am. J. Epidemiol.* 107, 96–103.
- Heineman, E.F., Zahm, S.H., McLaughlin, J.K., Vaught, J.B., 1995. Increased risk of colorectal cancer among smokers: results of a 26-year follow-up of US veterans and a review. *Int. J. Cancer* 59, 728–738.
- 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.
- Hilt, B., Langard, S., Andersen, A., Rosenberg, J., 1985. Asbestos exposure, smoking habits, and cancer incidence among production and maintenance workers in an electrochemical plant. *Am. J. Ind. Med.* 8, 565–577.
- Hilt, B., Andersen, A., Rosenberg, J., Langard, S., 1991. Cancer incidence among asbestos-exposed chemical industry workers: an extended observation period. *Am. J. Ind. Med.* 20, 261–264.
- 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.
- Hodgson, J.T., Jones, R.D., 1986. Mortality of asbestos workers in England and Wales 1971–81. *Br. J. Ind. Med.* 43, 158–164.
- Holt, P.R., 1999. Dairy foods and prevention of colon cancer: human studies. *J. Am. College Nutr.* 18, 379S–391S.
- Homa, D.M., Garabrant, D.H., Gillespie, B.W., 1994. A meta-analysis of colorectal cancer and asbestos exposure. *Am. J. Epidemiol.* 139, 1210–1222.
- Hughes, J.M., Weill, H., Hammad, Y.Y., 1987. Mortality of workers employed in two asbestos cement manufacturing plants. *Br. J. Ind. Med.* 44, 161–174.
- Imbernón, E., Goldberg, M., Guenel, P., Chevalier, A., Vatre, R., Bonenfant, S., the Matex Group, 1996. Validation of asbestos exposure assessment in a job-exposure matrix in the electricity and gas industry in France: the Matex Project. *Occup. Hyg.* 3, 193–198.
- Kanarek, M.S., Conforti, P., Jackson, L., Cooper, R.C., Murchio, J.C., 1980. Asbestos in drinking water and cancer incidence in the San Francisco Bay Area. *Am. J. Epidemiol.* 1123, 54–72.
- Koskinen, K., Pukkala, E., Reijula, K., Karjalainen, A., 2003. Incidence of cancer among the participants of the Finnish asbestos screening campaign. *Scand. J. Work Environ. Health* 29, 64–70.
- Levine, D.S., 1985. Does asbestos exposure cause gastrointestinal cancer? *Dig. Dis. Sci.* 30, 1189–1198.
- Levin, J.L., McLarty, J.W., Hurst, G.A., Smith, A.N., Frank, A.L., 1998. *Occup. Environ. Med.* 55, 155–160.
- Levy, B.S., Sigurdson, E., Mandel, J., Laudon, E., Pearson, U., 1976. Investigating possible effects of asbestos in city water: surveillance of gastrointestinal cancer incidence in Duluth, Minnesota. *Am. J. Epidemiol.* 103, 362–368.
- Liddell, F.D.K., 1993. Exposure-response: asbestos and mesothelioma. *Eur. Respir. Rev.* 3, 98–99.
- Liddell, F.D.K., McDonald, A.D., McDonald, J.C., 1997. The 1891–1920 birth cohort of Quebec chrysotile miners and millers: development from 1904 and mortality to 1992. *Ann. Occup. Hyg.* 41, 13–36.
- Marsh, G.M., 1983. A critical review of epidemiologic studies related to the ingestion of asbestos. *Environ. Health Persp.* 53, 49–56.
- Masson, T.J., McKay, F.W., Miller, R.W., 1974. Asbestos-like fibers in Duluth water supply, relation to cancer mortality. *JAMA* 228, 1019–1020.
- McDonald, J.C., Liddell, F.D.K., Gibbs, G.W., Dyssen, G.E., McDonald, A.D., 1980. Dust exposure and mortality in chrysotile mining, 1910–75. *Br. J. Ind. Med.* 37, 11–24.
- McDonald, A.D., Fry, J.S., Woolley, A.J., McDonald, J.C., 1983. Dust exposure and mortality in an American chrysotile textile plant. *Br. J. Ind. Med.* 40, 361–367.
- 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, J.C., McDonald, A.D., Armstrong, B., Sebastien, P., 1986. Cohort study of mortality of vermiculite miners exposed to tremolite. *Br. J. Ind. Med.* 43, 445–449.
- McDonald, J.C., Liddell, F.D.K., Dufresne, A., McDonald, A.D., 1993. The 1891–1920 birth cohort of Quebec chrysotile miners and millers: Mortality 1976–88. *Br. J. Ind. Med.* 50, 1073–1081.
- Meigs, J.W., Walter, S., Heston, J., Millette, J.R., Craun, G.F., Woodhull, R.S., Flannery, J.T., 1980. Asbestos-cement pipe and cancer in Connecticut, 1955–1974. *J. Environ. Res.* 42, 187–191.
- Melkild, A., Langard, S., Andersen, A., Tonnessen, C.N.S., 1989. Incidence of cancer among welders and other workers in a Norwegian shipyard. *Scand. J. Work Environ. Health* 15, 387–394.
- Meurman, L.O., Pukkala, E., Hakama, M., 1994. Incidence of cancer among anthophyllite asbestos miners in Finland. *Occup. Environ. Med.* 51, 421–425.
- Miller, A.B., 1978. Asbestos fibre dust and gastro-intestinal malignancies: review of literature with regard to a cause/effect relationship. *J. Chron. Dis.* 31, 23–33.
- Neugut, A.I., Wylie, P., 1987. Occupational cancers of the gastrointestinal tract. I. Colon, stomach and esophagus. *State Art Rev. Occup. Med* 2, 109–135.
- Nokso-Koivisto, P., Pukkala, E., 1994. Past exposure to asbestos and combustion products and incidence of cancer among Finnish locomotive drivers. *Occup. Environ. Med.* 51, 330–334.
- Nolan, R.P., Langer, A.M., Wilson, R., 1999. A risk assessment for exposure to grunerite asbestos (amosite) in an iron ore mine. *Proc. Nat. Acad. Sci. USA* 96, 3412–3419.
- Nomura, A., 1996. Stomach Cancer. In: Schottenfeld, David, Fraumeni, Joseph F., Jr. (Eds.), *Cancer Epidemiology and Prevention*, 2nd ed. Oxford University, New York.
- Ohlson, G.G., Hogstedt, C., 1985. Lung cancer among asbestos cement workers. A Swedish cohort study and a review. *Br. J. Ind. Med.* 42, 397–402.
- Ohlson, C.G., Klaesson, B., Hogstedt, C., 1984. Mortality among asbestos-exposed workers in a railroad workshop. *Scand. J. Work Environ. Health* 10, 283–291.
- Pang, Z.C., Zhang, A., Wang, Y., Zhang, H., 1997. Mortality from a Chinese asbestos plant: Overall cancer mortality. *Am. J. Ind. Med.* 32, 442–444.
- Peto, J., Doll, R., Hermon, C., Binns, W., Clayton, Goffe, T., 1985. Relationship of mortality to measures of environmental asbestos pollution in an asbestos textile factory. *Ann. Occup. Hyg.* 29, 305–355.
- Piolatto, G., Negri, E., Vecchia, C.L., Pira, E., Decarli, A., Peto, J., 1990. An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. *Br. J. Ind. Med.* 47, 810–814.
- Polissar, L., Severson, R.K., Boatman, E.S., Polissar, L., Severson, R.K., Boatman, E.S., Thomas, D.B., 1982. Cancer incidence in relation to asbestos in drinking water in the Puget Sound Region. *Am. J. Epidemiol.* 116, 314–328.
- Polissar, L., Severson, R.K., Boatman, E.S., 1983. Cancer risk from asbestos in drinking water: summary of a case-control study in Western Washington. *Environ. Health Persp.* 53, 57–60.
- Polissar, L., Severson, R.K., Boatman, E.S., 1984. A case-control study of asbestos in drinking water and cancer risk. *Am. J. Epidemiol.* 119, 456–471.
- Raffin, E., Lynge, E., Juel, K., Korsgaard, B., 1989. Incidence of cancer and mortality among employees in the asbestos cement industry in Denmark. *Br. J. Ind. Med.* 46, 90–96.
- Raffin, E., Villadsen, E., Lynge, E., 1996. Colorectal cancer in asbestos cement workers in Denmark. *Am. J. Ind. Med.* 30, 267–272.
- Reddy, B.S., 1995. Nutritional factors and colon cancer. *Crit. Rev. Food Sci. Nutr.* 35, 175–190.
- Rosler, J.A., Weitowitz, H., Lange, H., Weitowitz, R.H., Ulm, K., Rodelsperger, K., 1994. Mortality rates in a female cohort following asbestos exposure in Germany. *J. Occup. Med.* 36, 889–893.
- Rubino, G.F., Piolatto, G., Newhouse, M.L., Scansetti, G., Aresini, G.A., Murray, R., 1979. Mortality of chrysotile asbestos workers at the Balangero Mine Northern Italy. *Br. J. Ind. Med.* 36, 187–194.
- Sadler, T.D., Rom, W.N., Lyon, J.L., Mason, J.O., 1981. The Use of Asbestos-cement Pipe for Public Water Supply and the Incidence of Cancer in Selected Communities in Utah, 1967–1976. Graduate thesis, University of Utah.

- Sanden, A., Jarvholm, B., Larsson, S., Thiringer, G., 1992. The risk of lung cancer and mesothelioma after cessation of asbestos exposure: a prospective cohort study of shipyard workers. *Eur. Respir. J.* 5, 281–285.
- Schottenfeld, D., Winawer, S.J., 1996. Cancers of the large intestine. In: Schottenfeld, D., Fraumeni, J.F. (Eds.), Chapter 39: Cancer Epidemiology and Prevention, second ed. Oxford University Press, New York.
- Seidman, H., Selikoff, I.F., 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., Churg, J., Hammond, E.C., 1964. Asbestos exposure and neoplasia. *JAMA* 188, 22–26.
- Selikoff, I.J., Hammond, E.C., Seidman, H., 1979. Mortality experience of insulation workers in the United States and Canada, 1943–1976. *Ann. N.Y. Acad. Sci.* 330, 91–116.
- Selikoff, I.J., Seidman, H., Hammond, E.C., 1980. Mortality: effects of cigarette smoking among amosite asbestos factory workers. *JNCI* 65, 507–513.
- Severson, R.A., 1979. A Study of the Effects of Asbestos in Drinking Water and Cancer Incidence in the Puget Sound Region. M.S. Thesis, University of Washington, Seattle, Washington.
- Sigurdson, E.E., 1982. Description and comparison of two population-based studies of Duluth, Minnesota, as a follow-up of asbestos exposure and recommendations for facilitating similar studies in the future. *J. Environ. Sci. Health A17*, 463–471.
- Sigurdson, E.E., Levy, B.S., Mandel, J., McHugh, R., Michienzi, L.J., Jagger, H., Pearson, J., 1981. Cancer morbidity investigations: lessons from the Duluth study of possible effects of asbestos in drinking water. *Environ. Res.* 25, 50–61.
- Szeszenia-Dabrowska, N., Wilczynska, U., Szymczak, W., Laskowicz, K., 1998. Environmental exposure to asbestos in asbestos cement workers: a case of additional exposure from indiscriminate use of industrial wastes. *Int. J. Occup. Med. Environ. Health* 11, 171–177.
- Tarter, M.E., 1981. Pattern recognition in the context of an asbestos cancer threshold study. In: Proceedings of the 13th Annual Symposium on the Interface, Computer Science Statistic.
- 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.
- Toft, P., Wigle, D.T., Meranger, J.C., Mao, Y., 1981. Asbestos and drinking water in Canada. *Sci. Total Environ.* 18, 77–89.
- Tola, S., Kalliomaki, P.-L., Pukkala, E., Asp, S., Korkals, M.-L., 1988. Incidence of cancer among welders, platers, machinists, and pipe fitters in shipyards and machine shops. *Br. J. Ind. Med.* 45, 209–218.
- Trock, B., Lanza, E., Greenwald, P., 1990. Dietary fiber, vegetables, and colon cancer: critical review and meta-analyses of the epidemiologic evidence. *J. Natl. Cancer Inst.* 82, 650–661.
- Tsai, S.P., Waddell, L.C., Gilstrap, E.L., Ransdell, J.D., Ross, C.E., 1996. Mortality among maintenance employees potentially exposed to asbestos in a refinery and petrochemical plant. *Am. J. Ind. Med.* 29, 89–98.
- Tulchinsky, T.H., Ginsberg, G.M., Shihab, S., Goldberg, E., Laster, R., 1992. Mesothelioma mortality among former asbestos-cement workers in Israel 1953–90. *Israel J. Med. Sci.* 28, 543–547.
- Tulchinsky, T.H., Ginsberg, G.M., Iscovich, J., Shihab, S., Fischbein, A., Richter, E.D., 1999. Cancer in ex-asbestos cement workers in Israel, 1953–1992. *Am. J. Ind. Med.* 35, 1–8.
- Tuomi, T., Huuskonen, M.S., Virtamo, M., Tossavainen, A., Tammilehto, L., et al., 1991. Relative risk of mesothelioma associated with different levels of exposure to asbestos. *Scand. J. Work Environ. Health* 17, 404–408.
- Waage, H.P., Langard, S., Andersen, A., 1993. The incidence of asbestos-related cancer in a population cross-section: eight years of follow-up. *J. Occup. Med. Toxicol.* 2, 15–30.
- Weiderpass, E., Vainio, H., Kaupppinen, T., Vasama-Neuvonen, K., Partanen, T., Pukkala, E., 2003. Occupational exposures and gastrointestinal cancers among Finnish women. *J. Occup. Environ. Med.* 45, 305–315.
- Weiss, W., 1995. The lack of causality between asbestos and colorectal cancer. *JOEM* 37, 1364–1373.
- Wigle, D.T., 1977. Cancer mortality in relation to asbestos in municipal water supplies. *Arch. Environ. Health* (July/August), 185–190.

An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments

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Abstract

Amphiboles are hydrated mineral silicates five of which occur in asbestiform habits as asbestos grunerite (amosite) asbestos, riebeckite (crocidolite) asbestos, anthophyllite asbestos, tremolite asbestos and actinolite asbestos] and non-asbestiform habits (grunerite, riebeckite, anthophyllite, tremolite and actinolite). The asbestiform varieties are characterized by long, thin fibers while non-asbestiform varieties such as cleavage fragments form short fibers with larger widths. The U.S. regulatory method for counting asbestos fibers (aspect ratio $\geq 3:1$, length $\geq 5 \mu\text{m}$) does not distinguish between asbestos and cleavage fragments. The method biases toward increased counts of non-asbestiform cleavage fragments compared to long, thin asbestos fibers. One consequence of this regulatory approach is that workers can be erroneously classified as exposed to concentrations of asbestos (asbestiform amphiboles) above the U.S. 0.1 f/mL exposure standard when in fact they are not exposed to asbestos at all but non-asbestiform amphibole cleavage fragments. Another consequence is that the known carcinogenic effects of asbestos may be falsely attributed to non-asbestiform amphibole cleavage fragments of the same mineral. The purpose of this review is to assess whether amphibole cleavage fragments pose the same risk of lung cancer and mesothelioma characteristic of amphibole asbestos fibers.

We identified three groups of workers exposed to non-asbestiform amphiboles: two groups exposed to grunerite (Homestake gold miners and taconite miners) and one group exposed to industrial talc containing non-asbestiform tremolite and anthophyllite in St. Lawrence County, NY. In addition to assessing strength of association and exposure–response trends in the non-asbestiform amphibole cohorts, comparisons were also made with cohorts exposed to the asbestiform counterpart (positive control) and cohorts exposed to the mineral (e.g. talc) that does not contain amphiboles (negative controls).

The cohorts exposed to non-asbestiform amphiboles had no excesses of lung cancer or mesothelioma. Similar results were observed in the negative control groups, in stark contrast to the excess risks of asbestos-related disease found in the asbestos cohorts. The only possible exception is the twofold increased risk of lung cancer where exposure was to industrial talc containing cleavage fragments of tremolite and anthophyllite. However, this risk is not considered attributable to the talc or amphibole cleavage fragments for several reasons. A similar increased risk of lung cancer was found in Vermont talc workers, studied in the same time period. Their exposure was to relatively pure talc. There was no relationship between lung cancer mortality and exposure measured as mg/m^3 years and years worked. A case–control study reported that all the lung cancer cases were smokers (or former smokers) and attributed the excess to smoking. There were two mesothelioma cases among the NY State talc workers exposed to cleavage fragments of tremolite and anthophyllite, but talc is not a plausible cause because of too short latency and potential for previous asbestos exposure. The positive controls of tremolite asbestos and anthophyllite asbestos exposed workers showed excess risks of both lung cancer and mesothelioma and positive exposure–response trends. St. Lawrence, NY talc does not produce mesotheliomas in animals while amphibole asbestos does. In sum, the weight of evidence fully supports a conclusion that non-asbestiform amphiboles do not increase the risk of lung cancer or mesothelioma.

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Keywords: Amphiboles; Cleavage fragments; Lung cancer; Mesothelioma; Asbestos; Non-asbestiform amphiboles; Grunerite; Talc

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1. Introduction

Asbestos is a generic term applied to a group of hydrated fibrous mineral silicates. Their asbestiform habit permits them to be easily separated into long, thin, flexible, strong fibers and ultimately fibrils (single fibers). Included are the asbestiform serpentine (chrysotile) and the asbestiform amphiboles, riebeckite (crocidolite) asbestos, anthophyllite asbestos, grunerite (amosite) asbestos, tremolite asbestos and actinolite asbestos. These minerals also crystallize with non-asbestiform habits, their counterparts being lizardite or antigorite (chrysotile), riebeckite, anthophyllite, grunerite, tremolite and actinolite, respectively. Crystal habit is a description of the shapes in which a certain mineral is likely to occur, both in nature and when grown synthetically. Tremolite is a mineral in the tremolite-ferro-actinolite series that has fewer than 0.5 atoms of iron, and more than 4.5 atoms of magnesium per formula unit; actinolite has between 0.5 and 2.5 atoms of iron, and 2.5 atoms of magnesium per formula unit; ferro-actinolite has more than 2.5 atoms of iron per formula unit with the balance being magnesium.

By the early 1970s, airborne concentrations of asbestos fiber were being measured using “the membrane filter phase contrast method (PCM)”. In many countries, including the USA, this method was adopted for the regulatory control of asbestos. Fundamental to the method was the definition of a fiber as an elongated particle having a length: breadth ratio (aspect ratio) of at least 3:1 and a minimum length of 5 micrometers (μm). Such a definition does not allow the microcopist to distinguish between asbestos fibers and non-asbestos amphibole particles. Consequently, in work environments where there exist many elongated particles meeting the PCM fiber definition, they are counted as if they are “asbestos” even if they are neither asbestos minerals nor even amphiboles. This results in concern by workers and health professionals about health risks and potential economic impacts for companies mining ore deposits where amphibole minerals are present. This is because the amphiboles have cleavage planes such that when they are crushed they produce elongated prismatic particles called cleavage fragments.

All amphiboles that were once exploited commercially as asbestos have non-asbestiform counterparts. Hence, workers in industries where amphibole cleavage fragments are present, but not asbestos, are often erroneously reported as being exposed to asbestos based on current regulatory counting strategies and protocols. On the other hand, the evidence concerning the health consequences of exposure to cleavage fragments has never been widely understood. Industries involving exposure to cleavage fragments should not be exempt from similar controls to the asbestos industries, if elongated particles meeting the PCM definition of fibers pose qualitatively and quantitatively the same levels of health risk as their asbestiform counterparts. However, if cleavage fragments pose no or

a lesser risk than the asbestos minerals, they should be regulated accordingly.

The purpose of this paper is to compare, as far as possible, the cancer risks (lung cancer and mesothelioma) for workers exposed to airborne amphibole cleavage fragments with those associated with exposure to amphibole analogues that formed asbestos fibers. Pneumoconiosis risk will not be compared because some of the minerals associated with the amphibole cleavage fragments are recognized in their own right as causing lung fibrosis (e.g.: talc and crystalline silica). However, pneumoconiosis is sometimes used to assess whether exposure is high enough and latency long enough to detect carcinogenic risk and to evaluate the exposure-response.

2. Methods

The extent to which the carcinogenic risks of exposure to cleavage fragments differ from those associated with exposure to asbestos was examined in several ways.

The potential of particles to cause health effects depends on the characteristics of the particles (e.g.: size, shape, respirability, solubility, toxicity, carcinogenic potential), the level and duration of exposure as well as host and other factors. It is important to determine whether amphibole cleavage fragments differ sufficiently from asbestos fibers for them to pose different levels of health risk than their asbestos counterparts. To do this requires examination of the characteristics of the particle such as dimensions, shape and density that influence fiber respirability, and fiber dimensions and biopersistence that influence carcinogenicity.

Mesothelioma and lung cancer are the health endpoints examined for comparison of the relative effects of non-asbestiform and asbestiform amphiboles. Mesothelioma is considered the more important indicator because it is both more specific and perhaps more sensitive than lung cancer. Mesothelioma is a rare cancer that acts as a marker or “signal” tumor, which is primarily associated with exposure to amphibole asbestos and has occurred in some situations after what appears to be exposure at quite low concentrations. Lung cancer is more subject to being caused by confounding exposures such as smoking, which is the primary cause of lung cancer. Thus while lung cancer might be caused by asbestos, it is an effect that is not specific to asbestos exposure.

If smoking prevalence is not known, the effects of dust exposure and smoking in the occurrence of lung cancer cannot readily be distinguished. Mesothelioma is a more sensitive and specific indicator of amphibole asbestos exposure than lung cancer in that pleural mesothelioma may occur following what are ostensibly brief exposures (Roggli, 1990) and up to 80% of the cases in males may be associated with asbestos exposure (Price and Ware, 2004). The exposure-response curve is thought to be non-linear for both mesothelioma and lung cancer. While the shapes of relationships are still subject to debate, pleural mesothelioma has been reported to increase less than linearly with cumulative dose. For peritoneal mesothelioma the risk is thought to be proportional to the square of cumulative exposure while for lung cancer the exposure-response lies between linear and square of cumulative exposure (Hodgson and Darn-ton, 2000). As some mesothelioma have been reported to occur after relatively low and perhaps brief exposures one might anticipate that if amphibole cleavage fragments act like asbestos in causing mesothelioma there might be some cases even if cleavage fragment exposures were low. For mesothelioma to be attributed to amphibole cleavage fragments the time since first exposure must be more than about 20 years and there should be no previous exposure to asbestos or other confounding etiological factors.

The mortality from lung cancer and mesothelioma are compared to that expected in age- and sex-adjusted external populations. The comparison measure is the standardised observed/expected mortality ratio or standardized mortality ratio (SMR). When the incidence of lung cancer

and mesothelioma are compared to that expected in age- and sex-adjusted external populations, the comparison measure is the standardised observed/expected cancer incidence ratio or standardized incidence ratio (SIR). External comparisons for assessing lung cancer risk have inherent limitations such as differences in smoking and lifestyle between the study population and the external referent population. It is generally not feasible to adjust for these differences. An SMR less than 1.5 or a statistically non-significant SMR is suggestive, but not conclusive, of no association. A deficit in the lung cancer SMR could be due to exposure levels below a no-effect threshold, or a few highly exposed workers diluted by many workers with low exposure or negative confounding due to a low prevalence of smoking. A nonsignificant SMR might be due to the small size of the study population and the low power of the study to detect significant differences. Similarly, a positive finding of lung cancer could be due to differences in smoking prevalence between the study and reference populations rather than exposure to non-asbestiform amphiboles.

For mesothelioma, external comparisons using an SMR are often not possible because the expected number of cases is not known or not estimated. Therefore an internal proportional mortality ratio (PMR) is used to estimate risk of mesothelioma. PMR's have their limitations which must be taken into account when using them. For example, as a PMR can increase with length of follow-up of a cohort, attention must be given to the comparability of the follow-up period. Age differences in populations being compared are important as age determines the nature of diseases from which people die as well as the frequency of death. The ratio with total deaths to some extent adjusts for both differences in follow-up and age. Era of death may be important because of diagnostic trends. Nevertheless, comparison of PMRs between non-asbestiform amphibole-exposed and asbestos-exposed populations is a useful way to examine the question of whether non-asbestiform amphiboles cause cancer at the same rates as asbestiform amphiboles.

The actual measured risks of lung cancer and mesothelioma in persons exposed to amphibole cleavage fragments is compared to workers exposed to asbestiform amphiboles as follows:

- The lung cancer and mesothelioma experience of workers exposed to amphibole cleavage fragments is compared with the experience of workers exposed to their asbestiform equivalents. There are three main ore bodies containing non-asbestiform amphiboles where epidemiological studies have been conducted. These are a gold mine in South Dakota (grunerite–cummingtonite exposure), taconite mines in Minnesota (grunerite and other non-asbestiform amphiboles) and a talc mine in St Lawrence County, New York State (transition minerals, non-asbestiform anthophyllite and tremolite). Their experience was compared to that of workers exposed to asbestiform amphiboles. These “positive controls” were in amosite asbestos mines, mills and manufacturing facilities, anthophyllite asbestos mines and vermiculite mines (exposed to winchite asbestos also known as soda tremolite asbestos). In this report, winchite asbestos from the vermiculite mine in Montana, will be referred to as “tremolite asbestos” as this has been the terminology used in the medical literature.
- The mortality from lung cancer is examined in relation to estimated levels of exposure to “fibers” for workers exposed to asbestos and workers exposed to amphibole cleavage fragments. The existence of a positive gradient of increasing risk with increasing exposure after taking account of potential confounders would be good evidence that the cleavage fragments were posing an increased risk of lung cancer. A negative gradient would be strong evidence against a causal association. The presence or absence of an exposure–response gradient is among the strongest evidence for or against a lung cancer association with cleavage fragment exposure because smoking is the major cause of lung cancer and rarely, if ever, can external comparisons be fully adjusted for smoking.
- The lung cancer and mesothelioma experience of workers exposed to dusts from an ore-body containing amphibole cleavage fragments is compared with that of workers exposed to dusts from a similar ore-body which does not contain asbestos or amphibole cleavage fragments. This is called a negative control. If the experience of the amphibole

cleavage fragment exposed workers were worse than that of the negative control (non-cleavage fragment exposed workers), this would be suggestive of an increased risk due to the presence of asbestos cleavage fragments.

- In order to investigate this, the mortality for St. Lawrence County talc miners is compared to that of talc miners where it is claimed amphiboles are not present. Also, the mortality of iron ore miners exposed to taconite rocks containing non-asbestiform grunerite and actinolite is compared to that of miners exposed to iron ore (hematite) which does not contain amphiboles.
- The biological plausibility of a difference in the potential of amphibole cleavage fragments to cause cancer compared to amphibole asbestos fibers was assessed by review of the results of toxicological studies involving asbestos and amphibole cleavage fragments. There is a clear pattern of an increased incidence of mesothelioma in animals exposed to amphibole asbestos. Observing a similar pattern for animals exposed to non-asbestiform amphiboles would be evidence supporting the hypothesis that non-asbestiform amphiboles pose a carcinogenic hazard similar to asbestos. The lack of an increased incidence of mesothelioma would be strong evidence against the hypothesis.

3. The amphiboles

The crystallographic structure of amphiboles consists of double chains of silica tetrahedra. Their general chemistry incorporates $(\text{Si}, \text{Al})_8\text{O}_{22}(\text{OH})_2$. The amphibole group of minerals is made up of a number of mineral series. These series result from the substitution of different elements in the structure. For example tremolite and actinolite are part of a homologous series of minerals—tremolite–actinolite–ferro-actinolite with chemistry $\text{Ca}_2(\text{MgFe})_5\text{Si}_8\text{O}_{22}(\text{OH})_2$. Actinolite is $\text{Ca}_2(\text{Mg}_{4.5}\text{Fe}_{0.5})\text{Si}_8\text{O}_{22}(\text{OH})_2$ – $\text{Ca}_2(\text{Mg}_{2.5}\text{Fe}_{2.5})\text{Si}_8\text{O}_{22}(\text{OH})_2$. Ferro-actinolite is $\text{Ca}_2(\text{Mg}_{2.5}\text{Fe}_{2.5})\text{Si}_8\text{O}_{22}(\text{OH})_2$ – $\text{Ca}_2\text{Fe}_5\text{Si}_8\text{O}_{22}(\text{OH})_2$. Actinolite with less than $\text{Fe}_{0.5}$ would be tremolite.

In practice, these minerals can have a fairly wide range of composition within the broad range of substitutions possible. The mineral names are defined where the ranges of the substituted elements fall within certain arbitrary boundaries.

Grunerite is a member of the mineral series cummingtonite–grunerite with chemistry $(\text{MgFe})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$. As noted above, the asbestiform variety of grunerite is “amosite”. As with the tremolite–ferro-actinolite series, the minerals in this series may display a range of compositions.

Anthophyllite occurs as asbestos and in a non-fibrous form and is an end member of the anthophyllite–ferro-anthophyllite series, which is chemically $(\text{MgFe}^{2+})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$. Anthophyllite is the name reserved for the orthorhombic MgFe amphibole where the ratio of $\text{Mg}/(\text{Mg} + \text{Fe})$ is greater than 0.5; a lower amount of magnesium in the same type of amphibole requires the name ferro-anthophyllite.

Non-asbestiform riebeckite and crocidolite asbestos have the same chemistry which is $\text{Na}_2\text{Fe}_3^{2+}\text{Fe}_2^{3+}\text{Si}_8\text{O}_{22}(\text{OH})_2$. Amphiboles exhibit prismatic cleavage, a property of nearly all samples of the amphiboles regardless of habit. There are two cleavage directions, both parallel to the length of the double-silicate chains. Cleavage across

the crystal is usually poor so that the fracture of amphiboles produces long rods or prisms and repeated cleavage produces thinner rods with a rhombic outline consisting of bundles of I beams (i.e.: structural units of the amphibole) (Skinner et al., 1988). The presence of twinning or chain width errors may results in an additional direction of weakness parallel to the length, enhancing the aspect ratio of cleavage fragments (Langer et al., 1991).

4. Properties of asbestiform and non-asbestiform amphiboles

While the chemical compositions of the asbestiform and non-asbestiform amphibole minerals are identical, the characteristics resulting from their differences in crystal habit are significant. The properties of the amphibole asbestos minerals include fibrous habit with parallel fibers occurring in bundles, fiber bundles with split or splayed ends, fibers showing curvature and fibers with high tensile strength. The high tensile strength and axial nature of asbestos means the diameters of asbestos fibrils are largely unaffected by milling. On the other hand, the low tensile strength of non-asbestiform amphiboles means that milling can reduce both particle length and width. The asbestos fibers have good heat insulation qualities, low electrical conductivity, fire resistance, and suitability for weaving. All asbestos minerals separate readily into long flexible fibrils with diameters less than about 0.5 μm and with aspect ratios (length: width ratios) ranging to well over 10,000 (Ross, 1978).

In the hand specimen (that is a sample of the rock as it occurs in nature), the appearance of the non-asbestos minerals is distinctly different from that of the asbestos minerals. This difference persists when viewed by optical and electron microscopy where the non-asbestiform minerals appear as blocks, chunks or slightly elongated particles in contrast to the very evident fibrous nature of asbestos. The non-asbestiform counterparts tend not to grow with parallel alignment. The crystals normally fracture when crushed forming cleavage fragments, some of which may appear as acicular or needle-like crystals because of the way in which amphibole minerals cleave. These cleavage fragments have diameters which on average, are much larger than those of asbestos fibers of the same length. Some asbestiform tremolite fibers with the majority of fiber diameters exceeding 0.25 μm , tested by intra-peritoneal injection in rats were found to be highly carcinogenic (Davis et al., 1991; Lee, 1990). However, almost 70% of the fibers had aspect ratios greater than 10:1, 42% greater than 15:1 and 25% had aspect ratios more than 20:1. This contrasts with the observations that only about 6% of the aspect ratios of cleavage fragments exceed 15:1. The diameters of cleavage fragments appear to be rarely less than 0.25 μm (Table 1).

4.1. Fiber diameters

The aerodynamic behavior of fibers is determined mainly by their diameter (Timbrell, 1982). The majority

Table 1

The diameters of asbestiform and non-asbestiform amphiboles

"Fiber"	Reference	Percent diameter >0.25 μm
Amosite	Gibbs and Hwang (1980)	28–42% (>0.3 μm)
All amphiboles [Homestake Gold mine]	Virta et al. (1983)	100%
Taconite–Grunerite & Actinolite [East Mesabi Range]	Wylie (1988)	100%
Asbestiform tremolite [Swansea]	Lee (1990)	76%
Non-asbestiform tremolite, [Alada Stura, Italy]	Lee (1990)	98%
Non-asbestiform tremolite [Greenland]	Wagner and Berry (1969)	100%
All amphiboles [NY State]	Kelse and Thompson (1989)	100%

of airborne asbestos fibers have diameters less than 0.25 μm making virtually all airborne fibers, respirable. In contrast, only very small percentages of non-asbestiform cleavage fragments have diameters less than 0.25 μm (Table 1).

For the same length distribution, counting fibers by PCM will, based on fiber diameter differences, lead to higher counts of non-asbestiform cleavage fragments than asbestos fibers, because of their visibility by PCM. On the other hand, assuming the same density for fibers as for cleavage fragments, the respirability (i.e. ability of particles to enter the alveolar regions of the lung) of the cleavage fragments will be less than that of asbestos fibers because of their larger diameters. Thus, the PCM method as presently formulated is more stringent for cleavage fragments than for asbestos fibers.

Fiber width is an important parameter determining the potential for causing both lung cancer and mesothelioma. The characteristics of non-asbestiform fiber populations are contrary to the hypothesis of carcinogenicity, while the abundance of thin asbestos fibers supports the hypothesis (Wylie et al., 1993). The evidence from experimental animal studies indicate fibers >1 μm show no dose–response relationship with tumor incidence (<30% of population of non-asbestiform fibers $\geq 5 \mu\text{m}$ long are <1 μm wide). For fibers <1 μm (and >5 μm long) there is an S-shaped dose–response curve with a threshold and then rapid increase in tumor incidence as the number of thin fibers increases. In populations of asbestos fibers >90% are <1 μm wide and $\geq 5 \mu\text{m}$ long. Fiber width is also a major factor determining access to the lung. Even long, thin fibers (such as 200 μm long or more) are respirable and are found in lung tissue, while respirability decreases as width increases. Wide diameter cleavage fragments are more likely to be deposited in the upper airways and never gain access to the lower lung to cause disease. The potential for asbestos fiber bundles to disaggregate into increased numbers of even thinner fibers *in vivo* is one of their hazardous features and is not a characteristic of non-asbestiform minerals.

While it has been argued that a major determinant of carcinogenic potential is decreasing fiber width (Wylie et al., 1993), the precise role of the single parameter, diameter in carcinogenesis is still not clear (Addison and McConnell, 2008).

4.2. Fiber length

While the majority of asbestos fibers are in fact short (less than 5 μm) there are airborne amphibole fibers which exceed 100 μm in length. Complete particle size data (length vs. diameter) on distributions of airborne cleavage fragments and asbestos fibers are extremely limited in number, making it difficult to compare length distribution differences. What data are available indicate that asbestos fibers are longer. For example, Dement et al. (1976) observed that the median length of “fibers” in the airborne dust in the South Dakota Homestake Gold mine was 1.10 μm as seen using scanning electron microscopy. This is less than the median length of airborne grunerite (amosite) asbestos fibers in South Africa mines and mills which were 1.83 and 2.53 μm , respectively (Gibbs and Hwang, 1980) and of grunerite (amosite) asbestos from a pipe insulation operation, 4.9 μm (Dement et al., 1976).

There is other evidence for a clear mineralogical difference between grunerite (amosite) asbestos and grunerite cleavage fragments. Virta et al. (1983) examined airborne particles of grunerite from the Homestake gold mine in South Dakota, particles of cummingtonite, hornblende and actinolite from the Peter Mitchell iron ore pit in Minnesota and particles of grunerite asbestos samples from a shipyard and an electric company. Hornblende is an amphibole that is similar to the tremolite-ferroactinolite series but with aluminum substituted for some of the iron-magnesium as well as for some of the silicon in order to maintain the stoichiometric balance. There were two distinct particle size distributions. The non-asbestiform grunerite distributions from the mining sites were short, wide fibers (average length to width equal to 4.6×1.1 and $5.5 \times 1.2 \mu\text{m}$). The amosite fibers from the industrial sites were longer and narrower (average length to width equal to 8.2×0.4 and $15.6 \times 0.5 \mu\text{m}$, respectively). Although the populations of grunerite

cleavage fragment and grunerite asbestos are distinct, at the submicroscopic level it may be very difficult to be certain about the specific identity of an individual particle and may be extremely difficult, if not impossible to distinguish asbestos and non-asbestiform particles among the small number of fibers where the two fiber population overlap, especially when the source of the fiber is unknown (Langer et al., 1979).

The New York State talc deposit has been extensively studied for its mineralogy and presence of fibers and cleavage fragments. Commercially important deposits of zinc, lead, talc and wollastonite are found in the Grenville Series of sedimentary rock in St. Lawrence County of NY. Three zinc mines and eleven talc mines have been worked in the area between Balmat Corners and Edwards, NY, which are about eight miles apart. All of these holdings contain some non-asbestiform tremolite, encountered as either a gangue mineral or component of the recovered ore. Anthophyllite and transitional metals have also been identified in variable amounts both between and within mines. We will refer to the NY state talc as St. Lawrence County talc.

Campbell et al. (1979) note that 5–10% of the earth's crust is amphiboles and therefore many mining industries have amphibole fragments in the gangue mineral tailings. There are at least three habits of non-asbestiform tremolite, none of which have the long, thin fibers characteristic of tremolite asbestos as shown in Table 2.

Long narrow fibers have been shown experimentally to be best capable of inducing mesothelioma when placed directly onto the pleura in experimental animals (Stanton et al., 1981). As there are likely to be fewer long fibers and fewer narrow diameter “fibers” in the case of exposure to amphibole cleavage fragments, compared to asbestos, it would be anticipated that cleavage fragments would pose lower carcinogenic risk.

4.3. Aspect ratios

Asbestos fibers have thin diameters and do not readily break transversely. As a result, length/width ratios can be quite high. All “fibers” will by definition have aspect ratios $>3:1$. Around 30% of asbestos fibers will have aspect ratios $>10:1$ and nearly 20% greater than $20:1$.

Table 2

Proportion of tremolite particles longer than 10 μm and narrower than 3 μm from milled blocky (prismatic), acicular, fibrous and tremolite asbestos stratified by aspect ratio using petrographic microscopy^a

Aspect ratio	% $<3:1$ Non-regulatory	% $3:1$ to $5:1$	% $>5:1$ to $10:1$	% $>10:1$ to $20:1$	% $>20:1$ to $50:1$	% $>50:1$
<i>Non-asbestiform tremolite particles (cleavage fragments)</i>						
Blocky	87	6.5	5	1	0.5	0
Acicular	87	4	6	3	0.5	0
Fibrous	57	18.5	18.5	5.5	0.5	0
<i>Asbestiform tremolite</i>						
Asbestos1	48.5	6.5	13	13.5	13.5	5
Asbestos2	53.5	3.5	14.5	12	13	4.5

Non-regulatory designates particles that do not meet the length $>5 \mu\text{m}$, width $<3 \mu\text{m}$, and aspect ratio >3 criteria.

^a Modified from Table 2 of Campbell et al. (1979).

There were very few cleavage fragments with aspect ratios greater than 10:1. The common blocky variety of non-asbestiform tremolite had less than 2% in the >10:1 class. The acicular and fibrous habits had more particles in the range between 10:1 and 20:1 category than did the blocky variety, but none of the non-asbestiform varieties had more than 0.5% particles in the range between 20:1 and 50:1 and none had any particles >50:1. Nearly 90% of the blocky and acicular habits did not meet the regulatory definition of a fiber. If only fibers that meet regulatory dimensions are counted, 1/100 of non-asbestiform particles have aspect ratios >20:1 while about 35/100 asbestiform tremolite particles have >20:1 aspect ratios (Table 2). A composite aspect ratio distribution reported in the Pictorial Atlas of Mineral Fibers (in press) showed that for non-asbestiform particles with an aspect ratio of 3:1 or greater and length greater than 5 μm , 6% on average exceed an aspect ratio of 15:1 and for asbestiform particles, 80% on average exceed an aspect ratio of 15:1. The 3:1 aspect ratio is used principally to eliminate particulates and fiber clumps and improve the precision and accuracy of fiber counts. It is not a defining characteristic of asbestos fibers (Langer et al., 1991).

Wylie et al. (1993) point out that aspect ratio is not a useful parameter for sizing as it is dimensionless, provides no information on width, shows no association with risk of disease, and therefore is of little use in the discussion of risk or exposure.

4.4. Biopersistence

As far as we were able to ascertain, there have been no systematic studies of the biopersistence of cleavage fragments. It is known that for long amphibole asbestos fibers, the half-life is extremely long (Berry, 1999). However, short fibers (i.e.: less than 20 μm in length) can be removed from the lung by macrophage action (Allison, 1973; Bernstein et al., 1994). For later phases of lung clearance, particle solubility is a key factor. In the absence of data, there is no basis for concluding that cleavage fragments will be removed any faster than asbestos fibers during that phase. However, because of their shorter lengths, cleavage fragments are much more likely to be removed more rapidly than amphibole asbestos fibers during the early lung clearance phase. This will reduce their potential for carcinogenic action.

Ilgren (2004) notes dissimilarities that make cleavage fragments much less biopersistent than amphibole asbestos fibers. Surfaces of cleavage fragments have a high density of surface defects, which are preferred sites for dissolution from intracellular acidic enzymes of phagocytic cells that have engulfed them. Amphibole asbestos fibers are smooth and defect free and highly acid resistant. Cleavage fragments are weak, brittle and inflexible because of their weak surface structure, which is further weakened by chemical dissolution. The tensile strength of

amphibole asbestos fibers is 20–115 times greater than the non-asbestiform amphibole variety. This difference becomes greater as width decreases and biological relevance more pronounced. When long, thin biologically relevant cleavage fragments are deposited in the lung alveoli and engulfed by macrophages, the fragment begins to dissolve on all surfaces. They are already weak and inflexible and become thinner and weaker (greater surface area, more surface defects) with increasing susceptibility to chemical dissolution and breakage. The defect-free surface of the amphibole asbestos fiber is better able to resist acid attack. Many of the asbestos fibers are too long to be completely engulfed. Attempts at engulfment produce protein deposits that form an “asbestos body” and eventual death of the cell. In short, biopersistence is a characteristic of carcinogenesis. It is reasonable to conclude that cleavage fragments are likely to be far less bio-persistent than asbestos fibers.

Nolan et al. (1991) compared activity of tremolite cleavage fragments with that of samples of tremolite–actinolite asbestos. For the same surface area, tremolite cleavage fragments had lower ability to alter the permeability of red blood cells than amosite and approximately the same membranolytic activity as anthophyllite and crocidolite. The surface charge of non-asbestos tremolite was about 70% less than asbestos analogues. Schiller et al. (1980) reported that asbestos fibers and cleavage fragments of the same dimensions had the same net negative surface charge. Short fibers and cleavage fragments have a smaller net charge than highly elongated particles.

5. Comparison of the risk of health effects in persons exposed to asbestiform and non-asbestiform grunerite

5.1. Grunerite occurrence

Grunerite is the mineralogically correct name for amphiboles of the cummingtonite–grunerite series in which iron is at the 50% point in the 100 times $\text{Fe}/(\text{Fe} + \text{Mg})$ ratio. Amosite (from the “Asbestos Mines of South Africa”) is the commercial asbestiform product that was used in insulation and building materials. Grunerite asbestos is no longer mined.

The non-asbestiform variety of cummingtonite–grunerite (C–G) has no commercial use *per se* other than as an aggregate but occurs in nature in conjunction with other asbestiform and non-asbestiform amphiboles and other minerals in ore deposits mined for other purposes. In the USA, ore containing C–G has been mined in at least two locations. One location is the Homestake gold mine in Lead, SD, where gold had been extracted since 1876. The other location is Mesabi Range where taconite has been mined since the 1950s and shipped to Silver Bay, Minnesota for extraction of iron. Because of its relationship to grunerite (amosite) asbestos, studies were initiated to determine if these minerals had similar pathogenicity. There have been four cohort studies of

Homestake gold miners (Gilliam et al., 1976; McDonald et al., 1978; Brown et al., 1986; Steenland and Brown, 1995) and two studies of taconite containing amphiboles; one of the Reserve iron deposit (Higgins et al., 1983) and the other of the Erie–Minntac mine (Cooper et al., 1988, 1992) (Table 3).

Taconite iron ore contains actinolite and cummingtonite–grunerite (probably predominantly grunerite). In 1973, elongated grunerite particles, said to be similar to grunerite (amosite) asbestos, were found in the Duluth, Minnesota water supply. The source was mine tailings from the process plant at Silver Bay, Minnesota (MN) serving the Peter Mitchell Pit. In a suit against the Reserve Mining Company, the US Environmental Protection Agency (EPA) claimed that some of the particles were asbestos. This finding initiated a series of studies to determine if there were effects on the Duluth residents (Cook et al., 1974; Masson et al., 1974; Levy et al., 1976; Sigurdson et al., 1981). These studies of human health are not considered further because they are ecological studies without identification of individual exposures or responses, because the route of exposure is via ingestion and because experimental studies and the epidemiological studies described below have provided no evidence in support of any gastrointestinal cancer risk from ingestion. The other health studies are of taconite miners and millers (Clark et al., 1980; Higgins et al., 1983; Cooper et al., 1988, 1992).

A reasonably valid comparison can be made between the health risks of workers exposed to amosite asbestos in mining and manufacture and the health risks of workers involved in the extraction of minerals from ore bodies containing non-asbestiform grunerite.

6. Grunerite (amosite) asbestos

Amosite is the trade name given to a mineral that was previously mined in Penge region in the Transvaal of South Africa. The mineralogical name is grunerite asbestos. In the bulk specimen the fibers can be several inches long. The color, ranging grey to brown depends on whether the fiber was mined from a weathered or unweathered zone. The size distribution of the airborne fibers in the mine and mill have been reported by Gibbs and Hwang (1980). In mining and milling 12.6% and 6.6%, respectively, of airborne fibers exceeded 5 µm in length when all particles with length to breadth ratios greater than 3:1 were counted using transmission electron microscopy combined with light optical microscopy. The median lengths for mining and milling were 1.83 and 2.53 µm, respectively. The median diameters were 0.20–0.26 µm depending on the process and there were no airborne fibers with diameters exceeding 3 µm.

6.1. Grunerite (amosite) asbestos exposed cohort studies

The studies of cohorts of amosite-exposed workers include miners and millers in South Africa (Sluis-Cremer et al., 1992) and workers engaged in amosite insulation manufacture (Acheson et al., 1984; Seidman et al., 1979, 1986; Levin et al., 1998). Cohorts where the exposure also included riebeckite (crocidolite) asbestos and/or chrysotile have been excluded from consideration as the ratios of the risks of mesothelioma associated with these various asbestos fiber-types have been reported to be in the ratio of 500:100:1 for riebeckite (crocidolite) asbestos, grunerite (amosite) asbestos and chrysotile, respectively (Hodgson and Darnton, 2000). For lung cancer the differences are

Table 3

Mesothelioma/lung cancer experience—non-asbestiform grunerite^a Workers and negative non-amphibole controls

Study population	Follow-up period	Cohort <i>N</i> (% dead)	<i>N</i> mesothelioma/ <i>N</i> deaths (PMR)	Lung cancer: <i>O/E</i> = SMR (95% CI)
<i>Non-asbestiform grunerite cohorts (latest follow-up)</i>				
Homestake gold miners (Steenland and Brown, 1995)	Follow-up 1977–1990	3328 (46.6%)	0/1551 = 0 ^{7c}	115/101.8 = 1.13 (0.94–1.36)
Reserve taconite miners (Higgins et al., 1983)	More than 1 year in period 1952–1976	5751 (5.2%)	0/298	15/17.9 = 0.84 (0.47–1.38)
Erie mining of taconite (Cooper et al., 1992)	>3 months <1959, Erie–Minntac mine, 1947–1989	3431 (30.8%)	1 ^b 0/1058 = 0	62/92.2 = 0.67 (0.52–0.86)
Total		12510 (23.2%)	0/2907 = 0	192/211.9 = 0.91
<i>Negative comparison: hematite iron ore without amphiboles</i>				
Hematite mining in Minnesota [Lawler et al., 1985].	>1 year employment before 1966. Follow-up 1937–1979.	Ugd 4708 (55%) Surface 5695 (36%)	0/2642 = 0 0/2057 = 0	117/117.6 = 1.00 (0.83–1.20) 95/108 = 0.88 (0.71–1.08)

^a It is recognised that these workers were also exposed to non-asbestiform hornblende and actinolite.

^b Exposure began only 11 years before death making it unlikely that this mesothelioma is related to work in the taconite mine. He was previously a locomotive fireman and engineer.

^c There were seven cases [four cancers of the peritoneum and three other respiratory cancers] in categories that might include mesothelioma but no mention of mesothelioma on the death certificate or other evidence to support diagnoses of mesothelioma. No mention of mesothelioma was found in a review of deaths from lung cancer or other non-specified cancer, which at times are categories that include mesothelioma (Steenland and Brown, 1995).

not as great or as clear-cut. Crocidolite and amosite pose similar exposure-specific risks for lung cancer (about 5% excess per f/mL years), while the risk from chrysotile is estimated as 0.1–0.5% of the risk of crocidolite and amosite. Thus the risk differentials between the amphibole asbestos (crocidolite and amosite) and chrysotile for lung cancer are about 10–50:1 (Hodgson and Darnton, 2000). It should be noted that the chrysotile in these risk estimates included sources where the chrysotile contained traces of tremolite, the form of which was not investigated or reported.

Only one of the cohorts with pure grunerite (amosite) asbestos exposure was examined for a quantitative exposure–response relationship (Seidman et al., 1986). There was a clear increase in the risk of lung cancer with increasing exposure expressed in fibers/mL years.

7. Non-asbestiform grunerite cohorts

Several groups of workers from Homestake gold mine and the Minnesota taconite deposits have been exposed to cleavage fragments of grunerite and studied to assess possible “asbestos-related” diseases (Table 3). The non-asbestiform amphiboles present in these mines generally crystallize in a prismatic habit with well-developed cleavage so breaks occur both perpendicular and parallel to particle length.

7.1. Taconite miners

There are several studies of workers who were exposed to cummingtonite–grunerite particles from the above deposits. These include the Reserve taconite miners (Higgins et al., 1983) and the Erie–Minntac taconite miners (Cooper et al., 1988, 1992). Another group of Iron ore (hematite) miners in Minnesota is included for comparison as a negative “control” since the hematite ore does not contain amphiboles (Lawler et al., 1985).

Taconite is an iron-bearing rock that by 1978 was supplying nearly 90% of the iron ore used in the US iron and steel industry. More than 60% of this came from the Mesabi Range that is 110 miles long and 1–3 miles wide extending east to west from Babbitt, Minnesota to Grand Rapids, Michigan. Iron ore has been mined along the Mesabi Range since about 1892 (Langer et al., 1979). Taconite contains 20–50% quartz and 10–36% magnetite with smaller amounts of hematite, carbonates, greenalite, chamosite, minnesotaite, stilpnomelane and amphiboles which are non-asbestiform minerals in the cummingtonite–grunerite series, actinolite and hornblende (Nolan et al., 1999).

Taconite from the eastern end of the Mesabi Range contains non-asbestiform cummingtonite–grunerite (most probably grunerite) and actinolite with most elongated particles having aspect ratios greater than 3:1 and length less than 10 μm and are mostly acicular cleavage fragments. Respirable dust concentrations in the Reserve mining company ranged from about 0.02 to 2.75 mg/m^3 at a crusher.

The modal range in most jobs was 0.2–0.6 mg/m^3 , with occasional concentrations of 1–2 mg/m^3 but mostly below 1 mg/m^3 . Fiber concentrations were generally <0.5 fibers/mL. Area samples suggest no change in concentrations between 1952 and 1976 and exposure estimates were based on samples collected in the period 1975 and 1958 (Higgins et al., 1983).

In the Reserve mining cohort (Higgins et al., 1983) there were no exposure–response relationships between lung cancer and cumulative exposure to silica dust or taconite (measured as mg/m^3 years) and no excess lung cancer based on the SMR. There were no cases of mesothelioma. Higgins et al. (1983) concluded that the lack of any increased risk of cancer is not surprising given the low silica and fiber exposure plus movement of miners to lower exposed jobs with increased seniority. The average and maximum latencies of lung cancer were 15 and 25 years. At high exposure levels the latency for pneumoconiosis has been as short as about 5 years or even less. As dust levels have declined latency is more in the range of 13–20 years. The cohort was also relatively young with 5% overall mortality and the number of cases was small with 15 lung cancer cases (17.9 expected), 8 with >15 years since hire (7.9 expected). Exposure–response functions were estimated using cumulative total dust exposure and cumulative silica dust exposure in mg/m^3 years as the exposure metrics. The relationship with total dust exposure, which is of interest from the standpoint of cleavage fragments, was not monotonic and the SMRs were at or below 1.0 in the three highest exposure categories. Higgins et al. (1983) concluded there was no suggestion of an association with lung cancer.

In the Eastern Mesabi district, west of the Reserve Mine are the Erie and Minntac operations. The Minntac ore has had a different metamorphic history and contains the lowest percentage of amphiboles. The Erie ore is a blend of the high and low amphibole ores with more amphiboles than Minntac but less than Reserve. Nolan et al. (1999) reported 28–40% quartz in dust from the Erie mine and 20% quartz from the Minntac mine. Concentrations of fibrous particulates were nearly always <2 fibers/mL. These particulates were >5 μm in length and included elongated cleavage fragments.

The Erie–Minntac cohort of taconite miners (Cooper et al., 1992) showed “no evidence to support any association between low-level exposure to non-asbestiform amphibole particles or quartz” and lung cancer. The Erie–Minntac cohort is older and larger than the Reserve cohort with 31% mortality and a minimum time since hire of 30 years. There were deficits in lung cancer SMRs for miners ever working in high or medium dust areas and no trend with years worked. There was no analysis by cumulative exposure.

There was one case of mesothelioma that had been reported in the initial study (Cooper et al., 1988). In this case, exposure to taconite began 11 years before death. Previous employment included work in the railroad industry as a locomotive fireman and engineer. Nolan et al. (1999)

suggest it is unlikely that the mesothelioma is related to taconite because mesothelioma generally occurs after at least 25 years although latencies as short as about 18 years have been reported among insulation workers where asbestos exposure can be quite high. The more likely cause is from the railroad employment where there are opportunities for exposure to commercial amphibole asbestos from thermal lagging used on steam locomotives. Also, the time since hire in the railroad jobs is more consistent with the long latency characteristic of mesothelioma.

Although deposits of grunerite asbestos large enough for commercial exploitation are very rare, small deposits are occasionally found as a gangue mineral in a limited area of a mine that is otherwise asbestos-free. Nolan et al. (1999) described the occurrence of such a localized seam of grunerite asbestos in a small portion of an iron ore mine otherwise free of asbestos. Samples from the seam revealed three kinds of morphological types or habits. One kind was the asbestiform habit with fibers occurring as parallel fibrils and forming polyfilamentous bundles. There were two non-asbestiform habits, namely splintery fibers and massive anhedral nodules, which when crushed may form elongated cleavage fragments that morphologically resemble some asbestiform fibers. To evaluate potential asbestos exposure, 179 personal air samples were collected for all relevant jobs associated with work on this localized seam. The mean concentration of fibers $\geq 5 \mu\text{m}$ in length and aspect ratio $\geq 3:1$ was 0.05 f/mL and the highest was 0.39 f/mL. All sample results were below the Mine Safety and Health Administration (MSHA) standard of 2 f/mL but 13% were above the Occupational Safety and Health Administration (OSHA) standard of 0.1 f/mL.

Nolan et al. (1999) estimated the potential lifetime risk of lung cancer and mesothelioma based on a worst case scenario. Lifetime lung cancer risks of 0.1 and 0.6/100,000 for non-smokers and smokers respectively were estimated using the EPA risk model and assuming a linear exposure–response relationship, age of 45 years at beginning of exposure and continuous exposure for 22 days to 0.05 asbestos fibers/mL. This was considered approximately equivalent to smoking 2 or 12 cigarettes over a lifetime.

Nolan et al. (1999) also estimated risk based on grunerite asbestos fiber content in the lungs of mesothelioma cases from a British grunerite (amosite) asbestos factory (Gibbs et al., 1994). Nolan et al. (1999) estimated it would take 75–265 years of daily 8-h shifts to inhale the number of fibers found in the lungs of the mesothelioma cases, assuming no clearance. Fiber concentrations were about 45% higher in the lung cancer cases, suggesting about 100–380 years to reach similar fiber content in iron ore miner lungs.

Nolan et al. (1999) suggested concentrations were a minimum of 30 fibers/mL in the Paterson, NJ grunerite (amosite) asbestos factory (Seidman et al., 1986). No mesothelioma cases had less than 6 months employment and 20-years latency. Assuming breathing 0.05 fibers/mL from the gangue rock in the iron ore mine, Nolan et al.

(1999) estimated it would take about 300 years to achieve the minimum exposures estimated for the mesothelioma cases in the Seidman et al. (1986) cohort.

7.2. Hematite miners as negative control

Hematite from the Mesabi Range in Minnesota is a mixture of about 83% hematite (Fe_2O_3) and limonite (HFeO_2). The hematite deposit differs from taconite deposits in that there is the absence of all amphiboles. Some silica (about 8%) is present plus possibly low levels of radon.

Lung cancer mortality was not associated with years worked. Mesothelioma was not mentioned. Lawler et al. (1985) considered that the lack of an excess risk of respiratory disease was possibly due to strict prohibition of smoking while underground, apparent absence of significant radon daughter exposure and/or the aggressive silicosis control program. No estimates of dust exposure are available.

7.3. Gold miners

There are several studies of miners at the Homestake gold mine in South Dakota (Gilliam et al., 1976; McDonald et al., 1978; Brown et al., 1986; Steenland and Brown, 1995).

Ore containing cummingtonite–grunerite has been mined to extract gold in Lead, South Dakota, since 1876. An analysis of airborne “fibers” using electron diffraction and X-ray spectrometry was reported to show that it contained “80–90% amphiboles” with the amphiboles being “60–70% fibrous grunerite”, “1–2% fibrous cummingtonite” and “10–15% fibrous hornblende” (Gilliam et al., 1976). The free silica content of the respirable airborne dust was reported to be 13.1%. Low concentrations of arsenopyrite were also reported. The NIOSH researchers identified the fibrous grunerite as grunerite (amosite) asbestos. Closer examination of the fiber population statistics suggests strongly that the fibrous grunerite particles are non-asbestos amphibole cleavage fragments as noted in the section on fiber length.

Measurements of airborne concentrations of “fibers” in the mine in 1974 showed concentrations to be about 0.25 f/mL greater than $5 \mu\text{m}$ with the highest concentration being 2.8 f/mL based on 200 samples (Gilliam et al., 1976). The mean total fiber concentration in the mine as determined by electron microscopy was $4.82 (\pm 0.68)$ f/mL with the concentration of fibers greater than $5 \mu\text{m}$ being $0.36 (\pm 0.08)$ f/mL. Approximately 94% of fibers were less than $5 \mu\text{m}$ in length, the mean fiber diameter was $0.13 \mu\text{m}$ and the mean “fiber” length was $1.1 \mu\text{m}$. The US Bureau of Mines in 1960 reported average airborne dust concentrations of 1.7 million particles per cubic foot (mppcf) (Gilliam et al., 1976). This suggests a ratio of f/mL to mppcf of about $0.25/1.7 = 0.146$ f/mL per 1 mppcf.

Exposure–response relationships were developed by several of these researchers. Only the results of the latest follow-up by Steenland and Brown (1995) will be consid-

ered. However, the exposure–response developed by McDonald et al. (1978) based on semi-quantitative exposure estimates is of interest because this cohort of 1321 men with 21 or more years of service clearly had adequate latency to observe the occurrence of mesothelioma or increase in lung cancer. There were 17 deaths from respiratory cancer but no convincing evidence of an excess of respiratory cancer or grunerite related mesothelioma. This contrasts with the results of the earlier study by Gilliam et al. (1976), which involved 440 men who had worked more than 5 years underground. They reported 10 deaths from neoplasms of the respiratory system with 2.7 deaths expected. Conclusions from the study by Gilliam et al. (1976) are weakened by the fact that the study population is small, the SMR for men with latency less than 20 years (5.4) was greater than that for men with latency greater than 20 years (3.2) (McDonald et al., 1978), and the results are contradictory to later follow-up studies of the entire cohort (Brown et al., 1986; Steenland and Brown, 1995). While the reason for the high overall SMRs is not clear, selection bias is possible as the cohort was comprised of volunteers participating in a 1960 silica X-ray survey. The participation rate of workers from the mine was not reported.

The Homestake study comprises the largest and oldest cohort of workers exposed to non-asbestiform amphiboles with 47% mortality. In the Steenland and Brown (1995) study, there was a 2.6-fold excess of silicosis and a 3.5-fold excess of respiratory TB that were significantly associated with cumulative exposure and SMRs were significantly elevated in the highest exposure category for both dust-related diseases. Lung cancer was not associated with cumulative exposure in the SMR exposure–response analysis and there was a negative trend in the nested lung cancer case–control portion of this study, i.e., as exposure increased there was a trend for lung cancer risk to decrease. There were no mesothelioma deaths.

The mesothelioma and lung cancer experience of the grunerite (amosite) asbestos and non-fibrous amphibole workers will be compared separately below.

8. Comparison of mesothelioma experience

One method of assessing whether non-asbestiform grunerite acts similarly to grunerite (amosite) asbestos is to compare the proportional mortality from mesothelioma in grunerite (amosite) asbestos exposed workers and in non-asbestiform grunerite exposed workers. Mesothelioma is a cancer which can clearly be caused by amosite without known confounders such as smoking, although there are a small number of other potential causes (Pelmar, 1988; Price and Ware, 2004). Hodgson and Darnton (2000) argue that there is unlikely to be a threshold for asbestos-related mesothelioma, but that the exposure–response function may be non-linear. As previously discussed about 80% of mesotheliomas are asbestos related, mesothelioma is a more specific indicator of amphibole asbestos exposure

and also more sensitive as there may be an excess mesothelioma risk in the absence of an excess lung cancer risk (Hodgson and Darnton, 2000).

The measure of mesothelioma mortality used in this study is the percent of total mortality (labelled PMR in this context). To assume a work-related mesothelioma in the non-asbestiform grunerite cohorts there should be no previous asbestos exposure, no exposure to other potential etiological factors such as erionite or therapeutic radiation and the time of death should probably be 20 or more years since hire, or 15 or more years since hire if exposure was intense. Lanphear and Buncher (1992) estimated that for 1105 mesothelioma cases meeting strict histological and exposure criteria, 99% had a latent period (time since first exposure) of 15 years or more and 96% of 20 years or more. The median latent period was 32 years with a range of 13–70 years. The probability was 0% for <10 years and 0.45% for 10–14 years.

Although there were only 19% of persons dead in the grunerite (amosite) asbestos cohorts combined, there was an overall proportional mortality from mesothelioma of 1.2%. In contrast, 23% of persons were dead in the non-asbestiform cohorts combined and no mesothelioma linked to the exposures in the non-asbestiform cohorts (or 0.03% if the non-exposure related deaths are counted). It is well recognized that the proportion of mesothelioma increases with long follow-up as mesothelioma increases as a cubed function of the time since first exposure and so would increase as the percentage of deaths increase. Certainly on present evidence there is no increased risk of mesothelioma in non-asbestiform amphibole exposed workers at the levels of exposure encountered in these industries (Tables 3 and 4 and Fig. 1).

In view of the fact that there was no detected increase in mesothelioma, one would not anticipate an increased risk of lung cancer due to exposure to fibrous dust, as usually in amphibole-exposed workers the exposure necessary to produce an increased risk of lung cancer is much greater than that required to increase mesothelioma risk.

9. Comparison of lung cancer experience

There are statistically significant excesses of respiratory cancer in all the grunerite (amosite) asbestos industries (except mining). In contrast, it is very clear that, with the exception of the first small study of Homestake gold miners (Gilliam et al., 1976), there is no increased risk of lung cancer in the non-asbestiform amphibole exposed industries. The results from the study by Gilliam have not been reproduced in subsequent studies with complete ascertainment of the cohort and longer follow-up (Steenland and Brown, 1995; McDonald et al., 1978). In the taconite-exposed miners there were some statistically significant deficits of respiratory cancer. This is in spite of the fact that workers in those industries are exposed to significant crystalline silica in addition to non-asbestiform grunerite (if silica increases lung cancer risk).

Table 4

Mesothelioma/lung cancer experience–grunerite (amosite) asbestos exposed workers

Study population	Follow-up period	No. in cohort (% mortality)	No. meso/No. deaths = PMR	Lung cancer: obs/ exp = SMR (95% CI)
Amosite mining (Sluis-Cremer et al., 1992)	Miners 1945–1955. Follow-up to 1986	3212 (20.2%)	4/648 = 0.6%	26/18.8 = 1.38 (0.97–1.91)
Amosite Insulation manufacturing (Acheson et al., 1984)	1945–1978: Follow-up to 1980.	4820 (6.9%)	5/333 = 1.5%	61/29.1 = 2.10 (1.62–2.71)
Amosite insulation manufacturing (Seidman et al., 1986; follow-up of Seidman et al., 1979)	1941–1945; more than 5-year latency; follow-up to 1983	820 (72%)	6/593 = 1.01% (death certificates) 17/593 = 2.9% (best evidence)	102/20.51 = 4.97 (4.08–6.1)
Amosite insulation manufacturing (Levin et al., 1998)	1954–1972, >10 years latency; follow-up to 1994	755 (29.4%)	6/222 = 2.7%	35/12.6 = 2.77 (1.93–3.85)
Total		9607 (18.7 %)	21/1796 = 1.2%	224/81 = 2.77

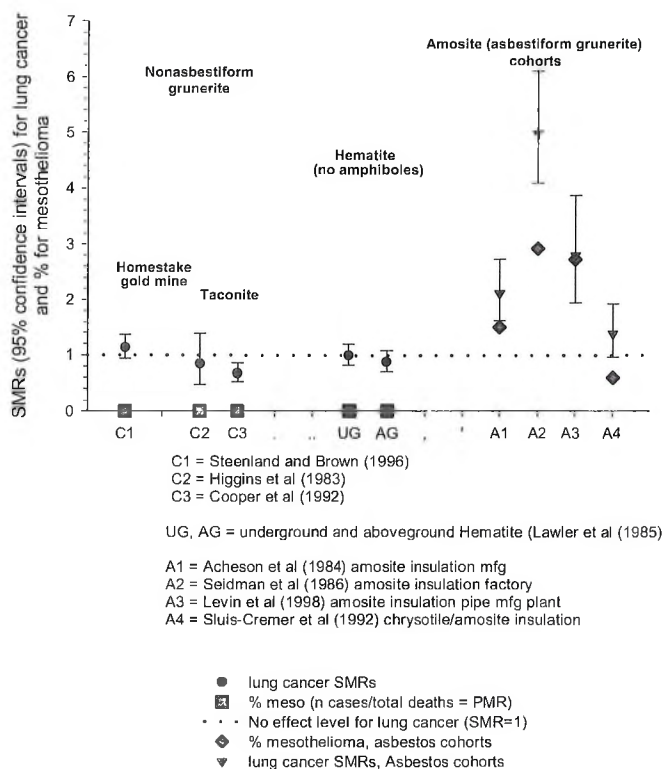


Fig. 1. Lung cancer and mesothelioma mortality in cohorts of workers exposed to non-asbestiform amphiboles (Homestake gold ore, taconite), hematite (no amphiboles, negative controls) and amosite asbestos cohorts of insulation factories and miners (positive controls).

Table 5

Lung cancer SMRs by cumulative exposure expressed as fiber/ml years for non-asbestiform grunerite [Steenland and Brown, 1995] and asbestiform grunerite exposures [Seidman et al., 1986]

Non-asbestiform grunerite [Steenland and Brown, 1995]				
mppcf-years ^a	<33.3	33.3–133.3	133.3–200	>200
Fiber/mL years ^b	<4.8	4.8–19.5	19.5–29.2	>29.2
SMR	1.17	1.01	0.97	1.31
Asbestiform grunerite [Seidman et al., 1986]				
Fiber/mL years ^b	<6	6–11.9	12–24.9	25–49.9
SMR	14/5.31 = 2.64	12/2.89 = 4.15	15/3.39 = 4.42	12/2.78 = 4.32
			17/2.38 = 7.14	9/1.49 = 6.04
				12/1.32 = 9.09
				11/94 = 11.7

^a Dust days in Table 2 of the paper by Steenland and Brown (1995) (i.e.: 1 day at 1 mppcf was converted to dust years by dividing by 240 days per year [i.e. 48 weeks × 5 day week]).

^b mppcf years converted to f/cc-years using a factor of 1 mppcf = 0.146 f/mL. The conversion is based on the average concentration of “fibers” greater than 5 μm and particles measured by the midjet impinger and reported by Gilliam et al. (1976) i.e.: 0.25 f/mL divided by 1.7 mppcf.

Another way to examine this question is to compare the exposure–response relationships for the various studies. In Table 5 the exposure–response relationships for the studies by Seidman et al. (1986) and Steenland and Brown (1995) are compared. While both have limitations in their exposure estimates, there is clearly no increasing trend of lung cancer with increasing exposure to non-asbestiform grunerite (and other non-asbestiform amphiboles). The exponential increase in pneumoconiosis (silicosis) with increasing exposure suggests exposure produced fibrotic but not carcinogenic effects (ratio lung cancer/silicosis mortality = 1.25). In contrast there is a steep and statistically significant slope for the lung cancer mortality in the grunerite (amosite) asbestos insulation manufacturing plant (lung cancer/asbestosis mortality ratio = 6.8) (Fig. 2).

Acheson et al. (1984) reported concentrations of 30 fibers/mL in the late 1960s in the factory using grunerite (amosite) asbestos. Exposures were probably much dustier before 1964 with improved conditions after 1964. However, Acheson et al. (1984) did not attempt to assess exposure–response trends.

It seems clear that exposure to non-asbestiform grunerite cleavage fragments and/or “fibers” at cumulative exposures below about 30 f/mL years has not resulted in an increased lung cancer risk for workers. The risk for workers exposed to grunerite (amosite) asbestos was increased at cumulative exposures <6 f/mL years.

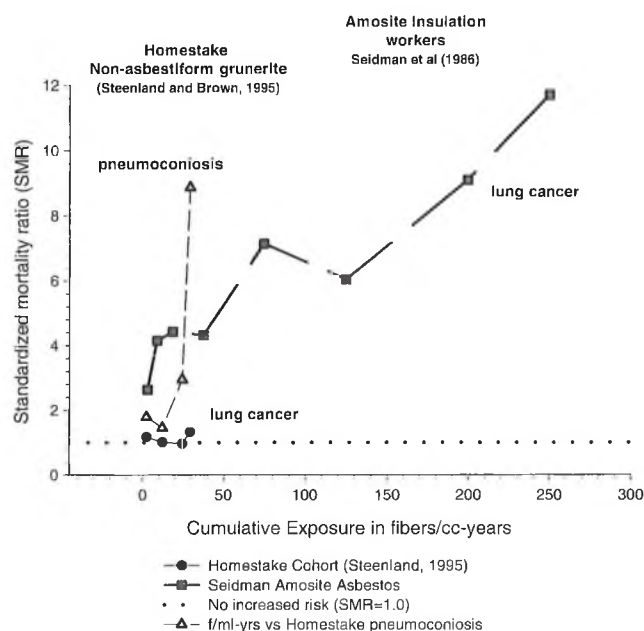


Fig. 2. Lung cancer SMRs by cumulative exposure (fibers/mL years) and pneumoconiosis for non-asbestiform grunerite (Steenland and Brown, 1995) and grunerite (amosite) asbestos (Seidman et al., 1986).

10. Overall conclusion concerning asbestiform and non-asbestiform grunerite

It is evident that the “fibers” to which the non-asbestiform amphibole workers were exposed were considerably shorter (and wider) than those to which grunerite (amosite) asbestos workers were exposed. While both studies of grunerite (amosite) asbestos and non-asbestiform grunerite (plus other non-asbestiform amphiboles) may have limitations as far as estimates of fiber exposure are concerned, the results indicate very large differences in the mortality from mesothelioma and from lung cancer from both external and internal comparisons. It seems unlikely that errors in the exposure estimates are responsible for these very large differences as the grunerite (amosite) asbestos factory shows a definite increase in risk of lung cancer with increasing exposure while there is no statistically valid increase in trend with non-asbestiform grunerite. The results are consistent with cleavage fragments having no (or negligible or very low) apparent carcinogenic hazard for mesothelioma and lung cancer in contrast to the obvious carcinogenic hazard shown by their asbestiform counterparts.

11. The evidence from studies of talc and vermiculite exposed workers

11.1. The mineral talc

The term talc is used in two ways. First, it is a term applied to a commercial or industrial product that contains finely divided mineral or rock powder that usually, but not always contains the mineral talc as its main component.

Second, it can refer to the mineral talc which is a phyllosilicate mineral with the chemical formula $\text{Mg}_3\text{Si}_2\text{O}_5(\text{OH})_2$. Since talc is a metamorphic mineral it is often associated with other minerals and is rarely found in its pure form. Co-exposures are specific to each site. Tremolitic talc is a commercial product that contains a high proportion of the amphibole tremolite in addition to the mineral talc; it also can contain other minerals including anthophyllite, a transitional talc/anthophyllite mineral as well as antigorite, lizardite and quartz. Cosmetic and pharmaceutical talcs have strictly controlled mineral contents; industrial talcs may contain other minerals.

Structurally, talc occurs in sheets that can be separated by slight pressure, so that when milled, talc can form cleavage fragments or elongated talc platelets (Wild et al., 2002).

12. The New York and Norwegian talc deposits

There are at least two talc deposits containing non-asbestiform tremolite and anthophyllite which have been studied, one in New York State and one in Norway (Table 6). The best known and best characterised is the industrial talc in New York. There has been considerable discussion in the literature concerning whether the tremolite and anthophyllite present in this talc is asbestiform or non-asbestiform. However, the evidence is supportive of non-asbestiform amphiboles (Skinner et al., 1988). Norwegian talc contains tremolite and anthophyllite said to be in trace amounts. However, the mineralogy of this talc is less studied and the cohort of exposed miners/millers is much smaller.

The health experience (mesothelioma and lung cancer mortality) of these two cohorts of talc workers exposed to non-asbestiform amphiboles will be compared to (1) anthophyllite asbestos miners, (2) to workers exposed to vermiculite contaminated with tremolite asbestos; and (3) to workers exposed to talc that is not contaminated with amphiboles from Vermont, Italy, France and Austria.

12.1. New York talc

The St. Lawrence County, New York talc deposit has been extensively studied for its mineralogy and presence of fibers and cleavage fragments. The mineralogy is complex and there has been a long and ongoing debate about the amphiboles present in the Gouverneur, NY talc, which is the only mine currently operating in the region. Dement et al. (1980) concluded that bulk Gouverneur talc samples contained both amphiboles (4.5–15% anthophyllite and 37–59% tremolite) and serpentines (10–15% lizardite and antigorite) and less than 2.6% free silica as determined by X-ray diffraction and petrographic microscope analysis. It appears that the mineral identified as anthophyllite by Dement et al. (1980), is, at least in part, a mixed phase mineral with talc evolving from the anthophyllite (Kelse and Thompson, 1989). The talc also contains talc fibers. Dement et al. (1980) considered the airborne dust “fibers”

Table 6
Lung cancer and nonmalignant respiratory disease (NMRD) mortality (SMR) among talc workers

Author	Years	Lung cancer SMR	Lung cancer mine SMR	Lung cancer mill SMR	NMRD overall SMR	NMRD mine SMR	NMRD mill SMR	Mesothelioma
NY, Brown et al. (1979)	1947–1959 Follow-up 1975 19% mortality	9/3.3 = 2.73 (1.25–5.18)			8/2.9 = 2.76 (1.19–5.13) Other 5/1.3 = 3.85 (1.25–8.96)			0
NY, Lamm et al. (1988)	1947–1978 >1-year tenure 14.8% mortality	6/3.1 = 1.93 (0.71–4.20)			7/2.5 = 2.78 (1.11–5.72)			
NY, Honda et al. (2002)	>1 day tenure 1948–1989	31/13 = 2.32 (1.57–3.29)	18/46 = 3.94 (2.33–6.22)	7/5.5 = 1.28 (0.51–2.63)	28/13 = 2.21 (1.47–3.20)	10/4.2 = 2.41 (1.16–4.44)		0
NY, Brown et al. (1990)	1947–1978; follow-up 1983; 23% mortality ≥1-year tenure	17/8.2 = 2.07 (1.20–3.31) 9/4.7 = 1.91 (0.88–3.64)			17/6.8 = 2.50 (1.46–4.01) 11/3.8 = 2.89 (1.45–5.18)			0
Vermont, Selevan et al. (1979)	1940–1975; >1-year tenure before 1970; 23% mortality	6/3.69 = 1.63 (0.60–3.54)	5/1.15 = 4.35 (1.41–10.1)	2/1.96 = 1.02 (0.12–3.68)	11/3.67 = 3.0 (1.50–5.36) Other = 11/1.79 = 6.15 (3.07–11)	2/1.23 = 1.63 (0.20–5.87) Other = 2/ 0.56 = (0.43–2.89)	7/1.72 = 4.07 Other = 7/ 0.89 = 7.87 (3.15–16.2)	0
Italy, Coggiola et al. (2003)	>1 year, 1946–1995 49% mortality	44/ 46.9 = 0.94 (0.68–1.26)	33/ 30.9 = 1.07 (0.73–1.50)	11/ 16 = 0.69 (0.34–1.23)	127/55.7 = 2.28 (1.9–2.72)	105/34.4 = 3.05 (2.5–3.7)	22/21.3 = 1.04 (0.65–1.57)	
France, Wild et al. (2002)	1945–1995, >1-year; 27.5% mortality	21/17 = 1.23 (0.76–1.89)			26/24.6 = 1.06 (0.69–1.55) Pneumoconiosis 3/0.5 = 5.56 (1.12–16.2)			
Austria, Wild et al. (2002)	1972–1996, >1-year; 12.4% mortality	7/6.6 = 1.06 (0.43–2.19)			1/3.7 = 0.27 (0.01–1.52)			0
Norway, Wergeland et al. (1990)	>1-yr: miners 1944–1972; 28.7% mortality >2-years millers 1935–1972; 30.5% mortality	SIR: 6/ 6.49 = 0.92 (0.34–2.01)	SIR: 2/ 1.27 = 1.57 (0.19–5.69)	SIR: 4/ 5.22 = 0.77 (0.21–1.96)	Diseases of Respiratory System SMR: 3/10.9 = 0.28 (0.06–0.80)	SMR: 1/ 2.5 = 0.40 (0.01–2.23)	SMR: 2 / 8.5 = 0.24 (0.03–0.85)	0

greater than 5 μm long to contain upward of 70% amphibole asbestos. Based on electron microscopy, Dement and Zumwalde reported that: “In the mine 38% of all fibers were anthophyllite. 19% were tremolite and 39% were unidentified”. In the mill 45 per cent of all fibers were anthophyllite, 12 per cent were tremolite and 38 per cent were unidentified. Three percent of the fibers in the mine and 2 percent in the mill reportedly gave chrysotile electron diffraction patterns. According to Thompson (1984) and Harvey (1979) all the amphibole minerals are cleavage fragments and in the non-asbestiform habit and it has now been shown that once the talc fibers are recognized, the talc does not contain asbestiform tremolite or asbestiform anthophyllite (Kelse and Thompson, 1989; Dunn Geoscience Corp., 1985; Langer and Nolan, 1989; Virta, 1985; Crane, 1986; Wylie et al., 1987; Wylie et al., 1993; Nolan et al., 1991).

A survey of the many mortality studies of workers exposed to St. Lawrence County, NY talc is summarised in Appendix A. Most of these have been variations of the original NIOSH cohort study (Brown et al., 1979; Dement et al., 1980). We will focus on the nested case-control study, which addressed three of the hypotheses raised about reasons for the increased lung cancer, namely smoking, other work exposures, and short-term workers (Gamble, 1993). Honda et al. (2002) added six more years update and estimated quantitative cumulative exposure to talc dust to address the question of exposure-response (Oestenstad et al., 2002).

Gamble (1993) conducted a case-control study nested in the Brown et al. (1990) cohort of NY talc workers. There were 22 cases and 66 controls matched on date of birth and date of hire. All cases were either smokers (91%) or ex-smokers compared to 27% non-smokers, 73% smokers or exsmokers among controls. Negative trends were consistently observed by years worked after controlling for smoking, 20 or more years latency, and exclusion of short-term workers. Lifetime work histories suggested no apparent association with non-talc exposures or non-Gouverneur talc exposures. The author concluded that “after adjustment for...smoking and the postulated role of very high exposures of short-term workers, the risk ratio for lung cancer decreases with increasing tenure”. The time occurrence of lung cancer was consistent with a smoking etiology, and was not consistent with a mineral dust relationship.

Honda et al. (2002) assessed cancer and non-cancer mortality among white male Gouverneur talc workers. The cohort analyzed for cancer endpoints consisted of 809 workers employed 1947–1989 and alive in 1950. The cohort analyzed for non-cancer endpoints consisted of 782 men employed during 1960–1989. The important additions in this study were 6 more years of follow-up (through 1989) and internal exposure-response analyses with cumulative exposure to talc dust as the exposure variable. Smoking status was not taken into account. The internal comparisons by cumulative exposure (mg/m^3 years)

showed a significant monotonic decrease in lung cancer risk with increasing exposure. The RR was 0.5 (0.2–1.3) in the highest exposure category. Mortality from ‘other NMRD’ and pulmonary fibrosis showed monotonic increases in risk as exposure increased with 2- and 12-fold increased risks in the highest exposure categories (Fig. 3).

Honda et al. (2002) concluded that talc dust was unlikely to have a carcinogenic potency similar to asbestos for several reasons. First, there were negative exposure-response trends. Second, although lung cancer mortality was increased nearly 4-fold among miners (SMR of 3.94; 95% CI 2.33–6.22, 18 observed (obs)) it was not excessive among millers (SMR of 1.28; 95% CI 0.51–2.63; 7 obs) although exposure was similar in both groups (medians of 739 and 683 mg/m^3 years, respectively). Third, the cumulative exposure was low for lung cancer cases compared to that of other workers. For example, if median cumulative exposure is set at 1.0 for lung cancer decedents, the relative median cumulative exposure is 1.1 for ischemic heart disease, 1.5 for all decedents, 3.5 for NMRD as underlying or contributory cause of death, and 10.8 for pulmonary fibrosis.

Honda et al. (2002) conclude that the lung cancer excess is unlikely to be due to talc dust *per se*. The reasons for the excess are unclear. Possible explanations for the excess include confounding by smoking or other risk factors or an unidentified constituent in the ore or mine environment that is poorly correlated with talc dust.

12.2. Norwegian talc

Norwegian talc contains trace amounts of quartz, tremolite and anthophyllite; the main minerals are talc and

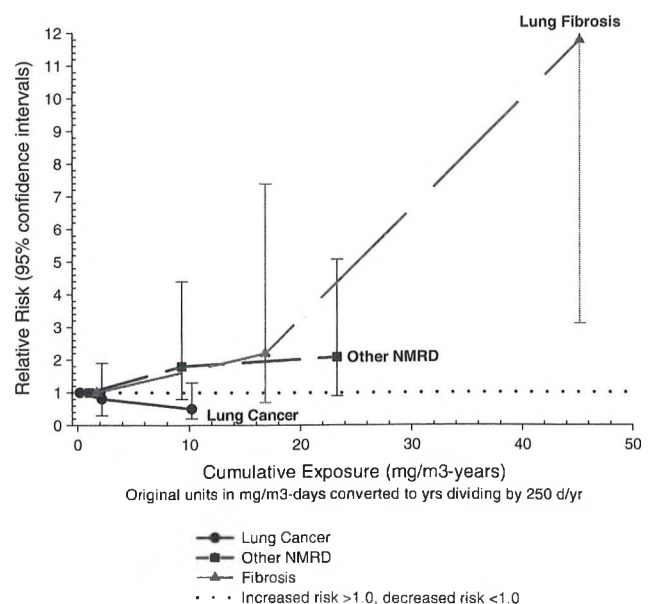


Fig. 3. Exposure-response of lung cancer, other non-malignant respiratory disease (other NMRD) and lung fibrosis by cumulative exposure (mg/m^3 years) Honda et al. (2002).

magnesite. Small amounts of magnetite, chromite, chlorite, and antigorite are in the ore, while the surrounding rock contains small amounts of serpentine, mica, feldspar, calcite, and non-asbestiform amphiboles (hornblende, tremolite). Personal air samples were collected 1982–1984. Exposures were somewhat higher in the mine with a range for total dust of 0.94–97.4 mg/m³ and peaks at drilling of 319 mg/m³. The range in the mill was 1.4–54.1 mg/m³ with peaks in the storehouse of 109 mg/m³. Fibers of tremolite, anthophyllite and talc with aspect ratios >3:1 by optical microscopy ranged from 0.2 to 0.9 f/mL (Wergeland et al., 1990).

The Norwegian male talc cohort consisted of 94 miners employed at least 1 year in talc-exposed jobs 1944–1972 and 295 millers employed at least 2 years 1935–1972 (Wergeland et al., 1990). In contrast to NY talc workers, this is a generally healthy work population with a significant deficit in all-cause mortality (SMR of 0.75; 0.62–0.89), which was below expected in both mine and mill. There were only 6 incident cases of lung cancer and 6.49 expected for an SIR of 0.92. There was a small positive trend with years worked because there were zero cases in the low tenure group but no significant excess (SIR) in the two groups with longer tenure. There were two lung cancer cases among miners (1.27 expected) and there were more expected (5.22) than observed (4) in the mill. There was no excess of NMRD cases (three cases of pneumonia), but numbers were too small to make any conclusions. There were no cases of mesothelioma.

It is unclear why the mortality and incidence of cancer are so far below expected. There is no excess NMRD mortality and no cases of pneumoconiosis as a cause of death despite the apparently very high dust exposures. There were three cases of pneumoconiosis as a contributing cause of death: two cases with silicosis, one case with talcosis. In 1981, smoking histories were obtained from 63 of 94 miners. A reduced prevalence of smoking is an unlikely cause of the reduced mortality as only 8% were non-smokers. In view of the small size of this cohort, interpretation is difficult.

13. Non-asbestiform amphiboles in South Carolina vermiculite

There are several small vermiculite pits in South Carolina containing nearly 50% tremolite/actinolite but is believed to be virtually free of fibrous tremolite (McDonald et al., 1988). Mining and the first part of the milling process are carried out wet. Four types of elongated fibers were identified in air samples using analytical transmission EM and energy dispersive X-ray spectroscopy (EDSX): tremolite–actinolite (48%), vermiculite fragments (8%), talc/anthophyllite (5%), iron-rich fibers (23%) and the rest unidentified. Mean fiber size was 1.1 µm diameter and 12.7 µm long. Mean fiber length seems to be quite large for the airborne fibrous dust cloud to be totally cleavage fragments. The mean expo-

sure was 0.75 f/mL years. Nolan et al. (1991) found tremolite cleavage fragments (some of which were >10:1 aspect ratio), but found no asbestos.

The mortality study comprises a small cohort of 194 men with 6 months or more tenure before 1971 and a minimum latency of 15 years. There were 51 total deaths and an all-cause mortality of 1.17 (0.87–1.51). There were four deaths from lung cancer and three from NMRD with SMRs of 1.21 and 1.22, respectively. There were no cases of mesothelioma and no deaths from pneumoconiosis. There was a negative exposure–response trend between cumulative fiber exposure and lung cancer (Fig. 4). Three of the four cases were in the lowest exposure category of <1 f/mL years (SMR = 1.71) and the 4th case was in the medium exposure category of 1–10 f/mL years (SMR = 0.73). Given the low fiber exposures (mean 0.75 f/mL years) and the small sample size the authors concluded there was inadequate power to detect an adverse effect in this population (McDonald et al., 1988).

The health experience of workers at this mine would be of considerable interest for comparison with the miners in Montana where exposures involve asbestiform “tremolite” and other fibers. Exposure levels were so much higher in Montana and the study population is so small and exposures so low in South Carolina that comparisons are difficult. In the longer term, the population is too small for confident conclusions concerning lack of risk. On the other hand, the exposure–response trends (Fig. 4) are suggestive that if tremolite asbestos were present instead of cleavage fragments there would likely have been an increase in lung cancer in the highest exposure category (and the work envi-

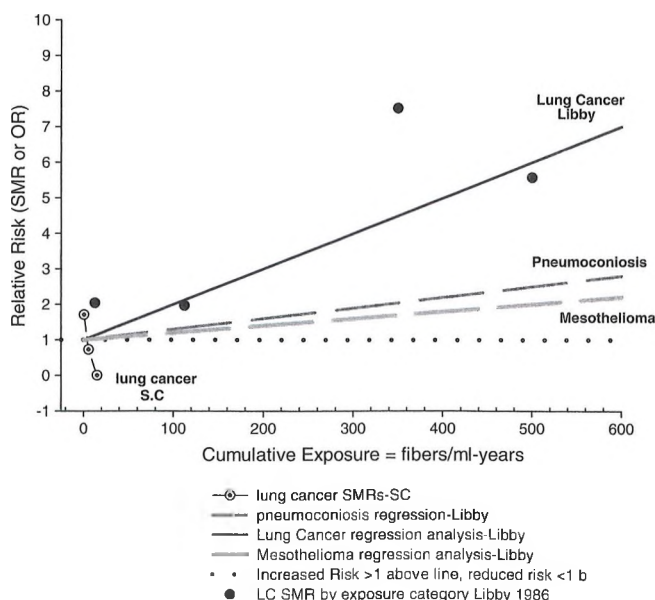


Fig. 4. Exposure–response trends for lung cancer, mesothelioma and Pneumoconiosis among Vermiculite workers exposed to Vermiculite Ore contaminated with tremolite asbestos in Libby, Montana (McDonald et al., 1986a,b) Vermiculite with non-asbestiform amphiboles in South Carolina (McDonald et al., 1988).

ronment would have been more dusty with higher exposures).

Although the actual percentage of “non-asbestiform” anthophyllite in the airborne dust is not clear in these studies, we will assume that the airborne dust contains a proportion of non-asbestiform anthophyllite and non-asbestiform tremolite. In view of this, comparison of the risk of mesothelioma and lung cancer in the NY and Norwegian talc mining industry will be compared with other talc studies (negative control) and with asbestos-exposed workers in anthophyllite mining and workers exposed to vermiculite contaminated with tremolite asbestos (positive comparison). South Carolina vermiculite will be compared with Libby, Montana vermiculite.

14. Other talc deposits

There are several mortality studies of talc where amphibole minerals are reported to be absent and the talc is relatively “pure” talc. These include studies of workers in the Vermont talc mines (Selevan et al., 1979), Italian talc mines (Coggiola et al., 2003), French and Austrian talc mines (Wild et al., 2002) (Table 6). According to Wild et al. (2002) “no asbestos contamination has ever been clearly documented in the talc deposits, at least not in the European sites”.

15. Lung cancer in New York and Vermont talc miners and millers

In contrast to the high levels of amphibole cleavage fragments in New York’s St. Lawrence County talcs, geological studies conducted since the early 1900s have shown no “asbestos” and little quartz in Vermont talc deposits (Boundy et al., 1979). Analyses of bulk samples collected in 1975/1976 from mines and mills of the three major Vermont talc companies showed talc and magnesite as major components (20–100%) and chlorite and/or dolomite as minor constituents (5–20%). There were trace amounts (<5%) of dolomite, calcite, quartz, biotite, ankerite, chromite, phlogopite and oligoclase and no asbestos.

Sampling surveys conducted in summer/winter of 1975/1976 at the three talc mines/mills resulted in respirable geometric mean concentrations in the mines ranging from 0.5 to 5.1 mg/m³ (median = 0.9) and in the mills from 0.5 to 2.9 mg/m³ (median = 1.0). Two methods were used to count “fibers” with aspect ratios $\geq 3:1$ and a “maximum width and minimum length” of 5 μm . Counts using phase contrast microscopy at a magnification of 437 $\times$ ranged from 0 to 60 fibers/mL (median = 4.1). Parallel fibers counted by SEM at a magnification of 5000 $\times$ ranged from 0 to 0.8 fibers/mL (median = 0). Cumulative exposures were not estimated, but past exposure levels commonly exceeded the MSHA and OSHA standards of 20 mppcf (Selevan et al., 1979).

The Vermont talc study provides the best comparison with the New York talc because the original studies were

conducted during the same time period using similar methods and some of the same investigators, and the mines were in adjacent US States (although different ore bodies).

The cohort comprised 392 men who had had a chest radiograph administered by the Vermont Health Department since 1937 and had been employed for more than 1 year in the Vermont talc industry between January 1, 1940 and December 31, 1969. Workers were followed through December 31, 1975. As the inclusion of workers in the cohort required a radiographic examination, it was thought that long-term workers were more likely to have participated than short-term workers. In the 1960s the Health Department reported that 70% of those missing from their radiographic surveys had less than 1-year employment. While the overall effect is not known, the original authors concluded that selection bias could not explain the observed excess mortality.

There were a total of 90 deaths with an overall SMR of 1.16. There was a six-fold excess mortality (11 obs, 1.79 exp) from NMRD (excluding influenza and pneumonia). The largest excess was among millers (7 obs, SMR = 7.87), but mortality was also increased among miners (2 obs, SMR = 3.6). Radiographic evidence of pneumoconiosis (80% > category 2/1) taken as part of the annual radiographic surveillance program of active workers, suggested to the authors that Vermont talc exposure was the causal agent. There was a non-significant 1.63-fold overall excess of lung cancer, which was significant among the miners (5 obs, SMR = 4.35) but not millers (2 obs, SMR = 1.02). There were no cases of mesothelioma (Selevan et al., 1979).

The most similar cohorts are Brown et al. (1979, 1980) and Lamm et al. (1988) (Table 6). Lamm et al. (1988) considered workers with >1 year tenure, which can be compared to Vermont. Brown et al. (1979, 1980) included all workers irrespective of tenure.

Risks of lung cancer were similar in Vermont and the NY talc workers with 1 or more year employment (1.63 versus 1.93, respectively) but elevated to 2.7 when all workers are included. The SMR for lung cancer among NY talc workers with less than 1-year tenure was 3.17 (6 obs) (Lamm et al., 1988). This supports the conclusion of Lamm et al. (1988) that the risk of lung cancer in NY talc workers is concentrated in short-term workers and is most likely due to risks acquired elsewhere.

Risks of NMRD were increased 3-fold in all three cohorts. Risk of pneumoconiosis appeared to be higher in Vermont as non-infectious respiratory disease mortality (possible surrogate for pneumoconiosis) was increased 6-fold compared to about 4-fold for both studies of NY talc workers.

In the Vermont mills the mortality from NMRD was twice that in the mines. However, the risk of lung cancer was four times greater in the mine than mill. Exposures in both mine and mill in Vermont were above the then standard of 20 mppcf, but cumulative exposures were thought to be higher in the mill than the mine because mine opera-

tions were more sporadic. Selevan et al. (1979) concluded that for NMRD, “additional etiologic agent(s) either alone or in combination with talc dust affect mine workers” because exposures were higher in the mill than in the mines yet mortality was higher in the mines. If this same reasoning is used for lung cancer, one would also conclude that other etiological agents were involved since SMRs for lung cancer were near the null among millers in both Vermont (Selevan et al., 1979) and the updated NY talc cohort (Honda et al., 2002) (Table 6).

A clear limitation of the Vermont study is the small number of deaths; there were only six lung cancer deaths and 11 deaths from NMRD. Nevertheless, the increased risk of lung cancer in talc miners in Vermont where there is no evidence of exposure to asbestos or amphibole cleavage fragments is consistent with a conclusion that amphibole cleavage fragments are not responsible for the increased risk of lung cancer in the New York Talc miners. On the other hand the increased risk of Non-Malignant Respiratory Disease (Pneumoconiosis) appears to be related to both Vermont and NY talc dust exposure. Further follow-up and quantitative exposure–response analysis of the NY talc cohort tested these hypotheses and found that cumulative exposure to talc dust showed a strong association with pulmonary fibrosis mortality, a moderate association with other NMRD and no association with lung cancer (Honda et al., 2002; Oestenstad et al., 2002).

It is informative to think about the history of these two cohorts of similar size and similar risks and hopefully learn some useful lessons. There has been no further follow-up of the Vermont talc cohort. The NY cohort has been re-analyzed several times both with and without further follow-up (Stille and Tabershaw, 1982; Lamm et al., 1988; Brown et al., 1990; Gamble, 1993; Oestenstad et al., 2002; Honda et al., 2002). From the earlier studies has come the common (and current) perception that talc in the Gouverneur Talc District contains asbestos and that “exposures to asbestiform tremolite and anthophyllite stand out as the prime suspected etiologic factors associated with the observed increase in bronchogenic cancer” (Brown et al., 1980). We offer two possible reasons for this incorrect perception.

First is the difference between including and not including short-term employees. The evidence that lung cancer risk was concentrated in short-term workers appears to have been outweighed by the known risks associated with asbestos and the presumption that NY talc workers were exposed to talc containing asbestos. The excess lung cancer among Vermont talc miners appears to have been discounted due to “talc free both of asbestiform minerals and significant quantities of free silica” and the potential for additional etiologic agents either alone or in combination with talc dust (e.g., radon).

Second, the most important limitation is with regard to the asbestos standard for regulating asbestos minerals. The OSHA–NIOSH definition of asbestos is inadequate for identifying and regulating non-asbestiform amphiboles. The crushing of rock containing non-asbestiform amphiboles

(and other minerals) produces cleavage fragments that conform to the OSHA–NIOSH definition of asbestos (e.g., $\geq 3:1$ aspect ratio, $\geq 5 \mu\text{m}$ length) but are not asbestos fibers.

Using this definition has produced errors regarding asbestos content of the ores that are the subject of this review, i.e., taconite tailings dumped into Lake Superior (see other presentations in this volume), asbestos exposure of Homestake gold miners (Gilliam et al., 1976) as well as talc. Other examples of the potential misuse of the federal fiber definition for asbestos include allegations of asbestos in play sand (Langer et al., 1991) and in crayons. The Agency for Toxic Substances and Disease Registry (ATSDR) in their Public Health Statement for Asbestos suggest that talc may contain asbestos. The Australian Government National Occupational and Health Commission say that industrial talc generally contains “asbestos fibers, notably tremolite”. By this standard one might include all the negative control talc cohorts as positive controls of workers exposed to asbestiform amphiboles. More examples are readily available on the internet. While amphiboles are sometimes present in some talc, asbestiform amphiboles occur very rarely as a geological curiosity and not as far as we are aware using a mineralogical definition in any commercial or industrial talc.

The reasons for the increased risks of lung cancer in the New York and Vermont mining areas still remain speculative. Exposure to radon may be one reason as levels were apparently elevated in the Vermont Mines. The possibility that miners worked in areas of high asbestiform tremolite in the past cannot be totally excluded on present evidence as in one closed mine in Vermont “cobblestones of serpentine rock which were “highly tremolitic” have been reported, although workers in the Vermont cohort were considered unlikely to have had such exposure (Selevan et al., 1979). Whether this was asbestiform tremolite is not described although this appears to be inferred.

16. Italian talc

Italian talc is very pure and is used in the pharmaceutical and cosmetic industries. Miners and millers in this industry were studied for mortality (Rubino et al., 1976, 1979; Coggiola et al., 2003). Miners were analyzed separately from millers because of silica exposure in the mine. The silica content of airborne dust in the mines was as high as 18% in drilling operations from footwall contact rocks, rock type inclusions, and carbonate, calcite and magnesite inclusions. The quartz content of the rock strata was inconsistent, ranging from 10% to 45%. Other minerals in the inclusions included muscovite, chlorite, garnet, and some carbonate material. A small amount of (non-asbestiform?) tremolite was detected in the inclusions but not in the talc samples. Talc samples were commonly contaminated with chlorite. From 1920 to 1950 there was dry drilling and no forced ventilation so exposures were over 10 times the TLV (which appears to have been about 25 mppcf at that time) in the mines and a little

over the TLV in the mills. Wet drilling and forced ventilation were introduced in about 1950 and dust concentrations dropped precipitously to about 1 mppcf and well below the TLV. Concentrations in the mills were reduced slightly and slowly and after about 1960 were higher than in the mines (Rubino et al., 1976).

Coggiola et al. (2003) updated the earlier talc studies by Rubino et al. (1976, 1979). The updated cohort comprised 1795 men with at least 1 year of employment 1946–1995 and national rates were used for comparisons. There were 880 observed deaths with an overall SMR of 1.20 (1.12–1.28). There were slight deficits in observed lung cancer and total cancer and there were no mesotheliomas.

The SMR for lung cancer was 1.07 (0.73–1.50) for miners, while there was a deficit of lung cancer with an SMR of 0.69 (0.34–1.23) in millers. There was a 2-fold excess of NMRD due mainly to silicosis with the excess occurring among miners with a significant SMR of 3.05 (2.50–3.70) compared to 1.04 (0.65–1.57) among millers. Exposure-response was examined using duration of exposure. This showed that for miners the only lung cancer excess was in the <10-year exposure group while for NMRD the exposure-response trends were flat with all categories of duration of exposure showing about a 2-fold excess mortality.

The authors concluded there was no association between lung cancer or mesothelioma and exposure to talc containing no asbestos fibers. But there was an association in miners between NMRD (primarily silicosis) and talc containing quartz.

17. French and Austrian talcs

Wild et al. (2002) conducted cohort studies of talc workers in France and Austria with nested case-control studies of lung cancer and NMRD. The French ore was a talc chlorite mixture with quartz contamination ranging from undetectable to less than 3%. In Austria, three mines were studied. At one site the ore was a talc-chlorite mixture with 0.5–4% quartz. Rock containing about 25% gneiss was not milled. A talc-dolomite mixture of 25% medium talc and <1% quartz in the final product was the product at the second mine. The ore at the third site did not contain talc but was mixture of approximately equal proportions of quartz, chlorite and mica. Workers were stratified into semi-quantitative exposure categories. The non-exposed group consisted of office workers not exposed to talc and personal dust samples averaged 0.2 mg/m³. The low exposure group was for workers with no direct contact to talc, such as maintenance workers, and concentrations were less than 5 mg/m³. The medium exposure category included workers exposed to concentrations between 5 and 30 mg/m³ for dustier areas such as bagging or milling and onsite maintenance. Quartz exposures occurred mostly in underground mining, tunneling and barrage building and milling products at site D. The highest exposure category was reserved for past production jobs (all before 1980) where concentrations were >30 mg/m³. Some samples produced concentra-

tions >50 mg/m³ and higher. Three samples taken on workers wearing personal protective equipment were 73, 82 and 159 mg/m³. To calculate cumulative exposures, values of 2.5, 10 and 40 mg/m³ were assigned to the low, medium and high exposure jobs.

The French cohort consisted of 1070 men with more than one year tenure between 1945 and 1995, with vital status follow-up through 1996. The Austrian cohort consisted of 542 men with >1-year tenure between 1972 through 1995 and vital status follow-up during this same period. Three controls per each case of NMRD and lung cancer from both the French and Austrian cohorts were matched on age and calendar year of employment.

Overall mortality was below expected. There were 294 deaths in the French cohort in the period 1968–1996 for an SMR of 0.93 (0.82–1.04). The Austrian cohort was smaller with 67 deaths and an SMR of 0.75 (0.58–0.95). In the French cohort SMRs were only slightly elevated for NMRD and lung cancer (1.06 and 1.23, respectively) but were increased over five-fold (SMR 5.56 CI 1.12–16.2) for the three cases with pneumoconiosis. There were zero mesotheliomas.

The case-control studies combined the French and Austrian cohorts. There were 40 combined deaths from NMRD: 10 from pneumoconiosis (including silicotuberculosis), 10 from chronic obstructive pulmonary disease (COPD, restricted to chronic bronchitis and airway obstruction), and 20 deaths from pneumonia and other diseases. When analyzed by exposure categories, the exposure-response trend for NMRD was not monotonic, with no apparent increased mortality below 400 mg/m³ years and 2-, and 2.5-fold increased risks in the two highest exposure categories respectively. When analyzed by conditional logistic regression there was a significant exposure-response trend with an 8% increased risk per 100 mg/m³ years exposure. The slope was even higher for pneumoconiosis, 1.17 for pneumoconiosis versus 1.08 for NMRD. The slope was only 1.02 for COPD. Adjustments for covariates in the regression analyses had little effect on these trends. Smoking prevalences were similar between cases and controls with about 40% non-smokers (Fig. 5).

There were 30 combined lung cancer cases. There was a negative exposure-response trend with odds ratios of 0.6 and 0.73 in the two highest exposure categories. The trend was unchanged when adjustments were made for smoking, quartz, working underground or when lagging the exposure estimates. Also, there were no trends when analyzed by maximum dose, latency, or duration of exposure (data not shown). About 40% of the controls were non-smokers compared to about 8% (1/19) among cases although smoking classification was unknown on about half of the cases.

Wild et al. (2002) concluded that the small excess of lung cancer was not due to talc, despite follow-up of over 50 years, high exposures and mean duration of exposure >20 years.

The pattern of mortality of workers exposed to cleavage fragments in the New York talc mines and mills (Fig. 3) is

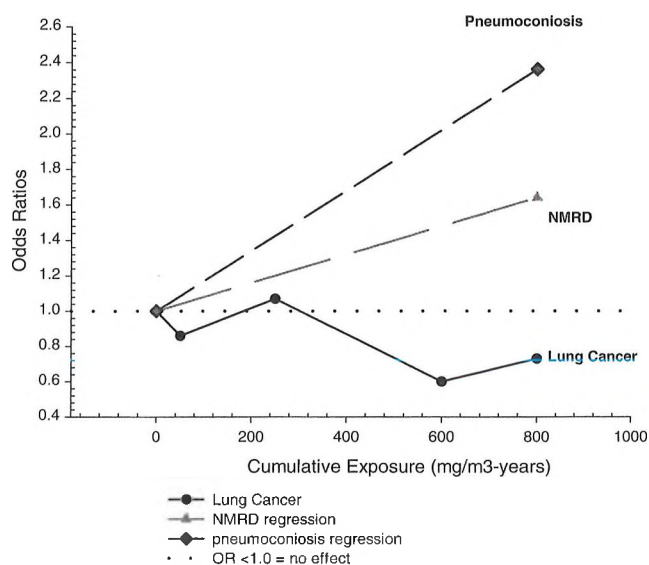


Fig. 5. Exposure-response trends for lung cancer Non-malignant respiratory disease (NMRD) and Pneumoconiosis by cumulative exposure ($\text{mg}/\text{m}^3\text{-years}$) to Talc not containing amphiboles Among French & Austrian Talc Workers Wild et al. (2002).

very similar to that of workers in the French and Austrian mines and mills where there was no exposure to cleavage fragments (Fig. 5). A limitation in these comparisons is the very large differences in cumulative exposures. If they are comparable, the dust to which the New York miners and millers are exposed is considerably more potent than that in the French and Austrian mines and mills from the standpoint of increasing lung fibrosis/pneumoconiosis. On the other hand, this “apparently highly potent pneumoconiosis producing dust” does not increase lung cancer risk.

These studies show that “pure” talc does not increase lung cancer risk. This is consistent with the observations for the New York millers, exposed to talc as there was no excess lung cancer in talc millers.

18. Asbestos-exposed cohorts for comparison with talc workers

There are two ore deposits containing tremolite asbestos or anthophyllite asbestos potentially suitable for comparison with the talc cohorts exposed to non-asbestiform tremolite and asbestos. One site is the vermiculite mine located in Libby, Montana with significant contamination from tremolite asbestos. The other is an anthophyllite asbestos mine in Finland.

18.1. Libby, Montana vermiculite mine contaminated with asbestiform amphibole

Ore fed to the mill in Libby, Montana contains 4–6% asbestiform amphiboles (about half tremolite asbestos and the other half a mixture of winchite and richterite in

the tremolitic series, Nolan et al., 1991). The health concern is the asbestiform amphibole contamination in these ores and not the vermiculite itself.

The raw ore and vermiculite concentrate from the Libby mine contain both asbestiform and non-asbestiform tremolite-actinolite and non-fibrous anthophyllite. Atkinson et al. (1982) found 21–26% fibrous tremolite-actinolite in the raw ore and 2–6% in the concentrate. Company data taken several years later indicated 3.5–6.4% at the head feed of the mill and 0.4–1% in the concentrate (Amandus et al., 1987a). After removal of coarse rock the ore contained about 20% vermiculite, 21–26% fibrous tremolite-actinolite and the rest augite, biotite, calcite, diopside, hornblende, magnetite, quartz, sphene, and apparently non-fibrous tremolite-actinolite (McDonald et al., 1986a,b).

Eight airborne samples from the mill and screening plant examined by phase contrast light microscopy indicated the asbestiform nature of the particles: 96% had aspect ratios >10 , 67% >20 and 16% >50 . In addition, 73% of the fibers were longer than $10\ \mu\text{m}$, 36% $>20\ \mu\text{m}$ and 11% $>40\ \mu\text{m}$ and width was $<2.5\ \mu\text{m}$ in all instances (Amandus et al., 1987a).

Two independent mortality studies of the Montana vermiculite have been conducted. McDonald et al. (1986a,b) conducted a radiological survey and a cohort and nested case-control study of 406 persons employed for at least a year prior to 1963 with follow-up until 1983. The cohort study was subsequently updated with follow-up to 1999 (McDonald et al., 2002, 2004). We will primarily focus on the up-dated analysis. Exposure was estimated from first exposure (1945) to 1982 when work histories were no longer available. By this date most of the cohort was no longer employed and fiber concentrations were about 0.1 f/mL. The plant closed in 1990. Before wet milling processes were installed, fiber concentrations were very high (estimates of $>100\ \text{f}/\text{mL}$). A wet mill was installed in 1955 and an entirely wet process replaced both wet and dry mills in 1974 so by 1980 nearly all concentrations were $<1\ \text{f}/\text{mL}$. Exposure-response was estimated by both categorical and linear exposure-response (E-R) Poisson regression models and excluding those with <10 years latency. Average and cumulative exposure metrics showed similar relationships with mortality (Table 7).

The overall all cause SMR was 1.27 (1.13–1.43). SMRs for lung cancer and NMRD were 2.40 (1.74–3.22) and 3.09 (2.30–4.06), respectively; the PMR for mesothelioma was 4.2%. Exposure-response trends were not linear, as risks of lung cancer, NMRD and mesothelioma increased steeply in the second quartile exposure category and showed less steep slopes in the third and fourth exposure quartiles (Fig. 4 and Table 7).

The other Libby cohort study was by NIOSH and published in 3 sections that included exposure estimates (Amandus et al., 1987a), cohort mortality study (Amandus and Wheeler, 1987b) and a cross-sectional radiographic study (Amandus et al., 1987c). Amandus and Wheeler

Table 7

Mesothelioma/lung cancer experience—non-asbestiform anthophyllite and anthophyllite asbestos miners and tremolite asbestos

Study population	Follow-up period	N in cohort (% deaths)	PMR (mesothelioma/total deaths)	Lung cancer SMR (95% confidence intervals)
Talc workers, NY State, Honda et al. (2002)	White men actively employed >1 day between 1948 and 1989 and alive in or after 1950. Follow-up 1950 thru 1989	809 (27%) Mill = 377 Mine = 311	2/209 = 0.96% ^a	31/13 = 2.32 (1.57–3.29) Mill: 7/5.5 = 1.28 (0.51–2.63) Mine: 18/4.6 = 3.94 (2.33–6.22)
Norwegian talc workers, Wergeland et al. (1990)	Miners >1 year 1944–1972; Millers >2 years 1935–1972; Follow-up 1953–1987	Total (M) 389 (30.1%) 94 miners (28.7%) 295 millers (30.5%)	0/117 = 0% 0/27 = 0% 0/90 = 0%	Incidence (SIR): 6/6.49 = 0.92 (0.34–2.01) 2/1.27 = 1.57 4/5.22 = 0.77
Finnish anthophyllite asbestos miners, Karjalainen et al. (1994), Meurman et al. (1994)	>3 months 1953–1967; Follow-up 1953–1991	999 (59.4%) M = 736 (68.3%) F = 167 (53.9%)	4/593 (0.7%) M = 4/503 (0.8%) F = 0/90 (0%)	Incidence: SIR M: 76/26.4 = 2.88 (2.27–3.6) Heavy Exp: 3.15 (2.37–4.09) Mod Exp: 2.35 (1.45–3.58)
Vermiculite miners, Libby, MN, McDonald et al. (2004)	>1 year before 1963, followed to 1999	406 70.2% mortality	12/285 = 4.2%	44/18.3 = 2.40 (1.74–3.22)
South Carolina Vermiculite, McDonald et al. (1988)	<6 months 1971–1986, followed to 1986 (>15 years latency)	194 51/194 = 27.8% (>15 years latency)	0/51 = 0%	4/3.31 = 1.21 (0.33–3.09)

^a See text. Cases were not considered to have resulted from work at the talc mine. One case had latency of 15 years and one was a draftsman during construction only.

Table 8

Dimensions of elongated particles associated with various amphibole exposure industries studied experimentally and/or epidemiologically

Cohort	Width (μm)	Length (μm)	Reference
Libby vermiculite; tremolite asbestos	46%, <0.25	62%, >5	Langer et al. (1974)
Homestake gold mine (CG = cummingtonite–grunerite) (TA = tremolite–actinolite) (GM = geometric mean)	69% CG: GM = 0.43 15% TA: GM = 0.27 0%, <0.25 minimum 0.3 mean 1.1	34%, >5; 32%, >5	Brown et al. (1986)
Taconite	0%, <0.25 min 0.25 mean 1.2	Mean 4.6; Max 17.5 Mean 5.5; Max 32.4	Virta et al. (1983)
Vanderbilt tremolitic talc	0%, <0.25		Wylie (1988)
Experimental studies			Kelse and Thompson (1989)
Korean tremolite asbestos >5 μm L	44.7%, <0.25	11.8%, >5 [1.9]	Addison (2004), Davis et al. (1985)
Californian white tremolite asbestos (Davis et al., 1991)	50%, <0.25	14.9%, >5 [3.2]	Addison (2004)
Swansea tremolite asbestos (Davis et al., 1991)	8.2%, <0.25	33.6%, >5 [1.0]	Addison (2004)
Italian tremolite (Davis et al., 1991)	13.3%, <0.25	9.7%, >5 [0.27]	Addison (2004)
Greenland tremolite, Wagner et al. (1982)	0%, <0.25	100%, <10	Wagner and Berry (1969), Wagner et al. (1982)
Dornie, Scotland tremolite, Davis et al. (1991)	13.7%, <0.25	22.5%, >5 [0.1]	Addison (2004)
Shinness tremolite, Davis et al. (1991)	13.8%, <0.25	10.6%, >5 [0]	Addison (2004)
Ferro-actinolite asbestos	Median: 0.24, range: 0.03–5.2	Median: 1.50, range: 0.3–52.5	Coffin et al. (1982)
UICC Amosite	Median: 0.22, range: 0.02–4.1	Median: 1.8, range: 0.15–378	Coffin et al. (1982)

Figures in [] = % >5 μm and less than 0.25 μm. Addison (2004) provided figures from Davis et al. (1991), calculated from the fiber numbers in the doses used in the experiments by Davis et al.

(1987b) also reported positive exposure–response trends for lung cancer with an almost 7-fold increased SMR in the high exposure category with more than 20-years latency. The PMR for mesothelioma was 2.2% considering only those with 20 years or more latency.

These results are a marked contrast to the decreasing trend of lung cancer with increasing exposure seen in the St. Lawrence, NY talc workers. There is little doubt that the mesothelioma experience of the Montana work force is considerably worse than that of the talc miners. This is

in spite of the fact that the New York talc workers are reported to have been exposed to dusts containing a very high percentage of non-asbestiform amphibole fibers (Kelse and Thompson, 1989).

The amphiboles in St. Lawrence, NY talc are non-asbestiform while they are asbestos in the Libby deposit (Kelse and Thompson, 1989; Langer and Nolan, 1989; Thompson, 1984; Dement et al., 1980).

Risk of pneumoconiosis, lung cancer and mesothelioma clearly increase as cumulative exposure to asbestiform tremolite increases (Fig. 4). For the talc workers exposed to non-asbestiform tremolite, the risk of NMRD and pneumoconiosis increase as exposure increases, but the trends are reversed for lung cancer (inverse trend) and for mesothelioma (no cases so there is no trend) (Fig. 3).

18.2. Finnish anthophyllite asbestos miners/millers

Dement et al. (1980) mentioned the study of Finnish miners by Meurman et al. (1974) in the belief that both the NY talc and Finnish anthophyllite asbestos cohorts were exposed to asbestiform anthophyllite. They recommended that the risk of mesothelioma should be further studied by further follow-up of the NY talc workers. Both the NY talc (Honda et al., 2002) and anthophyllite asbestos cohorts have had further follow-up so the maximum latency in Finland is now about 40 years (Karjalainen et al., 1994; Meurman et al., 1994), which is about the same as for NY talc workers (Honda et al., 2002).

In the updated Finnish study there was a significant 2.9-fold excess incidence of lung cancer overall with a somewhat higher risk in the heavily exposed males (SIR 3.15) than in moderately exposed (SIR 2.35). There were four mesothelioma cases for a significant 46-fold increased SIR (95% CI = 12.2–115) overall (or a PMR of 0.7%, 4/593). All of the cases were in the heavy exposure group where there was a 67-fold excess (95% CI = 18.3–172) and all four had asbestosis. Asbestosis was mentioned on 20% of all death certificates (Karjalainen et al., 1994; Meurman et al., 1994).

18.3. Mesothelioma comparison

In the NY talc cohort, Honda et al. (2002) reported two deaths from mesothelioma. One was coded as benign neoplasm of the respiratory system and the other as malignant neoplasm of the lung and bronchus, unspecified. One man worked for 15 years and died 15 years after starting work at the talc facility. He had been a carpenter and millwright for 16 years, 8 years as a lead miner and 5 years as a repairman in a milk plant. The other man worked briefly at the facility as a draftsman during mill construction in 1947–8. He would have had minimal talc exposure. He had been employed on the construction of a previous talc mine, and then installed oil burning heating systems. Honda et al. (2002) concluded it is unlikely that either of these cases occurred as a result of talc exposure in the mine or mill.

In essence, there are no mesothelioma cases that are plausibly related to occupational exposure to Gouverneur talc.

Vianna et al. (1981) reported a mesothelioma rate in Jefferson County twice that of New York State based on an incidence study of histologically confirmed mesothelioma cases. A total of six cases, four male and two female cases diagnosed between 1973 and 1978 were reported to have occurred in talc miners. Enterline and Henderson (1987) reported an excess mesothelioma incidence in Jefferson County from 1968 to 1981 with 4 female (0.6 expected) cases and 7 male (1.4 expected) cases for risk ratios of 6.7 and 5.0, respectively. These latter rates were the second and sixth highest in the USA and occur in the county next to the one where the talc mines are located.

Hull et al. (2002) drew attention to these elevated rates, added “five new mesothelioma cases,” and concluded that New York talc exposure was associated with an increased risk of mesothelioma. This conclusion is inconsistent with the limited available data as outlined in the following:

- The entire work histories of the “talc miners” with mesothelioma are apparently not known. Exposure to asbestos in other jobs is likely given the diagnosis of asbestosis and the smaller widths of the fibers in lung tissue.
- Hull et al. (2002) attempt to interpret the results of their tissue analyses based on only two mesothelioma cases. This sample is too limited to reach any reliable conclusions. Available data do not support a talc etiology.
- Fiber dimensions are consistent with asbestos exposure as the mean fiber widths in the two mesothelioma cases examined are less than 0.25 μm , which are the dimensions characteristic of asbestos.
- The source of the fibers in the lungs is unlikely to be NY talc mines. The average width of the fibers in the mesothelioma lungs was 0.15 μm , which is considerably less than the average width of 1.3 μm of anthophyllite and tremolite in milled talc samples (Siegrist and Wylie, 1980). Kelse and Thompson (1989) reported that 0% of the fibers in NY talc samples had widths less than 0.25 μm .
- Asbestos-related employment occurs among residents of both St. Lawrence and Jefferson counties. Fitzgerald et al. (1991) reported that 39% of workers with radiographic abnormalities of parenchyma and pleura had been employed for a year or more in asbestos-related industries (e.g., shipyard, construction, pipe and furnace insulation).
- Two of the five cases had worked only 4 and 2 years in occupations likely to be linked to the mining industry. One of these persons died at age 72 and the other at age 53. There was no information concerning their employment during the rest of their lives.
- A non-talc etiology for mesothelioma is plausible. As noted above, females in the talc mining counties have a greater risk of mesothelioma than males (Enterline

and Henderson, 1987). On the other hand, the cohort data on talc workers is based on men because less than 5% of those hired in the talc industry were women (Honda et al., 2002; Brown et al., 1990; Lamm et al., 1988).

- In the cohorts, the worker populations and exposures are well defined and no association is observed between talc or non-asbestiform amphibole exposure and mesothelioma in the absence of possible asbestos exposure. The cohort studies provide a more reliable estimate of risk than a small case report with limited information on exposure.
- Hull et al. (2002) indicate the “increased pleural mesothelioma mortality [is] in Jefferson County”. Jefferson County stopped producing talc about 100 years ago and all talc over the past century has been mined in St. Lawrence County.
- In the Libby cohort there were twelve mesothelioma cases. The PMR was 4.2%. Exposure to tremolite asbestos in the Libby vermiculite clearly increased the risk of mesothelioma significantly (McDonald et al., 2004). The risk of mesothelioma among anthophyllite asbestos workers was less than the risk among crocidolite miners but almost as great as among amosite miners (Meurman et al., 1994). These comparisons show a clear excess incidence of mesothelioma for workers exposed to asbestiform tremolite and anthophyllite, but no mesothelioma attributable to exposure to non-asbestiform tremolite/actinolite or anthophyllite. These comparisons are graphically displayed in Fig. 6.

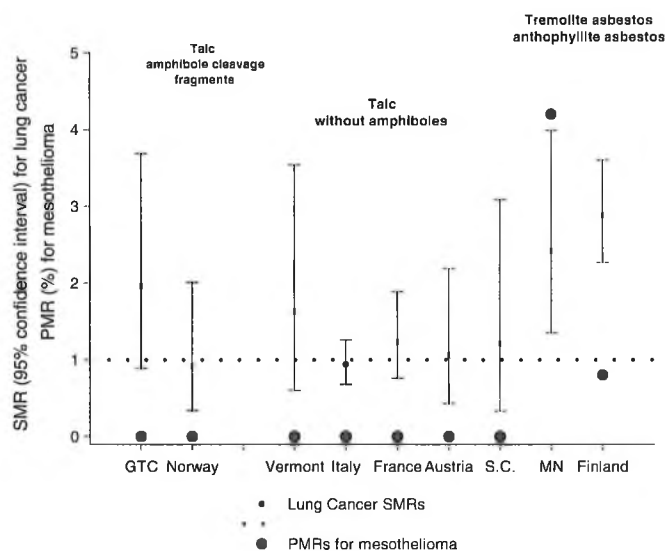


Fig. 6. Lung cancer and mesothelioma mortality in workers exposed to Talc containing non-asbestiform amphiboles in New York and Norway (Honda et al., 2002; Wergeland et al. (1990) Talc without amphiboles (Vermont, Italy, France/Austria) Selevan et al. (1979), Coggiola et al. (2003), Wild et al. (2002) and Vermiculite containing tremolite asbestos McDonald et al., 1986a,b Anthophyllite Asbestos (Karjalainen et al., 1994; Meurman et al., 1994).

18.4. Lung cancer comparison

There was an overall 2-fold increased rate of lung cancer in the Gouverneur talc miners and millers compared to the surrounding counties in which the mine was located. This excess of lung cancer was not associated with dust exposure but was concentrated in miners with an SMR of 3.94 (CI 3.33–6.22) while millers had only a small increased risk with an SMR of 1.28 (CI 0.51–2.63). In contrast, non-malignant respiratory disease mortality was associated with dust exposure as it was increased in both miners (SMR 2.41, CI 1.16–4.44) and in millers (SMR 2.27 CI 1.13–4.07) to almost the same extent. Smoking was clearly a confounding exposure as 100% of cases were smokers or ex-smokers but only 73% among controls. When exposure–response relationships were examined, the rate ratio for the highest respirable dust exposed workers to the lowest respirable dust exposed workers was 0.5 (0.2–1.3) for lung cancer and 11.8 (3.1–44.9) for pulmonary fibrosis (Fig. 3). One would expect that a respirable dust exposure index would reflect the respirable fractions of dust regardless of composition. Thus, the results indicate that the lung cancer excess in this industry is largely due to smoking and unlikely to be the result of exposure to the respirable fraction of dust (which would include talc and cleavage fragments of the various amphibole minerals). However the data suggest that the respirable dust did increase the risk of fibrosis.

In asbestos producing or using industries where midget impinger measurements were used as a basis for exposure estimates (Liddell et al., 1997), the risk of lung cancer increased with increasing levels of exposure. This illustrates the validity of exposure indices based on midget impinger measurements for assessing fiber-related risks, at least when exposures are high. However, in this talc mine, exposure estimates derived from midget impinger measurements (Oestenstad et al., 2002), showed no such relationship. If cleavage fragments were responsible for the lung cancer excess, an exposure–response relationship would have been anticipated.

To date a satisfactory explanation for the observation of an overall excess of lung cancer and for the concentration of the excess in miners rather than millers has not been found for workers exposed to either NY or Vermont talc, although at least part of the excess among NY talc workers is due to smoking (Gamble, 1993; Honda et al., 2002). If the airborne dust contained over 70% amphibole asbestos fibers as reported by Dement et al. (1980), there should be an overall increased risk of lung cancer, which there is. But there should also be a logical increasing risk of lung cancer with increasing dust exposure, with a very high risk of lung cancer in highly exposed workers. This is clearly not the case.

In Finland where the incidence of cancer has been studied in anthophyllite miners, it was found that among heavily exposed male workers, the standardized incidence ratio (SIR) for lung cancer was 5.54 (CI = 3.90–7.63) and among moderately exposed workers it was 1.63 (0.20–5.89). The

heavily exposed were those who worked in the mine or mill and the moderately exposed included all other personnel (Meurman et al., 1994). This exposure–response pattern is quite the opposite of that in the New York talc mines and mills.

There were consistent positive exposure–response trends for lung cancer risk as occurred with the increased asbestiform amphibole exposure in the Libby cohort. The slope of the exposure–response curve was steeper for lung cancer than for pneumoconiosis and for mesothelioma (Fig. 4).

The clear exposure–response trends for lung cancer to increase with increasing exposure to asbestiform tremolite and anthophyllite is in marked contrast to the negative exposure–response trend for lung cancer risk to decrease with increasing exposure to non-asbestiform tremolite and anthophyllite present in industrial talc. The pattern of increasing risk of fibrosis is consistent with exposure to mineral dust with or without the presence of tremolite asbestos. These lung cancer comparisons are graphically displayed in Fig. 6.

19. Biological plausibility

Biological plausibility is not a necessary prerequisite to establishing a causal association, but it is considered “helpful” (Hill, 1965). Experimental evidence is available to consider whether or not cleavage fragments are more or less carcinogenic than asbestos fibers. These issues have been independently evaluated by Addison and McConnell and Mossman, elsewhere in this volume.

Experimental studies have the potential advantage of precisely defining the characteristics of the minerals and amount of exposure. However there are also difficulties that affect the studies and their interpretation. Hence it is important to examine the overall pattern of biological responses to asbestos fibers and cleavage fragments rather than the results of single studies. Feeding studies have been considered elsewhere (Wilson et al., 2008).

Many experiments in animals have been used to assess the potential of fibers to produce mesothelioma-type neoplasms. For example, Stanton et al. (1981) counted as a positive response, pleural sarcomas that resembled the mesenchymal mesothelioma of man. The observed response is a measure of potential hazard rather than risk. Nevertheless such studies have been helpful in suggesting the morphological characteristics of particles in relation to “mesothelioma” producing potency. “Index particles” have been derived from these experiments. For example, based on the work of Stanton and colleagues the index particle is $>8\text{ }\mu\text{m}$ long and $<0.25\text{ }\mu\text{m}$ wide and is the best predictor of tumors without regard to the chemical composition of the particle. As far as we were able to ascertain, few if any cleavage fragments have the combination of diameter less than $0.25\text{ }\mu\text{m}$ and length greater than $8\text{ }\mu\text{m}$. This would suggest that cleavage fragments are not the most potent particles for the production of mesothelioma.

Different exposure techniques have been used, but most have not involved the inhalation route of exposure applicable to humans. Most experiments have involved placing fibers onto the pleural or into the peritoneal cavity or injections intratracheally, routes of exposure which are artificial. The incidence of tumors is therefore higher and the tests are likely to be more sensitive than by inhalation. However, these experiments ignore the factors which limit fiber passage to these sites and also the alterations to the particles during their passage to these sites if they get there at all. Nevertheless, these data are useful in hazard assessment, as the absence of “mesothelioma” occurrence when fibers are placed directly on the pleura or peritoneum in sufficient numbers, is strong evidence that human inhalation exposure is unlikely to be hazardous.

Samples used in experimental studies are not always related to the minerals to which workers are exposed. For example, no experimental studies of the Homestake gold ore were found. On the other hand, there are several studies of tremolitic talc samples from the Gouverneur mine in New York State (talc samples 6 and 7 used by Stanton et al. (1981); FD-14 used by Smith et al. (1979) and FD-275 (non-asbestiform tremolite) used by Smith et al. (1979) and by McConnell et al. (1983)) in feeding studies. Wylie et al. (1997) used *in-vitro* cell studies to compare the effects of asbestos fibers to talc fibers and transitional fibers in NY talc.

Fig. 7 shows the results of rat injection studies of asbestiform and non-asbestiform varieties of amphiboles, primarily tremolite. These data show a consistent pattern of high incidence of mesothelioma tumors with exposure to tremolite asbestos from South Korea, California, Swansea and Italy (Davis et al., 1985; Wagner and Berry, 1969; Wagner et al., 1982; Stanton et al., 1981). The mesothelioma incidence of both controls and samples was around 10%. The two Scottish tremolites studied contained relatively few asbestiform fibers and there was little difference between the control and exposed rats irrespective of whether the tremolite was asbestiform or not. Davis et al. (1991) noted that the intraperitoneal injection test used in their experiments is extremely sensitive so that any dust that produces fewer than 10% tumors is unlikely to show evidence of carcinogenicity by inhalation. Thus the non-asbestiform Scottish tremolite from Shinness was considered to pose no hazard.

The Scottish tremolite from Dornie was considered to be probably harmless as well. The latter sample was described as containing mostly cleavage fragments but also some very long, thin fibers, with a possible small asbestiform subpopulation. These results should be contrasted with those of asbestiform tremolite from Italy, California, Swansea and South Korea, which showed incidences of 70–100%. The Italian tremolite was described as a needle-like (byssolite) tremolite fiber but later shown to have an asbestiform component. For this fiber, the induction of tumors was much later than for the three asbestos types from California, Swansea and Korea. This is a normal response to a small

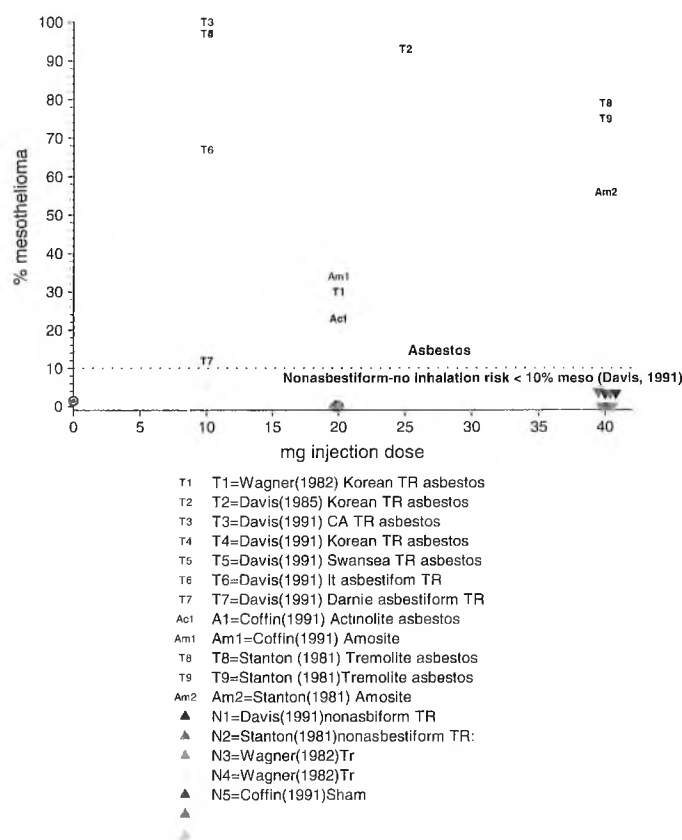


Fig. 7. Experimental studies of injections into rats of asbestiform amphiboles and non-asbestiform amphiboles.

dose of amphibole asbestos. Incidence was reduced to near zero for samples of non-asbestiform tremolite and talc fibers (Wagner et al., 1982; Stanton et al., 1981). Smith et al. (1979) assessed the incidence of tumors after injection of NY tremolitic talc and tremolite asbestos at two different doses. There were clear exposure-response trends for the asbestiform tremolite but no effect of non-asbestiform tremolite at either 10 or 25 mg exposures (Fig. 8).

20. Statistical analysis of potency by size, shape and mineralogy

Berman et al. (1995) conducted a statistical reanalysis of inhalation studies using data from studies of AF/HAN rats exposed to different types of asbestos to identify the exposure metrics that best predicted the incidence of lung cancer or mesothelioma. New exposure metrics were first generated from samples of the original dust because of limitations in the original characterizations. This analysis provided more detailed information on mineralogy [i.e., chrysotile, grunerite (amosite) asbestos, riebeckite (crocidolite), tremolite asbestos], type of structure (i.e., fiber, bundle, cluster, matrix), size (length, width) and complexity (i.e., number of identifiable components). In particular, transmission electron microscopy (TEM) was added to the descriptions so that asbestos structures less than

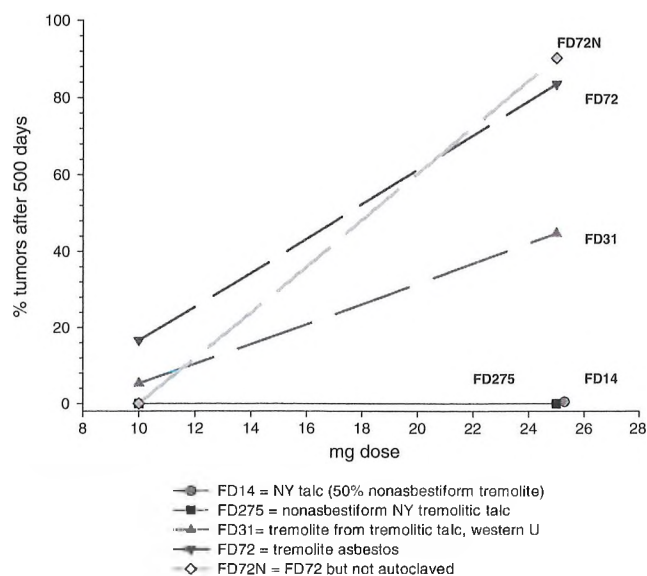


Fig. 8. Mesotheliomas in hamsters after intrapleural injection of tremolite asbestos and talc containing non-asbestiform tremolite Smith et al. (1979).

0.2 μm could be detected and identified and used in the statistical analysis of size distributions to evaluate combined effects of length and width.

Implantation and injection studies generally indicate long, thin fibers are most likely to induce mesothelioma. However, Berman et al. (1995) considered inhalation studies more relevant for assessing human risk because lung retention and transport from the lungs are likely to be important variables in potency but are bypassed in the implantation/injection studies. Also the exposure metrics from these studies are unable to satisfactorily predict tumor incidence (for example see Oehlert, 1991).

The analysis by Berman et al. (1995) indicated that particles contributing to lung tumor risk are long ($>5 \mu\text{m}$) thin ($<0.4 \mu\text{m}$) fibers or bundles with the potency increasing as length increases. For example, thin fibers longer than $40 \mu\text{m}$ are about 500 times more potent than thin fibers $5\text{--}40 \mu\text{m}$ in length. Long and very thick particles ($>5 \mu\text{m}$) may pose some risk, but these appear to be complex structures rather than fibers. It is hypothesized that these structures with large widths may break down and release additional long thin fibers or bundles. Short particles less than $5 \mu\text{m}$ in length do not appear to pose any lung cancer risk in this database. Thus in rats a particle length of $5 \mu\text{m}$ or less (or as Berman et al. suggest, $5\text{--}10 \mu\text{m}$ or less) appears to have zero potency.

The only other available data set for quantitatively assessing particle size is that of Stanton et al. (1981). The Berman et al. (1995) data set is considered more relevant because

1. It is based on an inhalation rather than implantation route of exposure;
2. It includes a range of representative samples of both asbestos fiber-types and particle sizes;

3. There is a more detailed characterization of long particles and complex structures than any other experimental study; and
4. The statistical analysis is more appropriate.

The analysis by Berman et al. (1995) is more appropriate as logarithms were not used, which avoided the problem of zero exposures in some size ranges and 0 tumors at some exposures. Also, an optimum exposure index was determined that provides a statistically adequate fit to the data. The models used by Stanton et al. (1981) do not fit the data well and therefore do not adequately describe the ranking of particle size potency.

In a statistical reanalysis of the Stanton et al. (1981) data, Oehlert (1991) confirmed the Stanton hypothesis that the primary ability of mineral particles to cause tumors are their dimensional properties, namely index particles that are long and thin ($>8\text{ }\mu\text{m}$ long and $<0.25\text{ }\mu\text{m}$ wide). Using improved models that fit the data better, Oehlert (1991) reinforced the idea that very long, very thin particles were the best predictors for tumors and that particles with dimensions outside the index class did not contribute to carcinogenicity. This is also in agreement with Berman et al. (1995) that non-index particles have essentially zero potency.

Oehlert (1991) disagreed with the Stanton hypothesis that dimensions alone determine carcinogenic potency. Model fit was significantly improved by assessing each mineral type separately, which indicates mineral type is also important. This disagreement was unfounded, as in fact, Stanton, himself noted that the solubility of the fiber was also important, a parameter that would be incorporated in any analysis by considering fiber type. Dimensions are necessary but are not alone sufficient to classify a substance as capable of inducing tumors. It is now well established that factors such as particle solubility and perhaps surface properties are also important. For example, fibrous talc from the Gouverneur talc deposit in New York is not equivalent (0% tumor probability) to grunerite (amosite) asbestos (93% tumor probability) in tumor producing potential although the dimensions are similar (Stanton et al., 1981).

In sum, the Oehlert (1991) reanalysis of the Stanton et al. (1981) data is consistent with Berman et al. (1995) that particles of certain dimensions are important predictors of tumor incidence. Long and thin particles are the significant dimensions. Also, the minerals comprising sufficient particles in these size ranges to produce tumors included asbestos (crocidolite, amosite, and tremolite asbestos) but not the non-asbestiform amphibole mineral (tremolitic talc).

Given the importance of width and length from these experimental data, it is useful to summarize available data on dimensions of amphiboles in the epidemiological studies summarized in previous sections (Table 8).

This analysis indicates the low amounts or absence of long, thin particles in the size ranges that predict lung

tumors or mesothelioma in the three ore bodies containing non-asbestiform amphiboles (NY talc, taconite and Homestake). A primary interest in studying these workers is the fact that they were exposed to non-asbestiform amphiboles. Steenland and Brown (1995) expressed the interest as follows: "Non-asbestiform amphibole fibers have not been shown to cause lung cancer, *but are suspect because of their similarity to asbestiform fibers* (emphasis added)". The data in Table 8 and noted above suggest that the similarity is applicable only to chemistry since there is no similarity in the occurrence of index particles. The long thin elongated particles (fibers) capable of inducing tumors are common in asbestiform amphiboles and absent in non-asbestiform amphiboles.

The absence of long thin particles in the size ranges identified by Stanton et al. (1981) and by Berman et al. (1995) as responsible for lung cancer and mesothelioma experimentally from ores containing non-asbestiform amphiboles detracts from the hypothesis that non-asbestiform particles have a carcinogenic potency similar to asbestos fibers. The other parameter which is now recognized as being important is biopersistence. As the cleavage fragments are in general shorter than the asbestos fibers they are likely to be more readily removed by macrophages than the asbestos. On the other hand, the solubility difference between cleavage fragments and fibers is not known, although Ilgren (2004) suggests greater solubility of cleavage fragments. However, it is possible that fibers, because they could split apart, would have greater surface areas and might be more soluble than cleavage fragments of the same dimensions. This would mean that they would have greater lung biopersistence than fibers. On this basis, long cleavage fragments would have the potential to pose a lung cancer/mesothelioma risk if cleavage fragments had the same biological potency as asbestos fibers of the same length.

In fact, this is not a real problem because the biopersistence of the amphibole fibers is known to be very high. Even if there were long cleavage fragments, their large diameters would reduce the risk compared to asbestos and their retention would be highly unlikely to render them more hazardous than the asbestos fibers. In this regard, it should be noted that the sample FD14 from the NY deposit did contain elongated particles that ranged up to $50\text{ }\mu\text{m}$ in length (Griegner and McCrone, 1972) and did not produce mesothelioma.

Conclusions about cleavage fragments from some of the other experiments are somewhat limited because, for example, the sample of Greenland non-asbestiform tremolite studied by Wagner et al. (1982) had no fibers greater than $10\text{ }\mu\text{m}$ in length and less than $0.25\text{ }\mu\text{m}$ in width. The sample FD 275-1 did not contain any particles longer than $10\text{ }\mu\text{m}$ in length and no particles with a width less than $1\text{ }\mu\text{m}$. Stanton (1973) showed that riebeckite (crocidolite) asbestos, pulverized to the state where 80% of the mass of fibres was in the size range less than $10\text{ }\mu\text{m}$ in length, produced a "negligible incidence" of mesotheliomas in pleural implantation studies.

While it is reassuring that none of the samples of non-asbestiform tremolite have produced elevated rates of mesothelioma in experimental animals, it is unfortunate that systematic studies have not been done to determine whether cleavage fragments of the same lengths as asbestos fibers produce the same risks as doses have generally been measured on a mass basis and not on the basis of number of fibers or cleavage fragments of particular lengths. An obvious problem with cleavage fragment studies is that in order to achieve similar numbers of long thin fibers to the tremolite asbestos in the dose, there would have had to be a very much larger mass of cleavage fragments injected, and that alone would have produced difficulties in animal survival. There do not appear to be cleavage fragment-related increases in lung cancer or mesothelioma risk in the studies. The lack of risk may be related to the fact that workers in those industries are not exposed to high concentrations of long cleavage fragments and the fact that because of their diameters such fragments would carry a much lower carcinogenic potency than their equivalent asbestiform mineral.

Our review of the experimental literature did not reveal any findings which would indicate that cleavage fragments have the same or greater carcinogenic potential than asbestos. In fact, they indicated that amphibole cleavage fragments have a much lower carcinogenic potential than their asbestiform counterparts by many orders of magnitude. In conclusion, there are still many unanswered questions relating to the extent to which the asbestiform habit of a mineral influences its biological behavior relative to that of a cleavage fragment (size for size). But the experimental data do provide strong support for the epidemiological findings that the risks of lung cancer and mesothelioma are considerably less [or absent] for persons exposed to amphibole cleavage fragments when compared to persons exposed to amphibole asbestos fibers.

21. Other amphiboles and other minerals

A search of the literature for studies containing both health outcomes and descriptions of exposure to cleavage fragments failed to identify additional studies that would be of immediate assistance in examining the health risks associated with cleavage fragments. The review did identify studies such as that in Finland where the percentages of asbestiform tremolite and cleavage fragments and fibrous wollastonite and cleavage fragments of wollastonite were characterised in metamorphic limestone and dolomite mines (Junttila et al., 1996). However, epidemiological studies to relate to the environmental studies do not appear to be available. The exposure to “Federal fibers” in quarrying industries and coal mines with their large workforces would be of interest. There were experimental studies and health evaluations of arfvedsonite asbestos in Russia (Kogan et al., 1970; Pylev and Iankova, 1975). There were well described studies of crocidolite-exposed populations,

but no health studies of workers exposed to non-asbestiform riebeckite have been identified.

There are potentially other populations of workers exposed to the hundreds of other minerals (e.g., erionite; fluoroedenite), which can occur with a fibrous morphology. There is some information on mesothelioma risks for some of these minerals, but no studies were found of populations exposed to the non-asbestiform fibers of these same minerals.

A chronic intraperitoneal injection study administered doses of asbestiform silicon carbide (SiC) whiskers and SiC cleavage fragments to rats. The purpose of the study was to compare potency by particle size. Cleavage fragments were defined as longer than 5 μm , narrower than 3 μm and aspect ratios greater than 3:1. Only 3.3% of cleavage fragments had aspect ratios greater than 10:1 compared to 96% for whiskers; lengths greater than 10 μm were 0% for cleavage fragments and 44% and 30% for low and high doses of asbestiform whiskers. Tumor rates for cleavage fragments were 0.8% and 0% for low and high doses respectively; 20% and 43% tumors rates were expected if cleavage fragments had the same potency as asbestiform whiskers (Rodelsperger and Bruckel, 2006). These data are consistent with the amphibole experimental data showing that cleavage fragments (or even federal fibers) “have a much lower carcinogenic potency than whiskers, if any at all.”

While the gaps in knowledge concerning the US studies need to be filled, a broader base of information would be helpful. In the absence of well defined occupational groups exposed to well-characterised cleavage fragments with well studied health outcomes, it may be useful to consider non-occupational settings. In some of these areas, there are definite concentrations of pleural calcification and definite areas of elevated rates of malignant mesothelioma. Perhaps mapping the geographical distribution of mesothelioma in various countries such as Southern Europe, New Caledonia and the Mediterranean region might identify clusters of cases which might be investigated for asbestiform amphibole exposure and non-asbestiform amphibole exposure in for example, case-comparison studies.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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Appendix A

There is some overlap between this appendix and the main text in order to maintain the historical development of knowledge concerning the NY talc deposit.

A.1. New York State talc

A.1.1. Early NY talc studies

Kleinfeld et al. (1967) conducted a PMR mortality study among 220 talc miners/millers with 15 or more years of exposure in 1940, with follow-up to 1965. There were 28 deaths (31%) attributed to pneumoconiosis and complications and a PMR of 3.44 for 9 deaths from lung cancer and 1 from fibrosarcoma of the pleura. Kleinfeld et al. (1967) also reported that in a small group of asbestos insulation workers with similar years of exposure, the asbestos workers had about twice the proportion of lung cancer deaths (24% vs 11%) and the significant excess was in both the 40–59 and 60–79 year age groups. This is “at variance” with the talc workers where the excess was only in the 60–79 year age group (PMR = 4.36) and a deficit (PMR = 0.96) in the 40–59 year age group. Overall, lung cancer mortality among the asbestos insulators was 2.5 times higher than among the talc workers, 8.43 versus 3.44.

Kleinfeld et al. (1974) added 4 more years of follow-up (to 1969), 40 more workers in the cohort (for a total of 260), 17 more total deaths (for a total of 108) and three more respiratory cancers (for a total of 13). Similar results to the 1967 study were obtained with the only significant excess of respiratory cancers in the 60–79 age range (PMR = 4.61) and not in the 40–59 year age group (PMR = 1.63). The authors thought it was noteworthy that the significant excess respiratory cancer mortality was in the years 1945–1959 (PMR = 3.37) and not in the years 1960–1969 (PMR = 1.35) when dust counts were appreciably reduced but fiber counts (fibers/mL >5 μ m) remained high. Ten of the 13 respiratory cancer deaths occurred in workers exposed 15–24 years (and about the same latency). The authors suggested a more susceptible group develops cancer between 15 and 24 years leaving a less susceptible group in spite of more years of exposure. The size of the cohort is too small to confirm this hypothesis. There was one case of peritoneal mesothelioma but no information regarding latency or other work exposures.

Exposure was characterized as predominantly talc admixed with silicates such as serpentine, tremolite, carbonates and a small amount of free silica. Exposures were quite high before 1945 when both pneumoconiosis and lung cancer cases began working. Wet drilling began after 1945, which reduced mine levels from 818 to 5 mppcf. Exposures were lower in the mill than the mine prior to

1945, but after 1945 were not reduced as much as in the mine and were now 5 times (or more) higher than in the mine. Workers with lung disease had initial exposures prior to 1945 before wet drilling began and when average dust counts in the mine were 818 (83–2800) mppcf for drilling and 120 (2–475) for mucking. In the mill, averages were 180, 69, 92 and 151 mppcf for crushing, screening, milling and bagging. After 1945 (1946–1965) average dust counts were reduced to about 5 mppcf in these jobs in the mine and in the mill averages were generally below 50 mppcf.

Kleinfeld et al. (1973) studied 39 workers exposed to commercial talc dust where tremolite and anthophyllite were the major fibrous components. They also examined 16 talc samples from different mining and milling operations as well as finished products from NY State. Analyses included polarized LM, TEM with selected area diffraction, X-ray diffraction and electron microprobe analysis. No data are provided on distribution by fiber sizes. The point is made that there was no correlation between fiber count (fibers >5 μ m) and mean dust counts (mppcf). Particles observed included “true talc, talc fibers, serpentine minerals and after fragments, and amphibole fibers and fragments”. Fiber counts “may not provide a true picture of exposure to asbestiform minerals because the fiber counts include talc fibers but exclude many small asbestos fibers and ‘aggregate fibers’ which may contain substantial amounts of asbestiform minerals”. The electron micrographs of amphibole fibers present in talc suggested amphibole cleavage fragments.

A.1.1.1. NY Tremolitic talc. Brown et al. (1980) reported the dimensions of fibers determined by electron microscopy. Only 3% of tremolite fibers and 8–10% of anthophyllite fibers were longer than 5 μ m; median lengths were about 1.5 μ m. Median aspect ratios of 7.5 and 9.5 were reported for *all* fiber lengths of tremolite and anthophyllite. Data were not provided on aspect ratios for fibers >5 μ m counted using phase contrast microscopy.

There then began a series of mortality studies of workers at the Gouveneur talc mine and mill in NY state (GTC) (Brown et al., 1979, 1980, Brown et al., 1990; Stille and Tabershaw, 1982; Lamm et al., 1988; Gamble, 1993; Honda et al., 2002; Oestenstad et al., 2002). The extensive literature on GTC talc centers on three major issues that started with the first NIOSH mortality and industrial hygiene study of GTC workers.

Is the reported excess SMR for lung cancer due to the alleged asbestiform amphiboles in the talc or due to confounding? Confounding factors could include other work exposure (primarily in the surrounding mines/mills), from life-style factors such as smoking or short-term employees.

Is the tremolite and anthophyllite content of the talc non-asbestiform cleavage fragments or is the talc contaminated with tremolite asbestos and anthophyllite asbestos?

Is there biological plausibility that the tremolitic talc acts like asbestos producing asbestos-like effects in animal studies?

A.2. Epidemiology of health effects of GTC talc

Brown et al. (1979, 1980) studied 398 white males first employed 1947–1959 with vital status determined as of 1975. There was a 2.73-fold excess risk of lung cancer. Risk increased with increasing latency with SMRs of 2.00 and 4.62 at 10–19 and 20–28 years latency, which was said to be “consistent with an occupational etiology”. There was no analysis by years worked although 4/9 cases had worked less than 1 year. Smoking was considered unlikely to account for all the increased risk by Brown et al. (1979, 1980). Exposures in surrounding mines and mills were higher but all were said to involve exposures to “asbestiform amphiboles”. Exposures to “asbestiform tremolite and anthophyllite stand out as the prime etiologic factors associated with the observed increase in bronchogenic cancer”.

Stille and Tabershaw (1982) studied 655 white males employed 1948–1977 with vital status determined at the end of 1978. Lung cancer was only significantly elevated among employees with any prior employment history. There was no analysis by years worked and latency was not taken into account.

Because of these conflicting findings, Lamm et al. (1988) reanalyzed these data. They studied 725 male talc workers who had ever worked at Vanderbilt since the plant opened in 1947 through the end of 1977 with follow-up through 1978. Previous employment obtained from job applications were classified as posing a prior risk, no prior risk or unclassifiable (no indication of prior work history) with regard to risk of lung cancer. Among those with more than 1-year employment the SMRs for lung cancer and non-infectious, non-neoplastic respiratory diseases were 1.93 and 3.70, respectively, compared to 3.00 and 0 for those with less than 1-year duration. Adding prior exposure history to the analysis showed that lung cancer risk appeared to be related to prior employment. The SMRs were similar for all job risk categories, although the number of cases was too small to be definitive. Mean latency was 20.8 years (12–25) and all those with less than 20 years latency since being hired at GTC had worked elsewhere. Five of the 12 cases had 3 months or less employment. The authors conclude the increased risk of lung cancer in this cohort of talc workers is concentrated in short-term workers, probably due to prior employment, smoking or other differences in behavioral characteristics.

At the request of RT Vanderbilt and Company, NIOSH conducted a health hazard evaluation (HHE) of the GTC cohort (Brown et al., 1990). Eight years of follow-up (through 1983) and an analysis by latency and tenure were added to the retrospective cohort study. Nearly a third (27%) of the cohort had died, with 161 total deaths and 17 lung cancer deaths with an overall SMR of 2.07. About 50% of the cohort had worked less than 1 year. Among the 13 lung cancer cases with 20 or more years latency, there was a 3.6-fold excess in the eight cases with less than a year tenure Vs. a nonsignificant SMR of 1.79 among the five

cases with >1-year tenure. There were also 17 NMRD deaths with an overall SMR of 2.50 (1.46–4.01). Six of the cases had worked for less than 1 year with an SMR of 1.94 (0.72–4.28). There was a 3-fold excess (SMR 2.89; 1.45–5.18) among those with more than 1-year tenure. This pattern for NMRD is “more consistently associated with an occupational exposure at GTC”. Principal limitations in this study were small size (especially those with long tenure), inability to precisely characterize past occupational exposures at GTC or elsewhere, and lack of reliable smoking history. The authors concluded it is unlikely these potential confounders alone could account for the observed excess risks.

Gamble (1993) conducted a case control nested in the Brown et al. (1990) cohort. Information was collected on smoking, time exposed to talc plus a risk ranking on non-talc exposure. There were 22 cases and 66 controls matched on date of birth and date of hire. There were zero non-smokers among the cases (91% smokers and 9% ex-smokers) compared to 27% non-smokers, 73% smokers or ex-smokers among controls. Inverse trends were consistently observed by years worked for different subsets of the study population; e.g., all cases and controls, smokers only, those with >20-years latency, total tremolitic talc years. The author concluded that “after adjustment for...smoking and the postulated role of very high exposures of short-term workers, the risk ratio for lung cancer decreases with increasing tenure”. The time occurrence of lung cancer was consistent with a smoking etiology, and was not consistent with an occupational relationship.

Finally, Honda et al. (2002) assessed cancer and non-cancer mortality among white male GTC talc workers. The cohort analyzed for cancer mortality consisted of 809 workers employed 1947–1989 and alive in 1950. The cohort analyzed for non-cancer mortality consisted of 782 men employed during 1960–1989. The important additions in this study were 6 more years of follow-up (through 1989) and internal exposure–response analyses with cumulative exposure to talc dust as the exposure variable. Overall mortality continued to remain elevated at 1.31 ((209/160) due largely to 2.32-fold excess from lung cancer (31/13) and 2.21-fold excess in NMRD (28/13). The patterns are consistent with previous results, in particular with the inverse lung cancer trends from the nested case–control study (Gamble, 1993) and the inverse relationships for NMRD and lung cancer reported by Lamm et al. (1988). Honda et al. (2002) reported that among workers with >20-years latency, there was a 3.3-fold excess lung cancer for <5-years tenure and 1. Ninefold excess for >5-years tenure. For other NMRD (COPD + pneumoconiosis and excluding pneumonia, influenza, asthma, emphysema and bronchitis) the SMRs were 2.71 and 3.02, respectively. The internal comparisons by cumulative exposure (mg/m³ years) and adjusted for age and latency, showed a significant monotonic decrease in lung cancer risk with increasing exposure with a RR of 0.5 (0.2–1.3) in the highest exposure category. Mortality from ‘other NMRD’ and

Table A1

Exposure differences between cases of lung cancer, Other NMRD and Fibrosis in NY talc workers (Honda et al., 2002)

	Lung cancer	Other NMRD	Fibrosis
Median years worked	1.0	8.3	11.8
Median cumulative exposure (mg/m ³ days)	347	1199	3759

pulmonary fibrosis showed monotonic increases in risk as exposure increase. Risks were increased 2- and 12-fold increased risks in the highest exposure categories (Fig. 3).

There were two cases of mesothelioma, but because of too short latency in one case and minimal exposure for a

short time, Honda et al. (2002) considered it unlikely that exposure to talc ore was the cause.

Because of too short latency, Honda et al. (2002) concluded that the cause of the increased lung cancer mortality in the cohort is unclear, but speculated that it could be due in part to smoking or "other unidentified risk factors". They suggest it is unlikely to be related to talc ore dust per se. Other NMRD (and in particular fibrosis) were considered causally related to talc ore dust, other dusts in other work environments and smoking. This conclusion is supported by the differences in years worked and median cumulative exposures among decedents with these three causes of death and the inverse E-R trend for lung cancer (Table A1).

Table A2

Summary of results for lung cancer and mesothelioma from studies of NY talc workers

Reference	Study characteristics	Lung cancer	Mesothelioma
Kleinfeld et al. (1967)	220 NY Talc Miners ≥ 15 years tenure in 1940; 1965 follow-up, 91 total deaths, PMR	PMR = 3.44 (1.65–6.3) (11 deaths)	1 peritoneal mesothelioma (1.1%)
Kleinfeld et al. (1974)	260 NY Talc Workers ≥ 15 years in 1940 or between 1940 and 1969; 108 total deaths, PMR, follow-up of Kleinfeld et al. (1967)	PMR resp cancer = 3.24 (1.72–5.54) (12 lung cancer, 1 fibrosarcoma of pleura)	1 peritoneal mesothelioma (0.93%)
Brown et al. (1979, 1980)	398 WM employed GTC 1947–1959, follow-up 1975; 18% <1 month, 24% 1–6 months, 50% <1 year; 44% <1950;	9/3.3 = 2.73 (1.25–5.18) ($p < 0.05$); 4 <1-year tenure	1/74 = 1.4% (16-year talc tenure, 11 years construction)
Stille and Tabershaw (1982)	655 WM employed GTC 1948–1978, vital status 1978;	10/6.4 = 1.57 (10 obs) Prior employment = 2.14 (8 obs) No prior work = 0.76 (2 obs)	
Lamm et al. (1988)	705 men employed GTC 1947–end 1977, vital status 1978	12/5 = 2.40 (1.24–4.19) >1 year 6/3.1 = 1.93 (0.71–4.20) prior risk = 3.08 (6/2) <1 year 6/1.9 = 3.16 (0.16–6.88) prior risk = 3.33 (3/0.9)	1 electrician 15-year latency; 20-years prior As miner, miller, construction
Brown et al. (1990)	710 WM employed at GTC 1947–1978 with vital status 1983; Not reported,	17/8.2 = 2.07 (1.20–3.31) <1-year = 3.64 (1.54–7.04) 1–9 years = 0.83 (0.02–4.57) 10–19 years = 4.0 (0.54–16.1) 20–36 years = 1.82 (0.21–6.36)	
Gamble (1993)	22 lung cancer cases at GTC 1947–1978 matched 3:1 on data of birth and date of hire.	OR lung cancer Tenure smokers >20-year latency <5 year 1.0 5–15 years 0.63 15–36 years 0.42 mg/m ³ days RR (n) <95 1.0 (11) <987 0.8 (9) 987 + 0.5 (9) Hired: <1955 SMR 2.86 (0.9–4.1) Hired > 1955 SMR: 0. (0.2–2.4)	
Honda et al. (2002)	809 WM talc workers employed GTC 1948–1989 follow-up Cancer: 1950–1989 Non-cancer mortality = 1960–1989		Two cases not considered causal due to short latency, Case 1 & Very low exposure, Case 2 (3.7%)

All but two of the studies (Kleinfeld et al., 1967, 1974) were the same cohort of GTC workers.

Pn, pneumoconiosis.

These results are not at all consistent with the dust causing fibrosis being responsible for the lung cancer excess.

A.3. Summary of results from studies of NY talc workers

The cohorts studied before 1979 by Kleinfeld and colleagues worked in talc mines in St. Lawrence County, NY. After 1978 the cohorts were comprised of workers at the Gouverneur mine and mill, some of whom had previous employment in other mines in St. Lawrence County, NY (Table A2).

The authors of the two NIOSH studies of GTC talc (Brown et al., 1979, 1980; Brown et al., 1990) concluded that the tremolite and anthophyllite were the most likely etiological agents. This conclusion is based on the following logic.

The excess risk of lung cancer and NMRD were consistent with the findings of Kleinfeld et al. (1967, 1973) among NY talc workers and Meurman et al. (1974, 1979) among anthophyllite asbestos miners. The etiological agents were considered to be "asbestiform tremolite and anthophyllite," which were said to be in both talc ores at concentrations well above standards. Smoking could not account for the excess lung cancer risk. Short-term workers may have had "very high exposures, especially in the early years of the mining operation," which might account for their excess risk (Brown et al., 1990). There was an increased risk of developing pleural changes (including pleural thickening and pleural calcification), and the prevalence is higher when there is exposure to anthophyllite (Dement et al., 1980).

The lack of an association with years worked could be due to a combination of factors above plus work in other talc operations and/or other work-related exposure to lung carcinogens.

Many of these arguments have been contradicted by further analyses.

Kleinfeld et al. (1967) compared lung cancer risk patterns of talc workers with (apparently) their own data for a similar group of asbestos insulation workers. The asbestos PMRs were 2–3 times higher among the asbestos workers for lung cancer and GI cancers. Kleinfeld et al. commented that a major difference was the increased risk of lung cancer in age groups of 40–59 and 60–79 among asbestos workers, but excesses for talc workers were among only the 60–79 age group. In addition, longevity of talc miners was longer than the national average. Age at death among the talc lung cancer cases was 3 years greater than the average of all deaths and 10 years greater than the U.S. average. The talc lung cancer cases occurred in persons exposed before wet drilling was introduced. Wet drilling reduced mean exposures 164-fold from an average of 818 mppcf to 5. Kleinfeld et al. (1967) suggested part of the reason for the earlier deaths of asbestos cases compared to talc cases "may be partly due to the greater carcinogenicity of asbestos dust or to an increased level of exposure to asbestos or both".

There was excess mortality among the NY talc workers, but considerably less than the risk of asbestos workers

exposed in the same time period. It is not possible to directly compare risks from the Kleinfeld et al. (1974) cohort with that of the GTC cohort. The Kleinfeld et al. cohort et al is older, had worked decades earlier than the GTC cohort, and consisted of workers with more than 15 years tenure. Vanderbilt workers included many short-term workers with 26 years as the maximum possible years worked and no analysis by years-worked (Brown et al., 1979, 1980). In addition, overall mortality was over twice as great in the Kleinfeld et al cohort, i.e., 42% vs. 19%. *When stratified by years worked in subsequent follow-ups there were two cases with >20 years tenure (SMR = 1.82) and five cases with >10-years tenure (SMR = 2.17) (Brown et al., 1990). Gamble (1993) reported risk ratios less than 1.0 for lung cancer cases with >15-years tenure and adjusted for smoking. These data are suggestive of a different mortality pattern of GTC talc workers compared to the Kleinfeld talc cohort.*

Smoking. Further updates of the GTC cohort revealed that all of the lung cancer cases were either smokers or former smokers, while only 73% of controls had ever smoked. Smoking latencies for GTC cases were consistent with latencies from studies of smokers. This is particularly true for short-term workers where the risk of lung cancer was highest and talc exposure too short to be plausible. Lung cancer risk among workers with more than 1-year exposure was increased about 2-fold compared to the US population. This degree of increased risk is in large part plausibly attributable to smoking (Gamble, 1993).

High exposure of short-term workers. Gamble (1993) matched on date of hire in the nested case control study of lung cancer. Thus, cases and controls had equivalent opportunities for very high exposures. Six of the lung cancer cases had less than 3-months tenure, several with only a few days, so there were very few opportunities for excessive cumulative exposure. Honda et al. (2002) showed that lung cancer cases had lower exposures than other subgroups. For example, median cumulative exposure of lung cancer decedents was 347 mg/m³ days, which was less than all decedents (520), ischaemic heart disease decedents (376), all NMRD decedents (888), other NMRD decedents, pulmonary fibrosis decedents (3759). Thus there is no evidence to support the speculation that excessively high exposure in short-term workers could explain their increased risk.

Pleural changes. Gamble et al. (1979a,b, 1982) showed that the prevalence of pleural changes in GTC talc workers was essentially the same among other workers exposed to talc containing no measurable quantities of amphiboles. Thus it would appear that the pleural thickening observed in NY talc workers and other talc workers is likely due to factors other than exposure to amphiboles.

Exposure–response (E–R). The inverse exposure–response trends with duration of exposure were present when adjustments were made for other talc exposures and potential exposure to other work-related carcinogens (Gamble, 1993). The inverse E–R trends for lung cancer and cumulative exposure are strong arguments against attributing increased risk

of lung cancer to talc exposure. This argument is further strengthened by the very strong exposure–response relationship between fibrosis and cumulative talc exposure as well as the higher exposure of NMRD and fibrosis cases compared to lung cancer cases (Honda et al., 2002).

References

- 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.
- Addison, J., McConnell, E.E., 2008. A review of carcinogenicity studies of asbestos and non-asbestos tremolite and other amphiboles. *Regul. Toxicol. Pharm.* 52, S187–S199.
- Addison, J., 2004. Personal communication 6, 2004.
- Allison, A.C., 1973. Experimental methods of cell and tissue culture: effects of asbestos particles on macrophages, mesothelial cells and fibroblasts. In: Bogovski, P., Gilson, J.C., Timbrell, V., & Wagner, J.C. (Eds.), *Biological Effects of Asbestos*. Proceedings of a Working Conference. Lyons, 2–6 October, 1972. Lyons, International Agency for Research on Cancer, pp. 89–93.
- Amandus, H.E., Wheeler, R., Jankovic, J., Tucker, J., 1987a. The morbidity and mortality of Vermiculite Miners and Millers exposed to tremolite–actinolite: Part I. Exposure estimates. *Am. J. Ind. Med.* 11, 1–14.
- Amandus, H.E., Wheeler, R., 1987b. The morbidity and mortality of vermiculite miners and millers exposed to asbestiform tremolite–actinolite. Part II. Mortality. *Am. J. Ind. Med.* 11, 15–26.
- Amandus, H.E., Althouse, R., Morgan, W.K.C., Sargent, E.N., Jones, R., 1987c. The morbidity and mortality of vermiculite miners and millers exposed to asbestiform tremolite–actinolite. Part III. Radiographic findings. *Am. J. Ind. Med.* 11, 27–37.
- Atkinson, G.R., Rose, D., Thomas, K., Jones, D., Chatfield, E.J., Goig, J.E., 1982. Collection, analysis and characterization of vermiculite samples for fiber content and asbestos contamination. MRI report for the Environmental Protection Agency, Project 4901-A32 under EPA contract 68-01-5915.
- Berman, D.W., Crump, K.S., Chatfield, E.F., Davis, J.M.G., Jones, A.D., 1995. The sizes, shapes, and mineralogy of asbestos structures that induce lung tumors or mesothelioma in AF rats following inhalation. *Risk Anal.* 15, 181–195.
- Bernstein, D.M., Mast, R., Anderson, R., Hesterberg, T.W., Musselman, R., Kamstrup, O., Hadley, J., 1994. An experimental approach to the evaluation of the biopersistence of respirable synthetic fibers and minerals. *Environ. Health Persp.* 102 (5), 15–18.
- Berry, G., 1999. Models for mesothelioma incidence following exposure to fibers in terms of timing and duration of exposure and the biopersistence of the fibers. *Inhal. Toxicol.* 11, 111–130.
- Boundy, M.G., Gold, K., Martin Jr., K.P., Burgess, W.A., Dement, J.M., 1979. Occupational exposures to non-asbestiform talc in Vermont. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publisher, Inc, Park Forest South, Illinois, pp. 365–378.
- Brown, D.P., Sanderson, W., Fine, L.J., 1990. Health hazard evaluation Report HETA No. 90-390-2065 and MHETA 86-012-2065. RT Vanderbilt Company, Gouveneur, NY.
- Dement, J.M., Zumwalde, R.D., Gamble, J.F., Fellner, W., DeMeo, M.J., Brown, D.P., Wagoner, J.P., 1980. Occupational exposure to talc containing asbestos, morbidity, mortality, and environmental studies of miners and millers i. environmental study, II. Cross Sectional Morbidity Study, III. Retrospective Cohort Study of Mortality, NIOSH Technical Report, DHEW (NIOSH) Publication No. 80-115.
- Brown, D.P., Dement, J.M., Wagoner, J.K., 1979. Mortality patterns among miners and millers occupationally exposed to asbestiform talc. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publisher, Park Forest South, Illinois, pp. 317–324.
- 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. 335–349.
- Campbell, W.J., Steel, E.B., Virta, R.L., Eisner, M.H., 1979. Characterization of cleavage fragments and asbestiform amphibole particulates. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publishers, Park Forest South, Illinois, pp. 276–285.
- Clark, T.C., Harrington, V.A., Asta, J., Morgan, W.K.C., Sargent, E.N., 1980. Respiratory effects of exposure to dust in taconite mining and processing. *Am. Rev. Respir. Dis.* 121, 959–966.
- Coffin, D.L., Palekar, L.D., Cook, P.M., 1982. Tumorigenesis by a ferroactinolite mineral. *Toxicol. Lett.* 13, 143–149.
- Coggiola, M., Bosio, D., Pira, E., Piolatto, P.G., Vecchia, C.L., Negri, E., Michelazzi, M., Bacaloni, A., 2003. An update of a mortality study of talc miners and millers in Italy. *Am. J. Ind. Med.* 44, 63–69.
- Cook, P.M., Glass, G.E., Tucker, J.H., 1974. Asbestiform amphibole minerals: detection and measurement of high concentrations in municipal water supplies. *Science* 185, 853–855.
- 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.
- Crane, D.T., 1986. Memorandum from OSHA Salt Lake City Analytical Laboratory—Microscopy Branch to Greg Piacitelli, NIOSH, Morgantown, West Virginia (November 26, 1986).
- Davis, J.M.G., Addison, J., McIntosh, C., Miller, M., Niven, K., 1991. Variations in the carcinogenicity of tremolite dust samples of differing morphology. *Ann. N. Y. Acad. Sci.* 643, 473–490.
- Davis, J.M.G., Addison, J., Bolton, R.E., Donaldson, K., Jones, A.D., Miller, B.G., 1985. Inhalation studies on the effects of tremolite and brucite dust in rats. *Carcinogenesis* 6, 667–674.
- Dement, J.M., Zumwalde, R.D., Wallingford, K.M., 1976. Discussion paper: asbestos fiber exposures in a Hard Rock Gold Mine. *Ann. N. Y. Acad. Sci.* 271, 345–352.
- Dement, J.M., Zumwalde, R.D., Gamble, J.F., Fellner, W.F., DeMeo, M.J., Brown, D.P., Wagoner, J.K., 1980. Occupational exposure to talc containing asbestos I. Environmental Study, DHEW (NIOSH) Publication No. 80-115, US DHEW/PHS/CDC/NIOSH, February, 1980.
- Dunn Geoscience Corp., 1985. An evaluation of mineral particles at Gouverneur Talc Company 1975 and 1982: a comparison of mineralogical results between NIOSHS and DGC, Contract analysis and report to the R.T. Vanderbilt Company, Inc (January 4, 1985).
- Enterline, P.E., Henderson, V.L., 1987. Geographic patterns for pleural mesothelioma deaths in the United States, 1968–81. *J. Natl. Cancer Inst.* 79, 31–37.
- Fitzgerald, E.F., Stark, A.C., Vianna, N., Hwang, S.A., 1991. Exposure to asbestiform minerals and radiographic chest abnormalities in a talc mining region of upstate New York. *Arch. Environ. Health* 46, 151–154.
- Gamble, J.F., 1993. A nested case control study of lung cancer among New York talc workers. *Int. Arch. Occup. Environ. Health* 64, 449–456.
- Gamble, J.F., Greife, A., Hancock, J., 1982. An epidemiologic-industrial hygiene study of talc workers. *Ann. Occup. Hyg.* 26, 841–859.
- Gamble, J.F., Fellner, W., DeMeo, M.J., 1979a. An epidemiologic study of a group of talc workers. *Am. Rev. Respir. Dis.* 119, 741–753.
- Gamble, J., Fellner, W., DiMeo, M.J., 1979b. Respiratory morbidity among miners and millers of asbestiform talc. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publisher, Park Forest South, Illinois, pp. 307–316.
- Gibbs, A.R., Gardner, M.J., Pooley, F.D., Griffiths, D.M., Blight, B., Wagner, J.C., 1994. Fiber levels and disease in workers from a factory predominantly using Amosite, *Environ. Health Perspect.* 102 (5), 261–263.
- Gibbs, G.W., Hwang, C.Y., 1980. Dimensions of Airborne Asbestos Fibers, In: Wagner, J.C. (Ed.), *Biological effects of mineral fibres*.

- Proceedings of a Symposium held at Lyons, 25–27 September, 1979. Lyons, International Agency for Research on Cancer, IARC Scientific Publications No. 30, vol. 1, pp. 69–78.
- Gilliam, J.D., Dement, J.M., Lemen, R.A., Wagoner, J.K., Archer, V.E., Blejer, H.P., 1976. Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. *Ann. N. Y. Acad. Sci.* 271, 336–344.
- Griegner, G., McCrone, W.C., 1972. McCrone associates analysis of tremolitic talc FD-14 5.
- Harvey, A.M., 1979. Tremolite I Talc-a Clarification in Industrial Minerals. Metal Bulletin Limited, Worchester Park Survey, England, pp. 23–59.
- 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.
- Hill, A.B., 1965. The environment and disease: association or causation? *Proc. Roy. Soc. Med.* 58, 295–300.
- 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.
- Honda, Y., Beall, C., Delzell, E., Oestenstad, K., Brill, I., Matthews, R., 2002. Mortality among workers at a talc mining and milling facility. *Ann. Occup. Hyg.* 46 (1), 575–585.
- Hull, M.J., Abraham, J.L., Case, B.W., 2002. Mesothelioma among workers in asbestiform fiber-bearing talc mines in New York State. *Ann. Occup. Hyg.* 46 (1), 132–135.
- Ilgren, E.B., 2004. The biology of cleavage fragments: a brief synthesis and analysis of current knowledge. *Indoor Built Environ.* 13, 343–356.
- Junttila, S., Tossavainen, A., Hartikainen, T., Harma, P., Korhonen, K., Suominen, V., Pyy, L., 1996. Airborne mineral fibers and quartz dust in Precambrian metamorphic limestone and dolomite mines in Finland. *Appl. Occup. Environ. Hyg.* 11, 1075–1080.
- Karjalainen, A., Meurman, L.O., Pukkala, E., 1994. Four cases of mesothelioma among Finnish anthophyllite miners. *Occup. Environ. Med.* 51, 212–215.
- Kelse, J.W., Thompson, C.S., 1989. The regulatory and mineralogical definitions of asbestos and their impact on amphibole dust analysis. *Am. Ind. Hyg. Assoc. J.* 50, 613–622.
- Kleinfeld, M., Messite, J., Langer, A.M., 1973. A study of workers exposed to asbestiform minerals in commercial talc manufacture. *Environ. Res.* 6, 132–143.
- Kleinfeld, M., Messite, J., Zaki, M.H., 1974. Mortality experiences among talc workers: a follow-up study. *J. Occup. Med.* 16, 345–349.
- Kleinfeld, M., Messite, J., Kooyman, O., Zaki, M., 1967. Mortality among talc miners and millers in New York State. *Arch. Environ. Hlth.* 14, 663–667.
- Kogan, F.M., Valagov, A.G., Bunimovich, G.I., 1970. Health evaluation of the production of magnesia-arfvedsonite. *Gig. Tr. Prof. Zabol.* 14 (10), 45–47 (in Russian).
- Lamm, S.H., Levine, M.S., Starr, J.A., Tirey, S.L., 1988. Analysis of excess lung cancer risk in short-term employees. *Am. J. Epidemiol.* 127, 1202–1209.
- Langer, A.M., Maggiore, C.M., Nicholson, W.J., Rohl, A.N., Rubin, I.B., Selikoff, I.J., 1979. The contamination of Lake Superior with amphibole gangue minerals. *Ann. N. Y. Acad. Sci.* 330, 549–572.
- Langer, A.M., Nolan, R.P., 1989. Mineralogical characterization of Vanderbilt Talc Specimens. Contract analysis and report to the RT Vanderbilt Company, Inc.
- Langer, A.M., Nolan, R.P., Addison, J., 1991. Distinguishing between amphibole asbestos fibers and elongate cleavage fragments of their non-asbestos analogues. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fibre Carcinogenesis*. Plenum Press, NY in Cooperation with NATO Scientific Affairs Division, pp. 253–267.
- Langer, A.M., Mackler, A.D., Pooley, F.D., 1974. Electron microscopical investigation of asbestos fibers. *Environ. Health Perspect.* 9, 63–80.
- Lanphear, B.P., Buncher, C.R., 1992. Latent period for malignant mesothelioma of occupational origin. *J. Occup. Med.* 34, 718–721.
- Lawler, A.B., Mandel, J.S., Schuman, L.M., Lubin, J.H., 1985. A retrospective cohort mortality study of iron ore (hematite) miners in Minnesota. *J. Occup. Med.* 27, 507–517.
- Lee, R.J., 1990. Letter to National Stone Association on results of width distributions of Addison and Davis tremolite samples, April 16, 1990.
- Levin, J.L., McLarty, J.W., Hurst, G.A., Smith, A.N., Frank, A.L., 1998. Tyler asbestos workers: mortality experience in a cohort exposed to amosite. *Occup. Environ. Med.* 55, 155–160.
- Levy, R.S., Sigurdson, E., Mandel, J., Laudon, E., Pearson, J., 1976. Investigating possible effects of asbestos in city water: surveillance of gastrointestinal cancer incidence in Duluth, Minnesota. *Am. J. Epidemiol.* 103, 362–368.
- Liddell, F.D.K., McDonald, A.D., McDonald, J.C., 1997. The 1891–1920 birth cohort of Québec chrysotile miners and millers: development from 1904 and mortality to 1992. *Ann. Occup. Hyg.* 41, 13–36.
- Masson, T.J., McKay, F.W., Miller, R.W., 1974. Asbestos-like fibers in the Duluth water supply: relation to mortality. *JAMA* 228, 1019–1020.
- McConnell, E., Rutter, H.A., Ulland, B.M., Moore, J.A., 1983. Chronic effects of dietary exposure to amosite asbestos and tremolite in F344 rats. *Environ. Health Perspect.* 53, 27–44.
- McDonald, J.C., Harris, J., Armstrong, B., 2004. Mortality in a cohort of vermiculite miners exposed to fibrous amphiboles in Libby, Montana. *Occup. Environ. Med.* 61, 363–366.
- McDonald, J.C., Harris, J., Armstrong, B., 2002. Cohort mortality study of Vermiculite miners exposed to fibrous tremolite: an update. *Ann. Occup. Hyg.* 46 (1), 93–94.
- McDonald, J.C., McDonald, A.D., Sebastien, P., Moy, K., 1988. Health of vermiculite miners exposed to trace amounts of fibrous tremolite. *Br. J. Ind. Med.* 45, 630–634.
- McDonald, J.C., McDonald, A.D., Armstrong, B., Sebastien, P., 1986a. Cohort study of mortality of vermiculite miners exposed to tremolite. *Br. J. Ind. Med.* 43, 434–444.
- McDonald, J.C., Sebastien, P., Armstrong, B., 1986b. Radiological survey of past and present vermiculite miners exposed to tremolite. *Br. J. Ind. Med.* 43, 445–449.
- McDonald, G.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.
- Meurman, L.O., Pukkala, E., Hakama, M., 1994. Incidence of cancer among anthophyllite asbestos miners in Finland. *Occup. Environ. Med.* 51, 421–425.
- Meurman, L.O., Kiviluoto, R., Kakama, M., 1974. Mortality and morbidity among the working population of anthophyllite asbestos mines in Finland. *Br. J. Ind. Med.* 31, 105–112.
- Meurman, L.O., Kiviluoto, R., Hakama, M., 1979. Combined effect of asbestos exposure and tobacco smoking on Finnish anthophyllite miners and millers. *Ann. N. Y. Acad. Sci.* 330, 491–495.
- Nolan, R.P., Langer, A.M., Oechsle, G.W., Addison, J., 1991. Association of tremolite habit with biological potential: preliminary report in mechanisms. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Fibre Carcinogenesis*. Plenum Press, NY in Cooperation with NATO Scientific Affairs Division, pp. 231–251.
- Nolan, R.P., Langer, A.M., Wilson, R., 1999. A risk assessment for exposure to grunerite asbestos (amosite) in an iron ore mine. *Proc. Natl. Acad. Sci. USA* 96, 3412–3419.
- Oehlert, G.W., 1991. A reanalysis of the Stanton et al. pleural sarcoma data. *Environ. Res.* 54, 194–205.
- Oestenstad, K., Honda, Y., Delzell, E., Brill, I., 2002. Assessment of historical exposures to talc at a mining and milling facility. *Ann. Occup. Hyg.* 46, 587–596.
- Pelnar, P.V., 1988. Further evidence of nonasbestos-related mesothelioma: a review of the literature. *Scand. J. Work Environ. Health* 14, 141–144.
- Pictorial Atlas of Mineral Fibers, in press. The importance of using mineral growth habits to distinguish between the potency of asbestiform and non-asbestiform fibers in the etiology of asbestos-related cancer. *Regul. Toxicol. Pharm.*

- Price, B., Ware, A., 2004. Mesothelioma trends in the United States: an update based on SEER data for 1973 through 2003. *Am. J. Epidemiol.* 159, 107–112.
- Pylev, L.N., Iankova, G.D., 1975. Carcinogenic activity of magnesiarfvedsonite (group of amphibole asbestos minerals) administered intrapleurally to nonbred rats. *Vopr. Onkol.* 21 (1), 71–76, In Russian.
- Rodelsperger, K., Bruckel, B., 2006. The carcinogenicity of WHO fibers of silicon carbide: SiC whiskers compared to cleavage fragments of granular SiC. *Inhal. Toxicol.* 18, 623–631.
- Roggli, V.L., 1990. Human disease consequences of fiber exposures: a review of human lung pathology and fiber burden data. *Environ. Health. Perspective* 88, 295–303.
- Ross, M., 1978. The 'asbestos' minerals: definitions, description, modes of formation, physical and chemical properties, and health risk to the mining community. National Bureau of Standards Special Publication 506. Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods held at NBS, Gaithersburg, MD, July 18–20, 1977, pp. 49–63.
- Rubino, G.F., Scansetti, G., Piolatto, G., Romano, C.A., 1976. Mortality study of talc miners and millers. *J. Occup. Med.* 18, 187–193.
- Rubino, G.F., Scansetti, G., Piolatto, G., Gay, G., 1979. Mortality and morbidity among talc miners and millers in Italy. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publisher, Park Forest South, Illinois, pp. 357–363.
- Schiller, J.E., Payne, S.L., Khalafalla, S.E., 1980. Surface charge heterogeneity in amphibole cleavage fragments and asbestos fibers. *Science* 209, 1530–1532.
- Seidman, H., Selikoff, I.J., Hammond, E.C., 1979. Short-term asbestos work 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.
- Selevan, S.G., Dement, J.M., Wagoner, J.K., Froines, J.R., 1979. Mortality patterns among miners and millers of non-asbestiform talc: preliminary Report. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publisher, Park Forest South, IL, pp. 379–388.
- Siegrist, H.G., Wylie, A.G., 1980. Characterizing and discriminating the shape of asbestos particles. *Environ. Res.* 23, 348–361.
- Sigurdson, E.E., Levy, B.S., Mandel, J., McHugh, R., Michienzi, L.J., Jagger, H., Pearson, J., 1981. Cancer morbidity investigations: lessons from the Duluth study of possible effects of asbestos in drinking water. *Environ. Res.* 25, 50–61.
- Skinner, H.C., Ross, M., Fondel, 1988. Asbestos and other fibrous materials. Oxford University Press, Oxford, pp. 1–204.
- 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.
- Smith, W.E., Hubert, D.D., Sobel, H.J., Marquet, E., 1979. Biologic tests of tremolite in hamsters. In: Lemen, R., Dement, J.M. (Eds.), *Dusts and Disease*. Pathotox Publisher, Park Forest South, IL, pp. 335–339.
- Stanton, M.F., 1973. Some etiological considerations in fibre carcinogenesis. In: *Biological Effects of Asbestos*. In: Bogovski, P., Gilson, J.C., Timbrell, V., Wagner, J.C. (Eds.), IARC Sci. Publication No. 8, IARC, Lyon, France, pp. 289–294.
- Stanton, M.F., Layard, M., Tegeris, A., Miller, E., May, M., Morgan, E., Smith, A., 1981. Relation of particle dimension to carcinogenicity in amphibole asbestos and other fibrous minerals. *J. Natl. Cancer Inst.* 67, 965–976.
- Steenland, K., Brown, D., 1995. Mortality study of gold miners exposed to silica and nonasbestiform amphibole minerals: an update with 14 more years of follow-up. *Am. J. Ind. Med.* 27, 217–229.
- Stille, W.T., Tabershaw, I.R., 1982. The mortality experience of upstate New York talc workers. *J. Occup. Med.* 24, 480–484.
- Thompson, C.S., 1984. Consequences of using improper definitions for regulated mineral. In: *Definitions for Asbestos and Other Health-Related Silicates (STP-834)*. ASTM, Philadelphia, PA, p. 182.
- Timbrell, V., 1982. Deposition and retention of fibres in the human lung. *Ann. Occup. Hyg.* 26, 347–369.
- Vianna, N.J., Maslowsky, J., Roberts, S., Spellman, G., Patton, R.B., 1981. Malignant mesothelioma; epidemiologic patterns in New York State. *N. Y. State J. Med.* 81, 735–738.
- Virta, R.L., 1985. The phase relationship of talc and amphiboles in a fibrous talc sample, U.S. Department of the Interior, Bureau of Mines Report of Investigations No. 8923.
- Virta, R.L., Shedd, K.B., Wylie, A.G., Snyder, J.G., 1983. Size and shape characteristics of amphibole asbestos (amosite) and amphibole cleavage fragments (actinolite, cummingtonite) collected on occupational air monitoring filters, Chapter 47. In: Marple, V.A., Liu, B.Y.H. (Eds.), *Aerosols in the Mining and Industrial Work Environments, Volume 2 Characterisation*, Ann Arbor Science Publishers, Ann Arbor, Michigan, pp. 633–643.
- Wagner, J.C., Chamberlain, M., Brown, R.C., Berry, G., Pooley, F.D., Davies, R., Griffiths, D.M., 1982. Biological effects of tremolite. *Br. J. Cancer* 45, 352–360.
- Wagner, J.C., Berry, G., 1969. Mesotheliomas in rats following inoculation with asbestos. *Br. J. Cancer* 23, 567–581.
- Wergeland, E., Andersen, A., Baerheim, A., 1990. Morbidity and mortality in talc-exposed workers. *Am. J. Ind. Med.* 17, 505–513.
- Wild, P., Leodolter, K., Refregier, M., Schnidt, H., Zidek, T., Haidinger, G., 2002. A cohort mortality study and nested case–control study of French and Austrian talc workers. *Occup. Environ. Med.* 59, 98–105.
- Wilson, R., McConnell, E.E., Ross, M., Axten, C.W., Nolan, R.P., 2008. Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. *Regul. Toxicol. Pharm.* 52, S232–S245.
- Wylie, A.G., Virta, R.L., Segretti, J.M., 1987. Characterization of mineral population by index particle: implication for the Stanton Hypothesis. *Environ. Res.* 43, 427–439.
- Wylie, A.G., Skinner, H., Marsh, J., Snyder, H., Garzzone, C., Hodgkinson, D., Winters, R., Mossman, B., 1997. Mineralogical features associated with cytotoxic and proliferative effects of fibrous talc and asbestos on rodent tracheal epithelial and pleural mesothelial cells. *Toxicol. Appl. Pharmacol.* 147, 143–150.
- Wylie, A.G., 1988. Relationship between the growth habit of asbestos and the dimensions of asbestos fibers. *Mining Eng.* 40, 1036–1040.
- Wylie, A.G., Bailey, K.F., Kelse, J.W., Lee, R.J., 1993. The importance of width in asbestos fiber carcinogenicity and its implications for public policy. *Am. Ind. Hyg. Assoc. J.* 54, 239–252.

A review of carcinogenicity studies of asbestos and non-asbestos tremolite and other amphiboles

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Abstract

Experimental animal studies comparing asbestos and non-asbestos varieties of tremolite indicate tremolite asbestos is markedly more carcinogenic. By direct analogy, the differences in carcinogenicity between tremolite asbestos and non-asbestos prismatic tremolite should be the same for the other types of amphibole that also crystallize in the asbestos and non-asbestos habits. The earliest of the experiment animal studies, done more than 25 years ago, have design limitations by modern standards including the use of injection or surgical implantation as the route of administration rather than the more relevant route of inhalation. However, the differences in the carcinogenicity of amphibole asbestos and non-asbestos amphiboles are sufficiently large to be clearly discernable even with the study limitations. Together with later studies on these and related minerals, there is strong evidence of a much lower hazard associated with the shorter, thicker fibers of the non-asbestos amphiboles, than is found for the asbestos analogues of the same mineral. It is possible that the non-asbestos amphiboles are no more hazardous than other silicate minerals widely considered nuisance dusts.

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1. Introduction

We will define some basic asbestos terminology to clarify the terms used. The glossary in 'The Health Effects of Mineral Dusts' produced by The Mineralogical Society of America (Guthrie and Mossman, 1993) has the following definition: "Asbestos is a term applied to asbestiform varieties of serpentine and amphibole, particularly chrysotile, 'crocidolite', 'amosite', asbestiform tremolite, asbestiform actinolite, and asbestiform anthophyllite. The asbestos minerals possess asbestiform characteristics". The Mineral Society's glossary goes on to define asbestiform as: 'an adjective describing inorganic materials that possess the form and appearance of asbestos. When applied to a mineral, the term 'fibrous' is applied when it 'gives the appearance of being composed of fibers, whether the mineral

actually contains separable fibers or not' (Veblen and Wylie, 1993). Asbestiform is a subset of fibrous, where asbestiform implies relatively small fiber thickness and large fiber length, flexibility, easy separability and a parallel arrangement of the fibers in native (unprocessed) samples. Often, asbestos fibers occur in bundles, i.e. they are often polyfilamentous. From the definition it is clear that not all fibers or fibrous minerals are asbestiform and not all fibrous minerals called asbestiform are asbestos.

A convention has developed that a fiber is any particle with an aspect ratio equal to or greater than 3:1. This stems from the fiber definition in the early UK and US fiber counting methods (Asbestosis Research Council, 1969; Asbestos Textile Institute, 1971; Langer et al., 1991), it could just as easily have been 5:1 or 10:1. In using these methods, the microscopist had to make a decision to count or not count a particle depending on whether the shape and size met certain size criteria. The decision was more easily and consistently made for particles with aspect ratios just

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higher or lower than 3:1, and much more difficult with the higher aspect ratio thresholds. Similarly, a minimum fiber length of 5 μm was arbitrarily introduced for a fiber to be counted by these methods.

The inclusion of the abundant short fibers (less than 5 μm length) in the count would have made it much less consistent or reliable. Since the aim of the fiber counting rules was to differentiate between asbestos and total particles the aspect ratio and length cut-off chosen were those that produced consistency and not the ratio or length that might have had greater toxicological significance. By convention then, for a fiber to be counted it has to have an aspect ratio equal to or greater than 3:1 and a length equal to or greater than 5 μm (and in some rules a diameter less than 3 μm , e.g. WHO, 1985). This counting strategy has nothing to do with a definition of asbestos per se; it is simply helpful to microscopists doing fiber counting method. Since fiber counting analysis is performed using a phase-contrast light microscope at a magnification of 400–450 $\times$, the minimum width that can be counted is 0.2–0.25 μm .

Many non-asbestos particles, including non-asbestos amphiboles and other minerals can have aspect ratio greater than 3:1, but that does not make them 'asbestos' even though they are technically fibers. However, it does mean that they would be counted *as if they were an asbestos fiber* when seen in the course of a count of fibers in a membrane filter sample of airborne dust. In addition, asbestos will produce asbestos dust particles that mostly have aspect ratios equal to or greater than 3:1, but it will also produce particles that have lower aspect ratio. That does not mean that these low aspect ratio particles are not asbestos, but simply that they would not be counted as asbestos in the membrane filter method. The same is true for asbestos fibers with lengths shorter than the 5 μm minimum specified in the fiber counting method.

The adoption by some scientists and regulatory agencies of the fiber counting protocol using a 3:1 aspect ratio and a length of 5 μm or greater as being in some way a definition of asbestos has no scientific basis. It has been useful an improved metric when compared to just counting particles for assessing workplace exposure to airborne fiber dust leading to better epidemiological correlations between asbestos exposures with disease.

2. Mineralogy

Tremolite is one member of the calcic amphibole group of minerals that all possess similar crystal structures, basic chemical formula, although the various crystal forms have profoundly different physical properties. The group is characterized by a crystal structure described as a double chain of silicon oxide tetrahedra that is common to all members of the group. Within this chain structure are between 7 and 8 metal cations allowing wide range in elemental composition that still maintains the basic crystalline form (Deer et al., 1997). This has produced the large number of named variants or species within the amphibole group (Leake

et al., 1997, 2004). Actinolite and ferro-actinolite are part of a solid solution series with tremolite and differ only in the amount of substitution of magnesium by iron.

All of the amphibole minerals, and particularly tremolite, are very resistant to chemical attack by strong acids and bases (Addison and Davies, 1990) so that their biopersistence when inhaled would be expected to be very high. In addition to the chemical variability there is further variability in what is known as the crystal habit of the minerals that may arise independent of chemistry (Dorling and Zussman, 1987). The habit of a mineral is a description of the way that the crystals are commonly formed, and might otherwise be described as morphology.

The most common crystal habit for any amphibole is that called prismatic; elongate prisms with a lozenge

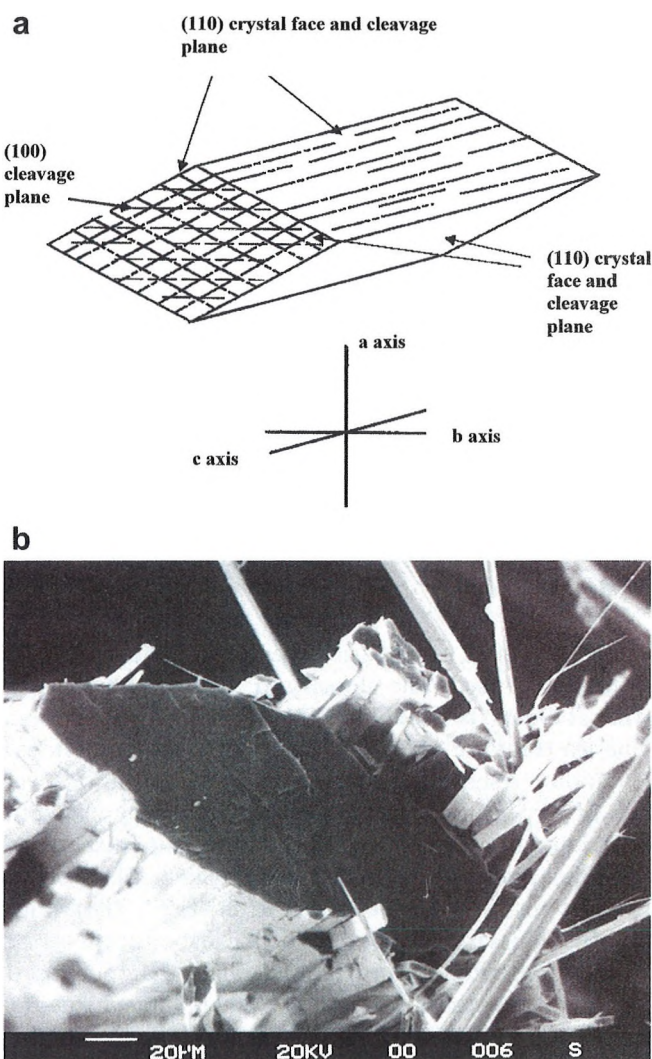


Fig. 1. (a) Typical prismatic crystal form of amphibole showing the main cleavages and prism faces. (b) Scanning Electron Microscope photomicrograph of Ala di Stura tremolite showing a large prismatic crystal with cross-section with a cross-section shape determined by (110) crystal faces; also evident are the traces of the (100) cleavage planes. Thin asbestiform tremolite fibers with diameters finer than 1 μm are also visible on the right-hand side of the image.

shaped cross-section that grade one way into short stocky prisms and in the other way into fine needle-like crystals or ultimately fine hair-like crystals (sometimes known as byssolite). The prismatic habit is the normal form for amphiboles in igneous and metamorphic rocks and is very widespread throughout the continental crust of the planet. Some amphiboles are also found in the habit that is termed asbestiform; this means that they have crystallized as bundles or matted masses of extremely fine fibers. The appearance of these forms usually implies some sort of secondary modification such as shearing and faulting or hydrothermal alteration. These may be found in three types of geological situations: (1) cross-fiber veins where the fibers have filled planar fissures, such as in the riebeckite (crocidolite) asbestos and grunerite (amosite) asbestos mines of South Africa; (2) in shear planes where slip fiber has formed in the plane of movement of a fault or shear plane; or (3) as disseminated fiber formed by hydrothermal alteration, such as in Libby, Montana (Meeker et al., 2003).

The differences in the manner of the formation of asbestos amphiboles, compared to the prismatic and other forms, have led to subtle differences in the details of the crystal structure that, while not sufficient to warrant a different mineral name, nevertheless lead to profound differences in physical properties (Langer et al., 1991). The commercial exploitation of the asbestos amphiboles depended upon these properties, including their capacity to be readily split into long, thin fibers with high tensile strength. These physical differences also lead to differences in the size distributions of dusts formed when the minerals are crushed, and arguably properties which impact the pathogenic potential of the material, especially their carcinogenic properties when these dusts are inhaled. Cleavage planes are planes of relative weakness along which certain minerals tend to fracture and are determined by the crystal lattice geometry. Mica, for example, is described as having a single perfect cleavage because it splits easily along the silicate sheet structure. Calcite has three perfect cleavages that form perfect rhombohedra when the mineral is crushed. Amphiboles have two sets of cleavage planes at 126° to each other and parallel to the long axis of the crystals (and parallel to the dominant prismatic crystal faces). In addition they also have a cleavage plane on (100).

These are not perfect cleavages; they are not persistent across or along the crystals and tend to be more widely spaced than the separations between the fibers of the asbestos amphiboles. The prismatic amphiboles, including byssolites, have relatively low tensile strength and the thin needle-like crystals fracture easily across the length. They also fracture along cleavage planes that are parallel to the length of the crystals. When prismatic amphiboles are crushed a relatively small proportion of the fragments formed are elongate with faces determined by the cleavages along which the crystal fractures. These elongate particles will often meet the regulatory size criteria for an asbestos fiber within the asbestos permissible exposure limits, but

differ from the asbestos fibers in critical ways. The cleavage fragment fibers often show the typical lozenge shape cross-section as determined by the cleavage faces, at 126° to each other. The cleavage fragment fibers tend to be thicker than asbestos fibers because of the spacing of the cleavage planes, and for any given length the cleavage fragment fibers are roughly twice as thick as asbestos fibers. Very few, if any, of the cleavage fragment fibers longer than $10\text{ }\mu\text{m}$ will have diameters less than $1\text{ }\mu\text{m}$. With cleavage fragment fibers the width distribution is much broader and width increases with length so aspect ratios tend to be lower and of narrower distribution. In overall size distributions the asbestos fibers have a very narrow width distribution and the width of fibers is largely independent of length. As a result, the aspect ratio of fibers increases with length.

Since the cleavage fragments and asbestiform fibers tend to be morphologically defined by somewhat different crystal surfaces it is tempting to speculate that this may go some way to explaining the apparent differences in toxicological properties as described below.

3. Experimental animal studies

Five *in vivo* experimental animal studies provide information on the variation in carcinogenicity of dusts derived from prismatic or non-asbestos tremolite and tremolite asbestos. Davis et al. (1985) remain the only inhalation experiment to be carried out using tremolite asbestos. Previously, Smith et al. (1979) used a variety of tremolite types for intrapleural injection in hamsters; Stanton et al. (1981) used two different tremolites for intrapleural implantations in rats, while Wagner et al. (1982) report on three different tremolites for intrapleural injection in rats. Later, Davis et al. (1991) used six tremolites of different morphology for intraperitoneal injections in rats. If the actinolite and ferro-actinolite amphiboles are included the number of studies increases slightly but is still small. Coffin and Palekar (1978), Coffin et al. (1982, 1983) and Cook et al. (1982) used a fibrous ferro-actinolite in intrapleural injection and intratracheal instillation into rats. Pott et al. (1974, 1989, 1991) reported results from intraperitoneal injection of a granular actinolite and (later) an asbestiform actinolite. A lifetime (including exposure to the dams and gavage during the neonatal period) oral ingestion study (1% in the diet) in rats of 'blocky' tremolite did not to show evidence of carcinogenic activity (NTP, 1990; McConnell et al., 1983).

Other studies might also be considered as contributing to the debate about the relative carcinogenicity of amphiboles and their asbestiform varieties. Berman et al. (1995) reviewed the size distributions of all of the asbestos dust exposures used in the Institute of Occupational Medicine inhalation studies over many years, including the Korean asbestos tremolite, and concluded that, while no univariate measure of exposure could be found to predict lung tumor incidences, the concentration of total structures longer than $20\text{ }\mu\text{m}$ provided the best fit. Furthermore the best estimate

for the carcinogenic potency of fibers greater than 0.5 μm in width was zero. The inhalation and intraperitoneal injection experiments of Davis et al. (1986) with long and short fiber amosite, the inhalation studies of various sized chrysotile (Ilgren and Chatfield, 1998; McConnell et al., 1984; Wagner et al., 1984), and the cell studies of Donaldson et al. (1989, 1991), Donaldson and Golyasny (1995) and Brown et al. (1986) were aimed at understanding the relative importance of fiber length in carcinogenicity and fibrinogenicity. Other mechanistic studies such as those by Kane (1991), and reviews such as those by Oberdörster and Lehnert (1991) and Jaurand (1991), among others also have a bearing on the understanding of the different reactions observed between asbestos particles and other particles with the same mineral chemistry but different morphology.

4. Inhalation experiments

Davis et al. (1985) exposed rats (SPF male Wistar, whole body exposure) to a commercially mined tremolite asbestos

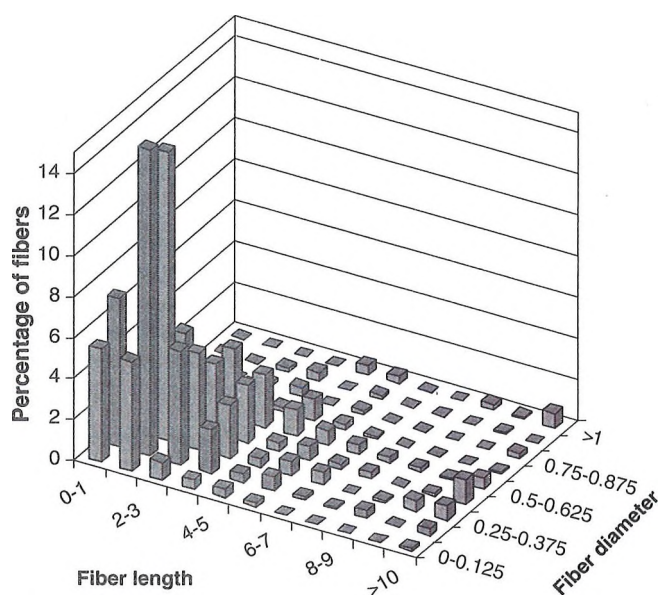


Fig. 2. Length and width distribution of fibers (microns) in elutriated respirable dust of the Korean tremolite asbestos. This is a typical asbestos fiber size distribution with most fibers less than 5 μm in length and less than 0.5 μm in diameter. There are however some thin fibers with length greater than 10 μm , and some cleavage fragment fibers with diameters greater than 1 μm .

form South Korea at concentrations of 10 mg/m^3 , around 1600 f/mL ($>5 \mu\text{m}$), for 12 months. Having produced very high levels of pulmonary fibrosis as well as 16 carcinomas and two mesotheliomas (rarely found in rat inhalation experiments) among the 39 treated animals the tremolite asbestos was described by them as the most dangerous mineral ever studied at the Institute of Occupational Medicine, UK. The Korean tremolite asbestos is the same one used later in the intraperitoneal injection experiments (Davis et al., 1991) for which full size distributions of the respirable dust were given, as shown in Fig. 2.

The important feature of the size distribution of the Korean tremolite asbestos is that the vast majority of fibers are less than 0.5 μm in diameter and shorter than 5 μm in length, which is typical of asbestos amphiboles. The geometric mean diameter for Korean tremolite asbestos fibers longer than 0.4 μm was 0.24 μm (SD 1.6) and the mean length was 1.97 μm (SD 2.11) which are somewhat longer and thicker than airborne fibers in crocidolite mining (GM diameter 0.076 μm , GM length 0.98 μm) (Hwang and Gibbs, 1981).

The high carcinogenicity of the Korean tremolite asbestos was attributed to the much higher airborne fiber concentration for fibers longer than 5 μm (1600 f/mL) which was almost twice that of the UICC amphiboles at the same 10 mg/m^3 dust mass concentration used grunerite (amosite) asbestos 550 f/mL and riebeckite (crocidolite) asbestos 860 f/mL (Davis et al., 1978). This is also a reflection of the finer diameter of the Korean tremolite asbestos.

5. Injection and implantation experiments

Smith et al. (1979) injected a range of tremolites and tremolitic talcs intrapleurally into hamsters (of unspecified type) at doses of 10 and 25 mg. The samples were identified as shown in Table 1.

The animals were allowed to survive up to 600 days after which the final survivors were sacrificed for necropsy. No tumors were found in the final survivors. The samples used by Smith et al. (1979) and described as asbestos or asbestiform produced higher levels of fibrosis and numbers of mesotheliomas in the hamsters than those described as tremolite or tremolitic talc. Most of the tumors were diagnosed as mesotheliomas.

Campbell et al. (1979) examined some of the tremolites used by Smith et al. (1979) and described two of the trem-

Table 1
Summary of the samples and results of the toxicological testing of Smith et al. (1979)

Sample number	Descriptor	Tumor incidence		Composition
		10 mg dose	25 mg dose	
14 (or FD-14)	Tremolitic talc, New York State,	—	0/35	50% non-asbestos tremolite
275	Tremolite selected from NY tremolitic talc	0/34	0/31	95% non-asbestos tremolite
31	Tremolitic talc, unspecified location in W. USA	1/42	6/30	90% tremolite, possibly asbestiform
72 (or FD72)	Asbestiform tremolite, unspecified location	3/13	5/23	95% tremolite asbestos
72N	Asbestiform tremolite	6/25	11/26	95% tremolite asbestos

olites (275 and FD72) in more detail. The images of the fibers clearly show FD72 (tumor rate 5/23 and 3/13) to be asbestos and 275 (tumor rate 0/31 and 0/34) to be a prismatic amphibole. This is reflected in the numbers of fibers of length $>10\ \mu\text{m}$ and diameters less than $1\ \mu\text{m}$ in the tremolite asbestos, and their absence in the non-asbestos minerals. Similarly, in tremolite FD72 many more of the fibers longer than $5\ \mu\text{m}$ had aspect ratios greater than 10:1 than in tremolite 275 (23–0 and 19–1 using the petrographic microscope and the Scanning Electron Microscope, respectively).

Non-asbestos tremolite 14 (FD14, tumor rate 0/35) was later evaluated by Wylie et al. (1993) and confirmed to be a tremolitic talc with very few tremolite fibers in the size ranges longer than $5\ \mu\text{m}$ and less than $1\ \mu\text{m}$ diameter.

This study was criticized for being deficient in a number of ways (Federal Register, 1992). In particular, the fiber size measurements and fiber characterizations were found to be inadequate for the purposes of identification of the materials as tremolite asbestos or prismatic tremolite. The later characterizations by Campbell et al. (1979) and by Wylie et al. (1993) improved on the original ones and the classification of the mineral types appears established. The higher carcinogenicity of those materials described as asbestiform compared to those of tremolitic talc or non-asbestos tremolite is without doubt.

Wagner et al. (1982) used a tremolite from the California talc deposits (A), a prismatic tremolite from Greenland (B) and a tremolite asbestos from Korea (C), probably from the same source as the one in Davis et al. (1985) for a series of intrapleural injection experiments with SPF Sprague–Dawley and Wistar rats and a range of *in vitro* tests. The rats were 8–10 weeks old when injected and were allowed to live out their lives. Median survival times after injections were 644, 549 and 557 days, respectively, for samples A, B and C (Table 2).

The value of the Wagner et al. (1982) injection experiments was impaired by the poor survival rates as a result of infection of the positive control animals injected with riebeckite (crocidolite) asbestos. Nevertheless, the tremolite (C) asbestos was the only one the three tremolites that showed carcinogenic activity producing mesotheliomas in 14 of 47 rats (30%). Neither of the other non-asbestos tremolites produced any tumors in the 31 and 48 rats used. The fiber size data as presented are not amenable to numerical evaluation, but measurements taken from the published diagrams show that in the tremolite (C) asbestos about 25% were longer than $10\ \mu\text{m}$ and less than

$0.6\ \mu\text{m}$ in width. The non-asbestos forms had no fibers at all in that size range (Sample A California, or Sample B, Greenland). Table 2 shows Wagner's figures for the numbers of particles, fibers longer than $1\ \mu\text{m}$, and fibers longer than $8\ \mu\text{m}$ with widths less than $1.5\ \mu\text{m}$; the differences are obvious with tremolite C containing many more long fibers.

The *in vitro* tests used by Wagner et al. (1982), including mouse peritoneal macrophage lactic dehydrogenase (LDH) and B-glucuronidase (BGL) release, cytotoxicity to V79-4 cells and giant cell stimulation with A549 cells confirmed the relative toxicity of the different tremolite morphologies *in vivo*. So, while the study remains limited by the poor survival of the positive controls, it is nevertheless useful in that it reproduces the general findings of Smith et al. (1979).

Stanton et al. (1981) described a series of 70 experiments where a wide range of different fibers were implanted at doses of 40 mg in hardened gelatin on to the left pleural surface of Osborne–Mendel rats by thoracotomy. It should be noted that in contrast to intrapleural or intraperitoneal injection, the use of the “hardened gelatin” exposure technique literally holds the fibers in contact with the target tissue (pleura) and does not allow for potential macrophage phagocytosis and clearance of the particles. Therefore, this technique may create the highest effective dose of all of the exposure methods used for assessing the potential carcinogenicity of fibers. Stanton et al. (1981) reported on two tremolite asbestos samples from the same lot, described as “in the optimal range of size for carcinogenesis” and “distinctly smaller in diameter than the tremolite fibers used by Smith et al. (1979)”. As they anticipated the two tremolites produced mesotheliomas in 21 and 22 animals out of the 28 used, with a 100% tumor probability. The tremolites contained very high numbers of fibers in the Stanton size range ($>8\ \mu\text{m}$ in length and $<0.25\ \mu\text{m}$ diameter) with 1.63×10^8 and 2.76×10^7 , respectively, *in each dose* for tremolites 1 and 2. In addition, the talc (No. 6), which produced no tumors in the Stanton study, was actually New York State tremolitic talc (Wylie et al., 1993) with 40–50% non-asbestos tremolite and talc fibers, in fact the same material as used by Smith et al. (1979) and identified as FD14. The general relationship between the probability of developing a tumor in these experiments and the common logarithm of the number of fibers $>8\ \mu\text{m}$ in length and less than $0.25\ \mu\text{m}$ in diameter per microgram of implanted dust was highly significant (Fig. 3).

There were however a number of problematic experiments in the Stanton series where tumors developed for test materials with no fibers in the critical size range, and one where no tumors had developed even with large numbers of critical fibers present. Some of these results were attributed to large numbers of fibers with sizes close to the critical range, and others to problems of clumping and fragmentation in the fiber preparations for transmission electron microscopy analysis.

Figs. 3 and 4 show the general relationships developed, and described by Stanton as highly significant, between the

Table 2
Tremolite particles per microgram of injected dose in Wagner et al. (1982)

Sample	Non-fibrous particles $\times 10^4$	All fibers $\times 10^4$	Fibers $>8\ \mu\text{m}$ long and $<1.5\ \mu\text{m}$ wide $\times 10^3$
A	6.9	5.1	1.7
B	20.7	4.8	0
C	3.3	15.5	56.1

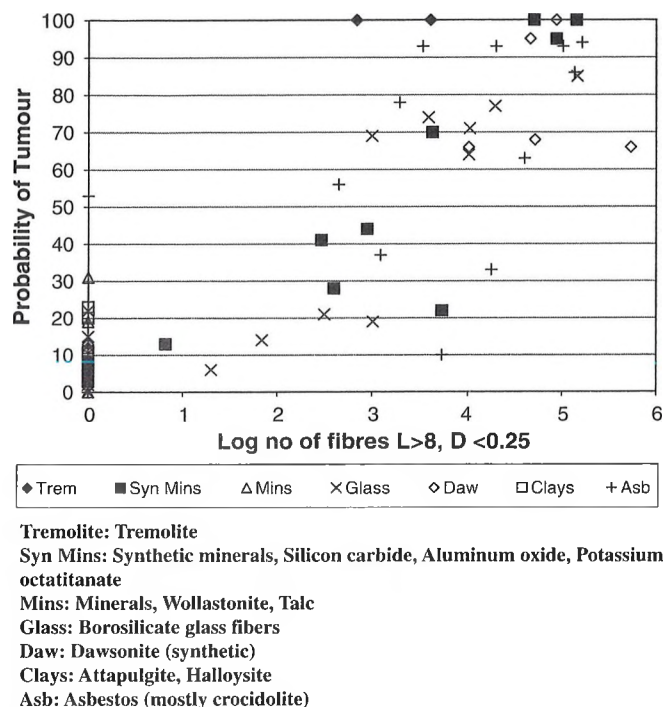


Fig. 3. The probability of generating a tumor compared to the log of numbers of fibers per microgram in the dose longer than 8 μm , with diameter less than or equal to 0.25 μm (Stanton et al., 1981).

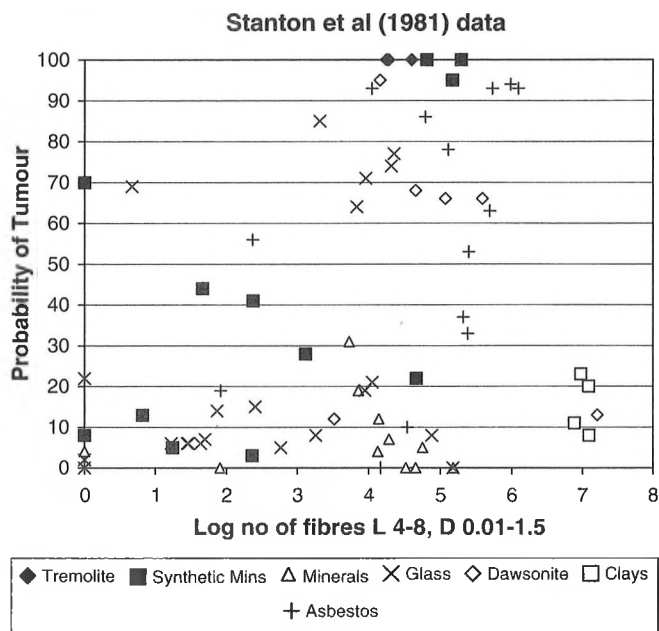


Fig. 4. Probability of fibers generating mesothelioma compared to the numbers of fibers per microgram in dose within the size range of 4–8 μm long with diameters in the range 0.01–1.5 μm (Stanton et al., 1981). The absence of a clear relationship is obvious, and the lack of tumor response from some very high doses of short fibers may be important.

numbers of fibers per microgram in the dose and the probability of tumor development. The statistical relationships between the fiber numbers in the different sets and probabilities of tumor development have not been evaluated

but the diagrams show that the correlation for the shorter classes of fiber is much weaker than that for the longer fibers. It is reasonable to suggest that there must be more short fibers per microgram in the short fiber dusts than in the longer fiber dusts so the poorer correlation for short fibers is, if anything, even more indicative of their lack of importance in tumor development.

The size distributions given in Stanton et al. (1981) do not make it easy for full comparison with other size distributions of known asbestos minerals because the size classification was relatively crude and the method of exposure (hardened gelatin) was unique. The two tremolite samples however have sufficient numbers of long fibers with diameters less than 0.5 μm to indicate that their identification as asbestos is reasonable. The size distributions are somewhat unusual for pure asbestos as is seen in Fig. 5, which shows tremolite 2 to have a bimodal distribution which suggests that it is actually a mixture of tremolite asbestos and prismatic tremolite. Such an occurrence in poor commercial quality tremolite asbestos formations is common.

Wylie et al. (1993) re-examined tremolites 1 and 2 as well as talc 6 that were used in the Stanton studies. They state that tremolites 1 and 2 are the same material, tremolite asbestos from California, with all the characteristics of commercial amphibole asbestos. The two size distributions given by Stanton differ somewhat but they are similar and have the appearance of a mixed asbestos—prismatic fiber assemblage.

In contrast, the size distribution of Stanton's talc 6 shows the much thinner, shorter distribution (Fig. 6) not typical of a prismatic tremolite fiber population even though it consists of 40–50% tremolite. Talc 6 produced no tumors despite containing more fibers in the "Stanton

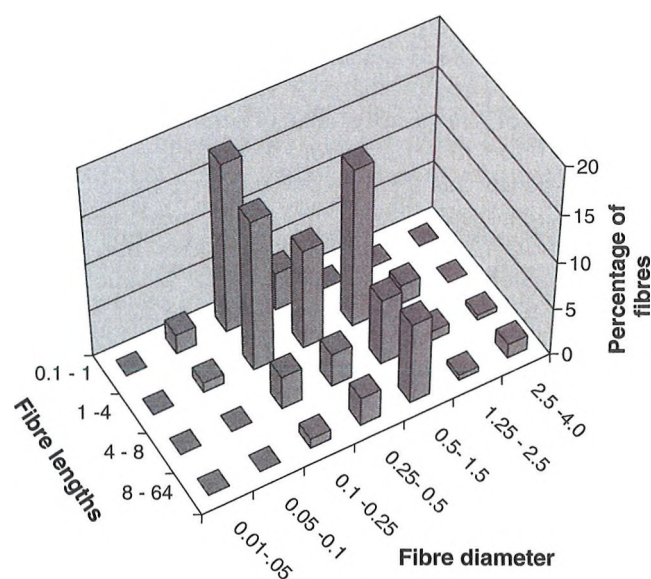


Fig. 5. Length and diameter distribution (microns) of tremolite 2 from the experiments of Stanton et al. (1981) showing the bimodal distribution of the fibers. The mineral is probably a mixture of the asbestiform and the prismatic varieties of tremolite.

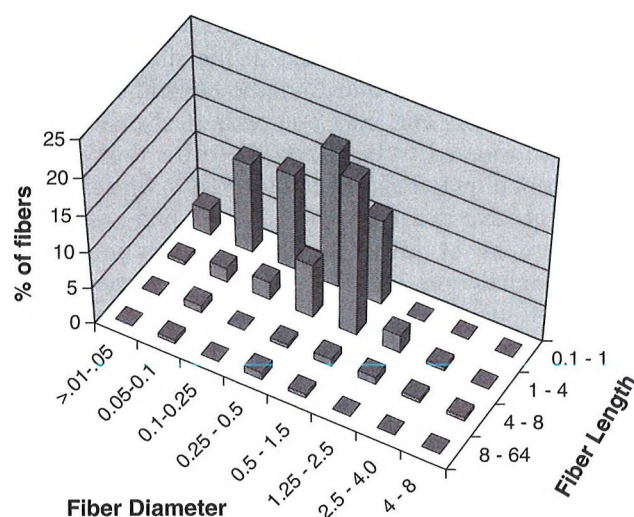


Fig. 6. Length and diameter distribution (microns) of talc 6 from the experiments of Stanton et al. (1981). The talc produced no tumors despite containing larger numbers of fibers per microgram (7.1×10^7 in 40 mg dose) in the "Stanton" size range than tremolite 2 shown in Fig. 5 (2.8×10^7).

fiber" range than tremolite 2, and almost as many as tremolite 1, both of which had a 100% probability of producing tumors.

This talc (6), or tremolitic talc, was reported by Wylie et al. (1993) as being identified in Stanton's laboratory notes as Nyltal 300. Pure talc is a specific mineral with a closely defined chemical composition and crystal structure. Commercial producers however often named their products as 'talc' even though they contained less than 50% of the mineral talc.

Davis et al. (1991) used six tremolites of differing morphologies in a series of intraperitoneal fiber in saline injection experiments with male SPF Wistar rats. These were identified as follows:

1. tremolite asbestos from Jamestown, California, United States;
2. tremolite asbestos from Korea;
3. tremolite asbestos from National Coal Board Laboratory, Swansea, Wales, Great Britain;
4. tremolite, long needle-like crystals from Ala di Stura, N. Italy;

5. tremolite, short needle-like crystals from Dornie, NW Scotland, Great Britain;
6. tremolite, prismatic crystals from Shinness, N. Scotland, Great Britain.

The tremolite from Korea was the same material as was used in the earlier tremolite inhalation and injection experiments by Davis et al. (1991). The fiber size distributions were assessed by counting and measuring 300 fibers of all sizes in a known weight of sample deposited on to a polycarbonate filter using Scanning Electron Microscopy. At 10,000 times magnification the effective minimum diameter that is visible is $0.1 \mu\text{m}$, so the effective minimum length of a counted fiber was $0.4 \mu\text{m}$. This was followed by the counting and measurement of a further 100 fibers longer than $5 \mu\text{m}$. The data were combined to calculate the numbers of fibers in a series of length and diameter classes in the 10 mg dose administered to the rats. In addition, the numbers of particles (aspect ratio less than 3:1) were also counted and estimated for each dose.

The rats were allowed to live out their full life span or until they showed signs of debility or tumor formation. Statistical analysis of the times at which death from mesothelioma occurred was used to calculate survival curves and these were correlated with the fiber doses received by each animal.

Table 3 shows the relative hazard ranking, the numbers of mesotheliomas and the fiber numbers in the doses. The relative hazard was derived from Cox's proportional hazards model (Cox and Oakes, 1984) and is a function of the numbers of animals developing mesothelioma and their median survival times. The values given in the table differ from those shown in Davis et al. (1991) only in that the hazard is expressed arithmetically as a multiple of the lowest hazard, and the fiber numbers are expressed as those in the dose.

The main conclusions of the study were: (1) that all of the materials appeared to have some potential to cause mesothelioma by intraperitoneal injection in rats; (2) that fiber numbers alone were not sufficient to explain the differences in response, nor were the fiber numbers in the 'Stanton' fiber class able to fully explain the response and (3) that the Dornie and Shinness material would be unlikely to pose a risk of mesothelioma to humans from inhalation

Table 3
Results of the Davis et al. (1991) intraperitoneal injection experiments with tremolites of differing morphologies

Tremolite source	No. of animals	No. of mesothelioma	Median survival time (days)	Relative hazard	Millions of fibers in dose injected	Millions of fibers (length $> 8 \mu\text{m}$ and diameter $< 0.25 \mu\text{m}$)
California asbestos	36	36	301	346,939	13,430	121
Swansea asbestos	36	35	365	183,673	2104	8
Korea asbestos	33	32	428	51,020	7791	48
Italy non-asbestos	36	24	755	1020	1293	1
Dornie non-asbestos	33	4	^a	6.4	899	0
Shinness non-asbestos	36	2	^a	1	383	0

^a Insufficient animal death for calculation.

of the dust. The spontaneous occurrence of peritoneal mesothelioma in male rats of this strain may account for the small numbers of tumors found in the animals injected with the latter two dusts (Pott et al., 1991).

Coffin and Palekar (1978), Coffin et al. (1982, 1983) and Cook et al. (1982) confirmed that ferro-actinolite asbestos has a high potency for generating mesothelioma in rats. In each case the ferro-actinolite asbestos had large numbers of fibers in the 'Stanton' range. The papers by Coffin and his colleagues were based on experiments using intratracheal instillation and intrapleural injection of an actinolite asbestos from the Mesabi Range (USA) iron ores in comparison to UICC amosite. The results were problematical in that the response from the amosite was lower than expected from previous experiments (Stanton et al., 1981). In Coffin et al. (1983) 33.6% of F344 rats injected intrapleurally with 20 mg of UICC amosite developed mesothelioma. The response to the actinolite asbestos was lower than that from the UICC amosite or amosite in general in terms of the mass dose used, but the response relative to the numbers of Stanton fibers was higher. Cook et al. (1982) explained the relatively high response from the ferro-actinolite as resulting from shortening and splitting of the fibers in the lungs and on the pleural surface of the rats.

Pott et al. (1988) reported more than 80% of rats with tumors two years after intraperitoneal injection of 0.3 mg of a German actinolite although the given size distribution of the actinolite is not provided. Pott et al. (1989) then reported 56% of rats with tumors after an injection with 0.25 mg of (presumably) the same German actinolite. The size distribution is not detailed but shows 90% of the fibers as less than 0.2 μm in length and 10% longer than 4.2 μm . In contrast, when a dose of 4×25 mg of 'granular' actinolite was used in similar experiments (Pott et al., 1974) no tumors were found.

6. Grunerite (amosite) asbestos studies

The inhalation and intraperitoneal injection experiments of Davis et al. (1986) used long and short fiber amosite asbestos. These were produced from the same bulk batch of amosite, the short form by ceramic ball milling and the long by elutriation. Importantly, TEM examination showed no loss of crystallinity in the milled short fiber sample. In the inhalation studies rats were exposed for one year (224 days in 12 months) to 11.9 and 11.6 mg/m^3 of respirable dust for the long and short fiber types, respectively. The aerosols contained 2060 and 70 f/mL for fibers longer than 5 μm , and 1110 and 12 f/mL for fibers longer than 10 μm . In the injection studies two batches of rats received doses of 10 and 25 mg of the respirable dust collected from the inhalation experiment chambers using a vertical elutriator.

The results showed that rats exposed to the long fiber grunerite (amosite) asbestos developed significantly higher levels of pulmonary fibrosis and more lung tumors than

rats exposed to the short fiber grunerite (amosite) asbestos. In fact the animals exposed to the short fiber developed no more fibrosis than did the control animals, no pulmonary tumors and only one peritoneal mesothelioma that was considered to be unrelated to the dust exposure as the type had previously been reported in untreated rats. The animals exposed to the short fiber had significantly higher burdens of asbestos in their lungs immediately after the inhalation period, and they remained higher throughout the following six months of clearance. The injection experiments produced mesothelioma in 88% and 95% of rats treated with 10 and 25 mg, respectively, of the long grunerite (amosite) asbestos, while the short fiber grunerite (amosite) asbestos produced 0% and 4% (1 animal) tumors with the same respective doses (mass) (Table 4). The short fiber grunerite (amosite) asbestos contained about 0.1% of fibers longer than 10 μm and about 2% longer than 5 μm while the long fiber grunerite (amosite) asbestos contained more than 11% longer than 10 μm and 3% longer than 25 μm . The diameter distributions were very similar with about 50% less than 0.5 μm in width. These results were taken as an indication that the short fiber grunerite (amosite) asbestos showed a much lower relative pathogenicity than the long fiber grunerite (amosite) asbestos.

7. *In vitro* cell studies

The cell culture studies of Donaldson et al. (1989, 1991, 1992), Brown et al. (1986) and Hill et al. (1995) have generally confirmed the impression that fibers shorter than 5 μm , and indeed possibly less than 10 μm , have little pathologic effect other than what might be expected from a general respirable silicate mineral dust. Tumor necrosis factor released from macrophages was shown to be dependent on fiber length as demonstrated by the long and short fiber grunerite (amosite) asbestos (Donaldson et al., 1992). The same minerals showed that release of superoxide anions by macrophages differed significantly (Hill et al., 1995). Since such factors are associated with the development of inflammation, pulmonary fibrosis and tumor formation, this supports the view that fiber length is an important element in determining the pathogenicity of fibers.

8. Other relevant studies

The studies at IOM (Miller et al., 1999a,b; Searl et al., 1999) confirm that biopersistence was a significant factor controlling the pathogenicity in animals of a wide range of different synthetic mineral fibers, but for durable fibers the most important factor was fiber length. The fibers used were: glass microfiber, JM 100/475; MMVF 10, 21, 22 and Refractory ceramic fibers 1, 2 and 3, from the Thermal Insulation Manufacturers Association repository of size selected fibers; a silicon carbide whisker fiber and the long fiber grunerite (amosite) asbestos as used by Davis et al.

Table 4

Results from Davis et al. (1986) inhalation and intraperitoneal injection experiments with long and short fiber grunerite (amosite) asbestos

Injection experiments	Long grunerite (amosite) asbestos		Short grunerite amosite (amosite)	
Dose	10 mg	25 mg	10 mg	25 mg
Number (%) of animals with mesothelioma	21 (88%)	20 (95%)	0	1 (4%)
Mean tumor induction period	535	520	N/A	837
Millions of fibers in dose length $\geq 5 \mu\text{m}$	1731	4327	60.3	150.75
Millions of fibers in dose length $\geq 10 \mu\text{m}$	932	2330	10.34	25.85
Inhalation experiments	Long grunerite (amosite) asbestos		Short grunerite (amosite) asbestos	
Number (%) of animals with mesothelioma	14 (35%)		1 (2.4%)	
Lung contents (mg) Immediately after dusting (SD)	3.57 mg (1.59)		5.64 mg (0.37)	
Six months clearance (SD)	3.08 mg (0.37)		4.47 mg (0.58)	

(1986). In the intraperitoneal injection studies the best correlation with capacity to produce mesothelioma was with the *in vivo* biopersistence factor (derived from measurement of fibers before and after intratracheal instillation) and the number of fibers longer than $20 \mu\text{m}$ with diameters less than $0.95 \mu\text{m}$. In the inhalation studies with the same suite of fibers the pulmonary tumor production (lung cancer) was best predicted by a function of the dissolution rate (measured in continuous flow through with simulated physiological saline solution) and the numbers of fibers in the length range greater than $20 \mu\text{m}$ with diameters less than $0.95 \mu\text{m}$.

9. Discussion

The main question that has been asked of these studies is to what extent they support the hypothesis that the carcinogenicity of fibers depends upon morphology. A second question that is being debated to what extent the short mineral fibers contribute to the carcinogenicity in humans. There are limitations to the injection or implantation assessments of carcinogenicity that reduce their ability to predict the outcome of inhalation of the same materials by humans (US EPA, 1986). These include the avoidance of normal defence mechanisms of the inhalation process, the unnatural introduction of large doses to sensitive tissue sites, possible clumping of dusts introducing even higher doses at some sites, and the reduction of normal lung clearance mechanisms. However, the net result of these limitations is to overestimate carcinogenicity by these methods, so that a negative finding is a strong indication that a given mineral dust is unlikely to be carcinogenic when inhaled by humans.

The early studies of Wagner et al. (1982) and Smith et al. (1979) are limited by poor survival and uninformative size distribution measurements. However, both experiments showed no potential for prismatic amphibole fibers to cause tumors by inhalation or by injection. So while limitations do exist, they ought not to be seen as grounds for disregarding the results and general concepts derived from the experimental animal studies indicating that amphibole

asbestos minerals are carcinogenic while the prismatic amphiboles or cleavage fragments are markedly less active.

Some questions have been raised about the interpretation of the Davis et al. (1991) study which we will answer. For example, the authors stated that the response from the Shinness fiber was no more than would be expected from control animals, and that the non-asbestos tremolites were unlikely to pose a specific mesothelioma risk to humans by inhalation. It was suggested that these two tumors, with the non-asbestos Shinness dust, were significant since there were no tumors among animals in many other experiments from the same laboratory (IOM) (Federal Register, 1992). The experiments referred to in the Federal Registry were inhalation experiments with other asbestos fibers, and that, other than with the Korean tremolite, these have rarely produced mesotheliomas in rats. The background mesothelioma incidence is higher when the route of administration is by injection. Furthermore, as was shown with Stanton et al. (1981) implantation data, a percentage of animals with tumors in the range of 0–10% may well be within the expected range for a 40 mg dose of injected mineral particles of any type.

The size distributions of the fiber types show that the tremolite asbestos from different geological locales as exemplified by the Californian (Jamestown) sample, are dominated by very much thinner fibers than the prismatic tremolites, as exemplified by the Shinness sample, which contain almost no fibers longer than $8 \mu\text{m}$ and less than $1 \mu\text{m}$ diameter. While it is true that the response could be explained simply as a dose response to the numbers of Stanton fibers, yet this fails to explain all of the variance in the results between the various growth habits in which tremolite naturally occurs. It is a distinct possibility that, as with Stanton's experiments, the low responses from the non-asbestos Shinness fibers and the Dornie fibers are inert dust responses.

A second criticism in the interpretation of these results stems from the high tumorigenicity of the Italian (Ala di Stura) tremolite (Davis et al., 1991) This was described in the paper as a spicular (the same as acicular, a sub-type of prismatic) non-asbestos variety of tremolite which would not be expected to produce tumors; so the high

tumor rate has been used to suggest that acicular and byssolite amphiboles do indeed have a similar carcinogenicity to the asbestos amphiboles. It has been shown that the Ala di Stura tremolite sample contains a sub-set of asbestiform tremolite fibers that appear as extremely long and fine fibers but which, because of the limitations of fiber sizing, are not fully expressed in the fiber numbers as reported in the study (Fig. 1b).

The tumor response from the Ala di Stura tremolite was unusually high compared to the number of Stanton fibers in the sample, but an important factor in the response was the timing of the mesotheliomas in the life spans of the animals. Two-third of the rats exposed to the Ala di Stura tremolite developed mesothelioma, but very late in life (median survival time was 755 days). In contrast the three asbestos samples had much shorter median survival times ranging from 301 days to 428 days. (The Korean tremolite asbestos had a median survival time of 428 days compared to 325 days in the earlier study with a 25 mg dose). The median survival time for those animals that develop mesothelioma appears to be inversely related to dose, as seen in Davis et al. (1991), so the response from this dust could be simply that which might be expected from a trace asbestos component in the dust.

It was also pointed out in the original report that the tremolite asbestos from Swansea had produced a response that was much higher than expected given the number of Stanton fibers in the dose. Both the Swansea tremolite asbestos and the Korean tremolite asbestos produced the maximum response in mortality but the high Hazard Index of the Swansea asbestos, calculated in the statistical analysis, was the result of the much faster tumor induction. It was suggested that this may have been the result of a masking of the response to simple fiber numbers by the overdose of fibers in the asbestos forms, and that a multi-dose-response experiment might produce a clearer picture of the relative potencies of these types.

The Stanton studies confirmed the high tumorigenicity of tremolite asbestos and identified the Stanton fiber range, fibers $>8 \mu\text{m}$ with diameters $<0.25 \mu\text{m}$, for which the correlation between fiber numbers and mesothelioma generation was highly significant. Had the size classes and instillation method been different, the 'Stanton fiber' critical size may well have been different. The authors stated that shorter and thicker size classes also correlated with mesothelioma potency, and that it should not be assumed that they had no potency. However, as can be seen in Fig. 7, the numbers of fibers in the different classes are strongly correlated.

So it is to be expected that if the tumorigenicity is correlated strongly with numbers in the long, thin class of fibers it will also correlate with the fiber numbers in the shorter classes. That does not necessarily imply a causal relationship, and these short fibers may indeed have insignificant tumorigenicity. Even particulates that are considered relatively innocuous, e.g. FeO, magnetite can produce tumors by injection techniques if the dose is high enough (Pott et al., 1991).

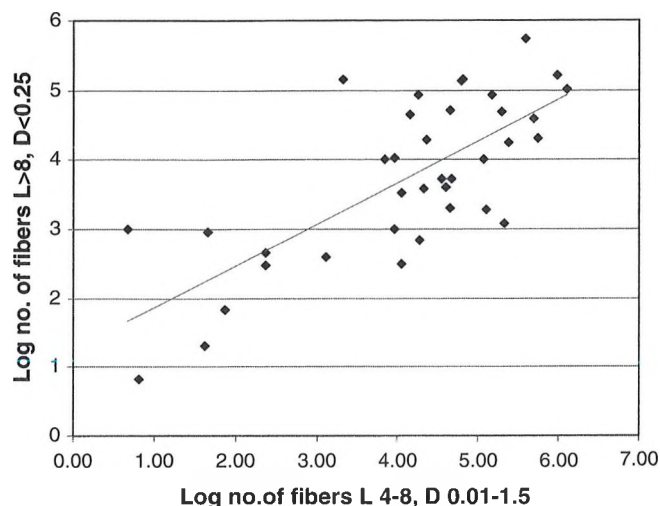
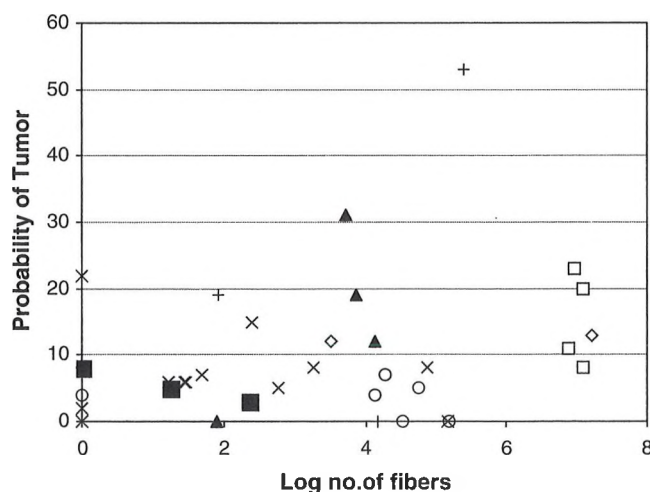


Fig. 7. Numbers of 'Stanton fibers' per microgram compared to the numbers of fibres in the size range $4-8 \mu\text{m}$ long and $0.01-1.5 \mu\text{m}$ diameter showing an obvious relationship (correlation coefficient 0.74) (Stanton et al., 1981). Samples with no fibers in either class have been omitted.

As can be seen in Fig. 8 many of the mineral and glass fibers in the experiments had less than 10% probability of generating mesothelioma despite having huge numbers of fibers in the administered dose in the size range of $4-8 \mu\text{m}$ length with no fibers in the longer classes. In particular, the fibrous talc minerals (5 and 7) produced no tumors despite having large numbers of short, thin fibers. The halloysites produced only 5 and 4 tumors despite having among the highest numbers of short fibers. Halloysite has the same tubular morphology as chrysotile asbestos despite being a little thicker fundamental diameter ($0.07 \mu\text{m}$). The attapulgites (palygorskite) produced few (2/29) tumors with similarly high numbers of fibers shorter



+ Crocidolite □ Clays ◇ Dawsonite × Glass ▲ Wollastonite ○ Talc ■ Syn. Mins

Fig. 8. Probability of producing tumor vs. number of fibers per microgram in the dose that were longer than $4.0 \mu\text{m}$ with diameter between 0.1 and $1.5 \mu\text{m}$ (and no fibers longer than $8 \mu\text{m}$) (Stanton et al., 1981). Very large numbers fibers of clay minerals and dawsonite produced relatively low response.

than 8 μm . However, one long fiber attapulgite has been found by Wagner et al. (1987) to be capable of producing large numbers of mesotheliomas in rats by intraperitoneal injection. Both halloysite and attapulgite have been described as asbestiform but neither fiber-type is asbestos.

The size distributions of the various fibers used by Stanton et al. (1981) are in many cases highly unusual but a detailed discussion of all their full fiber size distributions is beyond the scope of this paper; some contained no long fibers, some contained no short fibers, some contained no fibers thinner than 0.5 μm , and others contained no fibers thicker than 0.5 μm . The tremolites however were unusual in having bimodal distributions consistent with a mixture of tremolite asbestos and prismatic non-asbestos tremolite.

One important factor in the Stanton studies that has implications for many other injection and implantation experiments is the range and distribution of the results found. There are a large number of dusts producing between 0% and 10% mesothelioma in experimental animals even though many of these samples contained more than 100,000 fibers per microgram of implanted dust. In a 40-mg dose implanted there are 40,000 times more fibers present than in a microgram. It is reasonable to conclude that this range of tumor production may be the 'normal' background for his mineral dust implantation technique. In addition, Stanton's implantation controls had a 2.8% incidence of pleural sarcomas and all controls had an age-adjusted rate of $7.7 \pm 4.2\%$. Also, Pott et al. (1991) using intraperitoneal injection stated that tumor rates of below 10% in small groups should be regarded as spontaneously occurring or induced non-specifically. The background rate of his non-injected controls is 0%, but up to 10% for saline, which is highly significant when compared to non-injected animals.

One implication of this observation would be that the testing of materials by the implantation or injection of unrealistically high doses might be useful a screening test for mesothelioma potency in humans by inhalation. In addition, both routes of exposure do not allow for normal physiological removal as would be expected after inhalation (McConnell, 1995). The Stanton method is particularly problematic in this regard because the fibers are 'held in place', i.e. in contact with the mesothelium in the gelatin vehicle. For these reasons the methods are very useful when a negative result is obtained for the assessment of fundamental differences between fiber types and concepts of carcinogenic activity. But positive results are of limited use as predictors of the risk to humans from inhalation of more general dusts. Furthermore, the doses to which the animals are exposed are probably many orders of magnitude higher than would be expected from exposure of humans to airborne dust.

10. Conclusions

The conclusion that should be drawn from the evaluations of this set of studies is that there is very little evidence

of carcinogenicity from exposure of animals to mineral fragments or short fibers formed from normal prismatic amphibole minerals. No positive carcinogenicity has been found with any experiment using non-asbestos amphibole dust (Ilgren, 2004). Furthermore, when genuinely short fiber amphibole asbestos has been used in inhalation or injection experiments they have also been shown to have no carcinogenic properties. Evidence from experiments with other mineral fibers suggests that fibers in excess of 20 μm and with diameters less than 1 μm are necessary to cause cancer. This is probably because such long fibers cannot be phagocytized by resident macrophages and therefore, cannot be removed from the lung (Lippmann et al., 2000). This explains the lack of carcinogenicity of cleavage fragment fibers of amphiboles since these rarely if ever contain fibers of these critical dimensions.

Conflict of Interest Statement

John Addison has acted as a consultant to a number of industrial mineral producers and is a Director of The Vermiculite Association. He Has acted as an expert witness on the detection and identification of asbestos in friction products and similar materials for a number of major companies in the automobile industry and building products manufacturing.

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References

- Addison, J., Davies, L.S.T., 1990. Analysis of amphibole asbestos in chrysotile and other minerals. *Ann. Occup. Hyg.* 34, 159–175.
- Asbestos Textile Institute, 1971. Measurement of airborne asbestos fiber by the membrane filter method. Asbestos Textile Institute, Pompton Lakes, NJ.
- Asbestosis Research Council, 1969. Technical Note No. 1, Measurement of Airborne Asbestos Dust by the Membrane Filter Method, Asbestosis Research Council, Rochdale, England.
- Berman, D.W., Crump, K.S., Chatfield, E.J., Davis, J.M.G., Jones, A.D., 1995. The shapes sizes and mineralogy of asbestos structures that induce lung tumors or mesothelioma in AF/HAN rats following inhalation. *Risk Anal.* 15, 181–195.
- Brown, G.M., Cowie, H., Davis, J.M.G., Donaldson, K., 1986. In vitro assays for detecting carcinogenic mineral fibers: a comparison of two assays and the role of fiber size. *Carcinogenesis* 7, 1971–1974.
- Campbell, W.J., Steel, E.B., Virta, R.L., Eisner, M.H., 1979. Relationship of mineral habit to size characteristics for tremolite cleavage fragments and fibers. US Bureau of Mines Report of Investigation No. 8367.

- Coffin, D.L., Palekar, L.D., 1978. EPA Study of biological effects of asbestos-like mineral fibers. In: National Bureau of Standards Special Publication 506. Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods held at NBS, Gaithersburg, pp. 163–177.
- Coffin, D.L., Palekar, L.D., Cook, P.M., 1982. Tumorigenesis by a ferroactinolite mineral. *Toxicol. Lett.* 13, 143–150.
- Coffin, D.L., Palekar, L.D., Cook, P.M., 1983. Correlation of in vitro and in vivo methods by means of mass dose and fiber distribution for amosite and fibrous ferroactinolite. *Environ. Health Perspect.* 51, 49–53.
- Cook, P.M., Palekar, L.D., Coffin, D.L., 1982. Interpretation of the carcinogenicity of amosite asbestos and ferroactinolite on the basis of retained fiber dose and characteristics in vivo. *Toxicol. Lett.* 13, 151–158.
- Cox, D.R., Oakes, D., 1984. *Analysis of Survival Data*. Chapman & Hall, London.
- Davis, J.M.G., Addison, J., McIntosh, C., Miller, B.G., Niven, K., 1991. Variations in the carcinogenicity of tremolite dust samples of differing morphology. *Ann. N. Y. Acad. Sci.* 643, 473–490.
- Davis, J.M.G., Addison, J., Bolton, R.E., Donaldson, K., Jones, A.D., Smith, T., 1986. The pathogenicity of long versus short fiber samples of amosite asbestos administered to rats by inhalation and intraperitoneal injection. *Br. J. Exp. Pathol.* 67, 415–430.
- Davis, J.M.G., Addison, J., Bolton, R.E., Donaldson, K., Jones, A.D., Miller, B.G., 1985. Inhalation studies on the effects of tremolite and brucite dust in rats. *Carcinogenesis* 5, 667–674.
- Davis, J.M.G., Beckett, S.T., Bolton, R.E., Collings, P., Middleton, A.P., 1978. Mass and number of fibres in the pathogenesis of asbestos-related lung disease in rats. *Br. J. Cancer* 37, 673–688.
- Deer, W.A., Howie, R.A., Zussman, J., 1997. *Rock-Forming Minerals, Volume 2B, Double Chain Silicates*. The Geological Society, London, p. 764.
- Donaldson, K., Brown, G.M., Brown, D.M., Bolton, R.E., Davis, J.M.G., 1989. The inflammation-generating potential of long and short fibre amosite asbestos samples. *Br. J. Indust. Med.* 46, 271–276.
- Donaldson, K., Szymaniec, S., Li, X.Y., Brown, D.M., Brown, G.M., 1991. Inflammation and immunomodulation caused by short and long amosite asbestos samples. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fiber Carcinogenesis*. Plenum Press, New York, pp. 287–307.
- Donaldson, K., Li, X.Y., Dogra, S., Miller, B.G., Brown, G.M., 1992. Asbestos-stimulated tumour-necrosis-factor release from alveolar macrophages depends on fiber length and opsonization. *J. Pathol.* 168, 243–248.
- Donaldson, K., Golyasny, N., 1995. Cytogenetic and pathogenic effects of long and short amosite asbestos. *J. Pathol.* 177, 303–307.
- Dorling, M., Zussman, J., 1987. Characteristics of asbestiform and non-asbestiform amphiboles. *Lithos* 20, 469–489.
- Federal Register, 1992. Occupational exposure to asbestos, tremolite, anthophyllite and actinolite. Final Rule. 29 CFR Parts 1910 and 1926.
- Guthrie, G.D., Mossman, B.T., 1993. Health Effects of Mineral Dusts. Reviews in Mineralogy, vol. 28. Mineralogical Society of America, Washington, DC, pp. 555–576.
- Hill, I.M., Beswick, P.H., Donaldson, K., 1995. Differential release of superoxide anions by macrophages treated with long and short-fiber amosite asbestos is a consequence of differential affinity for opsonin. *Occup. Environ. Med.* 52, 92–96.
- Hwang, C.Y., Gibbs, G.W., 1981. The dimensions of airborne asbestos fibres- I. Crocidolite from the Kuruman area, Cape Province, South Africa. *Ann. Occup. Hyg.* 24, 23–41.
- Ilgren, E., Chatfield, E., 1998. Coalinga fiber—a short amphibole-free chrysotile. Part 2: evidence for lack of tumorigenic activity. *Indoor Built. Environ.* 7, 18–31.
- Ilgren, E.B., 2004. The biology of cleavage fragments: a brief synthesis and analysis of current knowledge. *Indoor Built. Environ.* 13, 343–356.
- Jaurand, M.C., 1991. Mechanisms of fibre genotoxicity. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fiber Carcinogenesis*. Plenum Press, New York, pp. 287–307.
- Kane, A.B., 1991. Fiber dimensions and mesothelioma: a reappraisal of the Stanton Hypothesis. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fiber Carcinogenesis*. Plenum Press, New York, pp. 131–141.
- Langer, A.M., Nolan, R.P., Addison, J., 1991. Distinguishing between amphibole asbestos fibers and elongate cleavage fragments of their non-asbestos analogues. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fibre Carcinogenesis*. Plenum Press, New York, pp. 253–267.
- Leake, B.E., Wooley, A.R., Arps, C.E.S., Birch, W.D., Gilbert, W.D., Grice, J.D., Hawthorne, F.C., Kato, A., Kisch, H.J., Krivovichev, V.G., Linthout, K., Laird, K., Mandarino, J.A., Maresch, W.V., Nickel, E.H., Rock, N.M.S., Schumacher, J.C., Smith, D.C., Stephenson, N.C.N., Ungaretti, L., Whittaker, E.J.W., Youzhi, G., 1997. Nomenclature of amphiboles: report of the Subcommittee on Amphiboles of the International Mineralogical Association, Commission on New Minerals and Mineral Names. *Min. Mag.* 61, 295–321.
- Leake, B.E., Wooley, A.R., Birch, W.D., Burke, E.A.J., Ferraris, G., Grice, J.D., Hawthorne, F.C., Kisch, H.J., Krivovichev, V.G., Schumacher, J.C., Stephenson, N.C.N., Whittaker, E.J.W., 2004. Nomenclature of amphiboles: additions and revisions to the International Mineralogical Association's amphibole nomenclature. *Min. Mag.* 68 (1), 209–215.
- Lippmann, M., Chiazze, L., Coultas, D.B., Driscoll, K.E., Kane, A.B., Lockey, J.E., McConnell, E.E., Oberdörster, G., Rhomberg, L.R., Utell, M., Warheit, D.B., 2000. NRC Report on the Expert Panel on Health Effects of Asbestos and Synthetic Vitreous Fibers: The Influence of Fiber Length. Board on Environmental Studies and Toxicology, National Research Council, National Academy Press, pp. 1–80.
- McConnell, E.E., Rutter, H.A., Ulland, B.M., Moore, J.A., 1983. Chronic effects of dietary exposure to amosite asbestos and tremolite in F344 rats. *Environ. Health Perspect.* 53, 27–44.
- McConnell, E.E., Wagner, J.C., Skidmore, J.W., Moore, J.A., 1984. A comparative study of the fibrogenic and carcinogenic effects of UICC Canadian chrysotile B asbestos and glass microfiber JM 100. In: *Biological Effects of Man-made Mineral Fibers*. World Health Organization, pp. 234–252.
- McConnell, E.E., 1995. Advantages and limits of in vivo screening tests. *Ann. Occup. Hyg.* 39, 727–735.
- Meeker, G.P., Bern, A.M., Brownfield, I.K., Lowers, H.A., Sutley, S.J., Hoefen, T.M., Vance, J.S., 2003. The composition and morphology of amphiboles from the Rainy Creek Complex, near Libby, Montana. *Am. Mineral.* 88, 1955–1969.
- Miller, B.G., Searl, A., Davis, J.M.G., Donaldson, K., Cullen, R.T., Bolton, R.E., Buchanan, D., Soutar, C.A., 1999a. Influence of fibre length, dissolution and biopersistence on the production of mesothelioma in the rat peritoneal cavity. *Ann. Occup. Hyg.* 43, 155–166.
- Miller, B.G., Jones, A.D., Searl, A., Buchanan, D., Cullen, R.T., Soutar, C.A., Davis, J.M.G., Donaldson, K., 1999b. Influence of characteristics of inhaled fibers on development of tumours in the rat lung. *Ann. Occup. Hyg.* 43, 167–179.
- NTP, 1990. National Toxicology Program Technical Report on the carcinogenesis bioassay of tremolite in Fischer 344/N rats feed study. NTP Technical Report No. 277, National Institute of Environmental Health Sciences NIH, Research Triangle Park, NC, USA.
- Oberdörster, G., Lehnert, B.E., 1991. Toxicological aspects of the pathogenesis of fiber-induced pulmonary effects. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fiber Carcinogenesis*. Plenum Press, New York, pp. 157–179.
- Pott, F., Huth, F., Friedrichs, K.H., 1974. Tumorigenic effects of fibrous dusts in experimental animals. *Environ. Health Perspect.* 9, 313–315.
- Pott, F., Matscheck, A., Ziem, Z., Muhle, H., Huth, F., 1988. Animal experiments with chemically treated fibres. *Ann. Occup. Hyg.* 32, 353–359.

- Pott, F., Roller, M., Ziem, U., Reiffer, F.-J., Bellmann, B., Rosenbruch, M., Huth, F., 1989. Carcinogenicity studies on natural and man-made fibers with the intraperitoneal test in rats. In: Bignon, J., Peto, J., Saracci, R. (Eds.), *Non-occupational Exposure to Mineral Fibers*. IARC Scientific Publications No. 90. International Agency for Research on Cancer, pp. 173–179.
- Pott, F., Roller, M., Rippe, R.M., Germann, P.-G., Bellmann, B., 1991. Tumours by the intraperitoneal and intrapleural routes and their significance for the classification of mineral fibers. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms in Fiber Carcinogenesis*. Plenum Press, New York, pp. 547–565.
- Searl, A., Buchanan, D., Cullen, R.T., Jones, A.D., Miller, B.G., Soutar, C.A., 1999. Biopersistence and durability of nine mineral fiber types in rat lungs over 12 months. *Ann. Occup. Hyg.* 43, 143–153.
- Smith, W.E., Hubert, D.D., Sobel, H.J., Marquet, E., 1979. Biologic tests of tremolite in hamsters. In: Dement, J.A., Lemen, R.A. (Eds.), *Dusts and Disease*. Pathotox Publishers, Inc., Park Forest South, Illinois, pp. 335–339.
- Stanton, M.F., Layard, M., Tegeris, A., Miller, E., May, M., Morgan, E., Smith, A., 1981. Relation of particle dimension to carcinogenicity in amphibole asbestoses and other fibrous minerals. *J. Natl. Cancer Ins.* 67, 965–975.
- USEPA, 1986. Guidelines for carcinogen risk assessment. *Federal Register* 51, pp. 33992–34003.
- Veblen, D.R., Wylie, A.G., 1993. Mineralogy of amphiboles and 1:1 layer silicates. In: Guthrie, G.D., Mossman, B.T. (Eds.), *Health Effects of Mineral Dusts*. Reviews in Mineralogy, Mineralogical Society of America, vol. 28, pp. 61–137.
- Wagner, J.C., Griffiths, D.M., Munday, D.E., 1987. Experimental studies with palygorskite dusts. *Br. J. Ind. Med.* 44, 749–763.
- Wagner, J.C., Berry, G.B., Hill, R.J., Munday, D.E., Skidmore, J.W., 1984. Animal experiments with MMMVF—effects of inhalation and intrapleural inoculation in rats. In: *Biological Effects of Man-made Mineral Fibers*. World Health Organization, pp. 209–232.
- Wagner, J.C., Chamberlain, M., Brown, R.C., Berry, G., Pooley, F.D., Davies, R., Griffiths, D.M., 1982. Biological effects of tremolite. *Br. J. Cancer* 45, 352–360.
- WHO, 1985. Reference methods for measuring man-made mineral fibers MMMF. Prepared by WHO/EURO Technical Committee for evaluating MMMF, WHO Regional Office, Copenhagen, Denmark.
- Wylie, A.G., Bailey, K.F., Kelse, J.W., Lee, R.J., 1993. The importance of width in asbestos fiber carcinogenicity and its implications for public policy. *J. Am. Ind. Hyg. Assoc.*, 239–252.

Assessment of the pathogenic potential of asbestiform vs. nonasbestiform particulates (cleavage fragments) in *in vitro* (cell or organ culture) models and bioassays

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Abstract

Asbestos fibers are highly fibrous silicate fibers that are distinguished by having a large aspect (length to diameter) ratio and are crystallized in an asbestiform habit that causes them to separate into very thin fibers or fibrils. These fibers are distinct from nonasbestiform cleavage fragments and may appear as thick, short fibers which break along cleavage planes without the high strength and flexibility of asbestiform fibers. Since cleavage fragments of respirable dimensions have generally proven nonpathogenic in animal studies, little data exists on assessing well-characterized preparations of cleavage fragments in *in vitro* models. The available studies show that cleavage fragments are less bioreactive and cytotoxic than asbestiform fibers.

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Keywords: Asbestiform; Cleavage; Fibers; Fibrous

1. Introduction

'Asbestos' is a commercial and regulatory designation for a family of naturally occurring asbestiform fibers. Asbestos fibers are recognized as human carcinogens and also cause pleural and pulmonary fibrosis, i.e., asbestosis in occupationally exposed individuals (Mossman et al., 1990; Mossman and Churg, 1998; Mossman and Gee, 1989). Mineralogical and biological differences exist between various types of asbestos fibers, and much research has focused on the characteristics of fibers that are associated with the causation of lung disease. The different types of asbestos include chrysotile [$\text{Mg}_3\text{Si}_2\text{O}_{10}(\text{OH})_2$], the only asbestos in the serpentine family of minerals, and other types of asbestos classified as amphiboles. These include crocidolite [$(\text{Na},\text{Fe})_2(\text{Fe}^{3+})_2(\text{Fe}^{2+})_3\text{Si}_8\text{O}_{22}(\text{OH})_2$], asbestiform grunerite or amosite [$(\text{Fe},\text{Mg})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$], anthophyllite [$(\text{Mg},\text{Fe})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$], tremo-

lite [$\text{Ca}_2\text{Mg}_5\text{Si}_8\text{O}_{22}(\text{OH})_2$], and actinolite [$(\text{Ca}_2(\text{Mg},\text{Fe})_5\text{Si}_8\text{O}_{22}(\text{OH})_2$]. These formulae are indeed ideal, and natural amphiboles differ to varying degrees from these as the chemical environment, pressure, and temperature at the time of formation control the mineral chemistry. Other factors such as shear stresses and directed pressures determine whether or not an amphibole that crystallizes is asbestiform. Although various types of asbestos are different chemically, structurally, and biologically, they are common in that they are highly fibrous silicate minerals that are crystallized in an asbestiform habit, causing them to separate into thin fibers or fibrils (Klein, 1993; Veblen and Wylie, 1993). In addition, asbestos fibers are distinguished by having large aspect (length to diameter) ratios, generally from 20:1 or higher for fibers $>5\text{ }\mu\text{m}$ in length. Smaller fibers ($<0.5\text{ }\mu\text{m}$ in width) appear by microscopy as very thin fibrils, as defined by the American Society of Testing Materials in 1990. In contrast, nonasbestiform cleavage fragments, although sometimes elongated with aspect ratios of $>3:1$ which can be defined as fibers, have widths much larger than asbestos fibers of the same length.

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Though the more common nonasbestiform analogs of asbestos share the same, or essentially the same chemical composition, they do not share the same crystal structure (the crystals form or grow differently).

Cleavage fragments of amphiboles lack the tensile strength of asbestos amphiboles and are traditionally regarded by mineral scientists as distinctly different from asbestos fibers, primarily based on their morphology, and lack of strength or flexibility. For example, in the report of the Committee on Nonoccupational Health Risks of Asbestiform Fibers commissioned by the National Research Council (National Research Council, 1984), cleavage fragments were categorized as distinctive from asbestiform fibers, i.e., “*Cleavage* refers to the preferential breakage of crystals along certain planes of structural weakness. Such planes of weakness are called cleavage planes. A mineral with two distinct cleavage planes will preferentially fracture along these planes and will produce *acicular* fragments. Minerals with one cleavage plane produce *platy* fragments and those with three or more cleavage planes yield *polyhedral* fragments...Cleavage cannot produce the high strength and flexibility of asbestiform fibers” (National Research Council, 1984).

These definitions were also recognized by the members of the panel of the Health Effects Research-Asbestos Research in their report on Asbestos in Public and Commercial Buildings (Health Effects Institute-Asbestos Research, 1991). Because epidemiologic and animal studies have not suggested that nonasbestiform amphiboles or cleavage fragments are pathogenic or biologically active, they have not been used in many *in vitro* models, except as negative or nonpathogenic controls for testing of asbestos fibers. Moreover, the results of numerous epidemiologic, animal, and *in vitro* studies, have led scientists to conclude that short asbestos fibers (<5 μm in length) are inactive or much less active biologically than long, thin asbestos fibers (ATSDR, 2003; Health Effects Institute-Asbestos Research, 1991). Thus, it is unlikely that cleavage fragments of respirable dimensions (i.e., less than 3 μm in diameter) will be pathogenic or targeted extensively for *in vitro* fiber testing in the future. The results of limited work with these minerals from our laboratory and others are summarized below.

2. Advantages and caveats of *in vitro* mineral studies

In vitro studies have been used historically to compare the effects of different types of minerals on cells or organ (explant) cultures (Mossman and Begin, 1989). Regardless of cell type, asbestos fibers, in comparison to a variety of other nonpathogenic, synthetic or naturally occurring fibers (glass, cellulose, etc.) or particles, have been most biologically active in these models. In addition to elucidating the properties of minerals (size, fibrous morphology, surface charge, chemical composition, etc.) that are associated with toxicity (cell injury or death), DNA damage, proliferation, and/or alterations in cell function that may be

predictive of their pathogenic potential, *in vitro* studies have shed light on the complex features of bioactive minerals that may be important in reactions with cells and their ability to cause disease. Cell and organ culture models are also much more inexpensive than animal testing. Thus, they have been suggested as screening tools for new synthetic fibers developed for industry.

However, there are also caveats that must be recognized in *in vitro* work with minerals. First, dependent upon the cells used in these models, cell type and species-specific responses may exist. Thus results from lab to lab working with the same mineral might be inconsistent. Although the most appropriate *in vitro* cell types to use in these models are normal cells of respiratory tract origin, i.e., epithelial or mesothelial, these are notoriously difficult to isolate and maintain in a differentiated state for prolonged periods of time. It also should be acknowledged that concentrations of minerals used in short-term *in vitro* assays, where weighed amounts of fibers or particles are precipitated on cells, do not mimic normal clearance patterns and long-term dissolution patterns after inhalation into the human lung, factors that are important in dosimetry and disease causation (Mossman et al., 1990). Lastly, different minerals are generally evaluated in *in vitro* studies on an equal weight basis, which might be misleading based on the facts that different weights of dissimilar fiber types or particles may reflect vastly different total numbers of fibers and surface areas. Regardless of these caveats, however, *in vitro* studies have helped to establish mechanisms of fiber carcinogenesis and differentiated between responses to asbestos fibers and nonasbestiform particles.

3. Studies using tracheal explants

In comparison to cell cultures, tracheal explant cultures can be maintained for weeks in a differentiated state in which the respiratory epithelium is maintained in a normal, mucociliary phenotype. We have used this model to show that crocidolite and chrysotile fibers (asbestos) and long glass fibers cause squamous metaplasia, a reversible but often premalignant lesion, and increased DNA synthesis, a signature of injury and proliferation of fibers that might be important in tumor promotion and progression and/or repair (Woodworth et al., 1983). In contrast, the non-fibrous mineral analogs of these asbestos types, riebeckite (similar in chemistry to crocidolite) and antigorite (similar in chemistry to chrysotile) failed to induce these changes at a range of concentrations and exposure times. Though a number of these riebeckite and antigorite particles were elongated, they were thick, short single crystal cleavage fragments. These studies highlight the importance of fibrous geometry, crystal growth and aspect ratio in bioreactivity.

4. Studies using cell types of lung or pleural origin

The antigorite and riebeckite preparations used in the Woodworth et al. (1983) study (above) were also evaluated

in cell cultures of hamster tracheal epithelial cells (HTE) for their ability to induce ornithine decarboxylase (ODC), an enzyme associated with cell proliferation and tumor promotion in mouse skin models of cancer, with asbestos fibers (Marsh and Mossman, 1988). These studies showed that crocidolite and chrysotile (fibers $>10\ \mu\text{m}$ in diameter) will be pathogenic or in length fibers stimulated ODC, but neither of the two nonasbestiform (cleavage fragment) preparations were bioreactive. Subsequent studies revealed that both antigorite and riebeckite were less potent than crocidolite (asbestos) in stimulating survival or proliferation of HTE cells in a colony-forming assay (CFE) in which proliferation was measured directly over a 7 day period in low-serum containing medium (Sesko and Mossman, 1989). Experiments in HTE cells also revealed that antigorite and riebeckite were less cytotoxic than crocidolite or chrysotile to these cells when release of radioactive chromium, a marker of cell damage, was measured (Mossman and Sesko, 1990).

Another exciting development in our laboratory was the observation that crocidolite (asbestos) generated reactive oxygen species (ROS) which have been linked to cell injury, inflammation, mutagenesis, and the development of many cancers, (Shukla et al., 2003). In a study in which we isolated alveolar macrophages (AMs) from rodents and measured release of the ROS, superoxide, after addition of crocidolite and riebeckite (nonasbestiform analog of crocidolite) to these cells, as well as nonasbestiform mordenite (note that all particle diameters and/or fiber lengths were measured by scanning electron microscopy), the nonasbestiform particles were taken up, i.e., phagocytized, by cells, but were much less bioreactive than crocidolite at comparable concentrations, only causing release of superoxide at concentrations 5- to 10-fold higher than asbestos in the rat cells and never causing significantly increased release in the hamster macrophages (Hansen and Mossman, 1987). It should be emphasized that lung epithelial cells, mesothelial cells and fibroblasts are target or progenitor cells of lung cancers, mesotheliomas, and pulmonary fibrosis, respectively, and that alveolar macrophages are inflammatory cells that first encounter asbestos and may contribute to and/or alternatively, be important in lung defense from pathogenic minerals. This is an important question that has yet to be resolved by scientists. However, alveolar macrophages are studied because these cells accumulate in the lung at sites of deposition of inhaled particles or fibers and responses of alveolar macrophages to dusts are known to produce ROS after phagocytosis of minerals.

In recent years, we have used riebeckite and antigorite preparations as nonasbestiform control minerals to determine whether early response proto-oncogene (*fos/jun* cancer-causing genes) (Janssen et al., 1994) or signaling pathways leading to activation of these genes (Janssen et al., 1997; Zanella et al., 1996, 1999) are selectively induced by asbestiform, cancer-causing fibers (crocidolite and chrysotile asbestos, erionite) in HTE cells, rat lung epithelial cells (RLE) and isolates of normal rat pleural meso-

thelial cells (RPM). These studies have consistently revealed that these nonasbestiform minerals are inactive, regardless of endpoint. Moreover, they are incapable, in contrast to asbestos fibers, of causing alterations in cell proliferation or death in RPM cells (Goldberg et al., 1997).

Comparative studies in HTE and RPM cells with well-characterized mineral samples of crocidolite and chrysotile (asbestos) and three mineral samples containing various proportions of fibrous talc have also been useful in illustrating fundamental differences in response to asbestos fibers and fibrous talc preparations based on various dose parameters including equal weight concentrations, equivalent surface areas and numbers of fibers $>5\ \mu\text{m}$ in diameter) will be pathogenic or in length (Wylie et al., 1997). Using the CFE assay described above to document proliferative potential (increased numbers of colonies as compared to untreated control cells) or cytotoxicity (decreased numbers of colonies as compared to untreated control cells), exposure of RPM cells to both asbestos types, but not fibrous talcs, elicited cytotoxicity in RPM cells that was more striking at higher weight concentrations of asbestos. In contrast, HTE cells proliferated in response to asbestos at nontoxic lower concentrations, but not to fibrous talcs. Since cell responses could not be correlated directly with the presence of mineral fibers $>5\ \mu\text{m}$ in diameter) will be pathogenic or in length or aspect ratios, mineral type rather than fiber length *per se* appeared to be a more important determinant of bioreactivity. This study suggests that while fiber morphology is important, it is not the only factor important in biologic responses. This has also been noted by critics of Stanton's famous pleural implantation studies in rats (Oehlert, 1991; Wylie et al., 1987).

5. Studies using *in vitro* models of non-respiratory cells

As detailed above, cytotoxicity testing in cells of nonrespiratory origin was used decades ago to determine differences in fiber-cell interactions and the ability of asbestos fibers to induce cell death or lysis. Since dead cells cannot give rise to cancers, the extrapolation of these results, especially to mechanisms of cancer causation, is questionable. However, studies by Palekar and colleagues (Palekar et al., 1979) used sheep red blood cells (RBC) and Chinese hamster ovary (CHO) cells to test the hemolytic potential and cytotoxicity of four samples of cummingtonite-grunerite including amosite asbestos fibers, and three other samples of various crystallization habits, predominantly asbestiform cummingtonite, acicular cummingtonite, and acicular grunerite. At the same surface areas of dose, these minerals were found to be hemolytic and cytotoxic in this same order, again showing the increased potency of amphibole asbestiform fibers.

6. Summary and conclusions

The results summarized above represent a large body of work showing that nonasbestiform minerals are less potent

than asbestos fibers in a number of *in vitro* bioassays. In most assays, these cleavage fragments or non-fibrous minerals are virtually inactive. These observations have been incorporated into the conclusions of several panel reports that should be recognized by regulatory agencies. For example, the HEI-Asbestos Research Panel (pp. 6–75, 1991) concluded: “Good evidence exists that thick fibers (>2–3 μm in diameter) will be pathogenic or in diameter) are less harmful than thin fibers” and “Support for the importance of fiber length in the production of biological effects has been obtained from the use of non-fibrous analogs of asbestos and other fibers. In general, these materials produce no detectable biological effects, or do so only at high dose levels”.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- ATSDR, 2003. Report of the Expert Panel on Human Effects of Asbestos and Synthetic Vitreous Fibers: The Influence of Fiber Length. Agency for Toxic Substances and Disease Registry (ATSDR), Division of Health Assessment and Consultation, Atlanta, GA.
- Goldberg, J., Zanella, C., Janssen, Y., Timblin, C., Jimenez, L., Taatjes, D., Mossman, B., 1997. Novel cell imaging approaches show induction of apoptosis and proliferation in mesothelial cells by asbestos. *Am. J. Respir. Cell Mol. Biol.* 17, 265–271.
- Hansen, K., Mossman, B., 1987. Generation of superoxide ($\text{O}_2^{\cdot-}$) from alveolar macrophages exposed to asbestiform and nonfibrous particles. *Cancer Res.* 47, 1681–1686.
- Health Effects Institute-Asbestos Research, 1991. Asbestos in Public and Commercial Buildings: A Literature Reviewed Synthesis of Current Knowledge. Health Effects Institute, Cambridge, MA.
- Janssen, Y., Driscoll, K., Howard, B., Quinlan, T., Treadwell, M., Barchowsky, A., Mossman, B., 1997. Asbestos causes translocation of p65 protein and increases NF-kappa B DNA binding activity in rat lung epithelial and pleural mesothelial cells. *Am. J. Pathol.* 151, 389–401.
- Janssen, Y., Heintz, N., Marsh, J., Borm, P., Mossman, B., 1994. Induction of c-fos and c-jun proto-oncogenes in target cells of the lung and pleura by carcinogenic fibers. *Am. J. Respir. Cell Mol. Biol.* 11, 522–530.
- Klein, C., 1993. Rocks, minerals and a dusty world, In: Guthrie, G.D., Mossman, B. (Eds.), *Health Effects of Mineral Dusts*. Washington, DC, pp. 7–59.
- Marsh, J.P., Mossman, B.T., 1988. Mechanisms of induction of ornithine decarboxylase activity in tracheal epithelial cells by asbestiform minerals. *Cancer Res.* 48, 709–714.
- Mossman, B., Bignon, J., Seaton, A., Corn, M., Gee, J., 1990. Asbestos: scientific developments and implications for public policy. *Science* 247, 294–301.
- Mossman, B., Churg, A., 1998. State-of-the-Art: mechanisms in the pathogenesis of asbestosis and silicosis. *Am. J. Respir. Crit. Care Med.* 157, 1666–1680.
- Mossman, B., Gee, J.B.L., 1989. Asbestos related disease. *N. Engl. J. Med.* 320, 1721–1730.
- Mossman, B., Sesko, A., 1990. In vitro assays to predict the pathogenicity of mineral fibers. *Toxicology* 60, 53–61.
- Mossman, B.T., Begin, R., 1989. Effects of Mineral Dusts on Cells, NATO ASI Series on Cell Biology. Springer-Verlag, Berlin.
- National Research Council, 1984. Asbestiform Fibers: Nonoccupational Health Risks. National Academy Press, Washington, DC.
- Oehlert, G.W., 1991. A reanalysis of the Stanton et al. pleural sarcoma data. *Environ. Res.* 54, 194–205.
- Palekar, L.D., Spooner, C.M., Coffin, D.L., 1979. Influence of crystallization habit of minerals on in vitro cytotoxicity. *Ann. N.Y. Acad. Sci.* 330, 673–686.
- Sesko, A., Mossman, B., 1989. Sensitivity of hamster tracheal epithelial cells to asbestiform minerals modulated by serum and by transforming growth factor beta 1. *Cancer Res.* 49, 2743–2749.
- Shukla, A., Gulumian, M., Hei, T., Kamp, D., Rahman, Q., Mossman, B., 2003. Multiple roles of oxidants in the pathogenesis of asbestos-induced diseases. *Free Radic. Biol. Med.* 34, 1117–1129.
- Veblen, D.R., Wylie, A.G., 1993. Mineralogy of amphiboles and 1:1 layer silicates, in: Guthrie, G.D., Mossman, B. (Eds.), *Health Effects of Mineral Dusts*. Washington, DC, pp. 61–137.
- Woodworth, C., Mossman, B., Craighead, J., 1983. Induction of squamous metaplasia in organ cultures of hamster trachea by naturally occurring and synthetic fibers. *Cancer Res.* 43, 4906–4912.
- Wylie, A., Skinner, H., Marsh, J., Snyder, H., Garzone, C., Hodgkinson, D., Winters, R., Mossman, B., 1997. Mineralogical features associated with cytotoxic and proliferative effects of fibrous talc and asbestos on rodent tracheal epithelial and pleural mesothelial cells. *Toxicol. Appl. Pharmacol.* 147, 143–150.
- Wylie, A.G., Virta, R.L., Segreti, J.M., 1987. Characterization of mineral population by index particle: implication for the Stanton hypothesis. *Environ. Res.* 43, 427–439.
- Zanella, C., Posada, J., Tritton, T., Mossman, B., 1996. Asbestos causes stimulation of the ERK-1 mitogen-activated protein kinase cascade after phosphorylation of the epidermal growth factor receptor. *Cancer Res.* 56, 5334–5338.
- Zanella, C., Timblin, C., Cummins, A., Jung, M., Goldberg, J., Raabe, R., Tritton, T., Mossman, B.T., 1999. Asbestos-induced phosphorylation of epidermal growth factor receptor is linked to c-fos expression and apoptosis. *Am. J. Physiol. (Lung Cell Mol. Physiol.)* 277, L684–L693.

Rapporteur's Report Session 5: Experimental animal and epidemiological studies of asbestos and non-asbestos tremolite including ingestion studies: Bertram Price

Paper 1: Risk of gastrointestinal cancers from inhalation and ingestion of asbestos, John F. Gamble

Selikoff suggested the hypothesis that asbestos exposure is causally associated with increased risk of gastrointestinal (GI) cancers in an early study of insulation workers. In this paper, John Gamble reports on his extensive review and reanalysis studies that address the relationship between asbestos exposure and GI cancers. The purpose of the review was to evaluate the association between asbestos exposure and risks of stomach, colorectal, colon, and rectal cancers separately.

Gamble evaluated exposure–response (E–R) relationships using surrogate exposure methods “because few individual studies of GI cancer have reported exposure–response analyses.” The principal asbestos exposure surrogates are: (1) the rate ratio (RR) for lung cancer; and (2) the percent of mesothelioma among exposed workers. Analyzing SMRs for GI cancers from individual studies versus the risk of lung cancer and mesothelioma provides crude estimates of E–Rs for asbestos exposure and GI cancer. Briefly, Gamble justifies the surrogate approach as follows:

- Asbestos exposure causes lung cancer and mesothelioma and the risks are dependent on the level of exposure.
- Higher risks of lung cancer and mesothelioma are associated with higher asbestos exposures in the worker cohort studies.
- Therefore, using SMRs for GI cancers from individual studies and stratifying by risk of lung cancer and mesothelioma provides crude estimates of E–R for asbestos exposure and GI cancer. Mesothelioma risk is considered the better indicator since asbestos exposure is the best known/most common cause of mesothelioma; smoking does not appear to increase the risk of mesothelioma, so the mesothelioma risk is relatively unconfounded by smoking or other factors. On the other hand, a major cause of lung cancer is smoking, so the

lung cancer SMR might be overestimated (biased) because of higher smoking among asbestos-exposed workers than among the comparison group.

Gamble found that E–R trends based on the surrogate asbestos exposure methods were not consistent and the strengths of associations were weak or non-existent. Gamble summarized results for the four cancers he analyzed as follows:

For stomach cancer the data show a consistent pattern of weak associations with a high proportion of SMRs less than 1.0. There are no biological gradients using surrogate exposure estimates and a consistent lack of E–R in the few individual studies where a gradient was assessed.

For colorectal cancer, the weight of evidence suggests asbestos is not a cause because there is a consistent lack of associations in external comparisons and lack of E–R using surrogate exposures as well as individual-level assessments. When there are associations, they are weak and not related to surrogates of exposure.

For colon cancer, the analysis provides similar relationships to those observed for colorectal cancer, but with somewhat less data and greater heterogeneity in the risk estimates. The strength of the association is consistently weak. Of the two statistically significant findings, one has a risk ratio significantly less than 1.0 and the other a risk ratio significantly greater than 1.0, but neither of these statistically significant findings is related to surrogate exposures.

For rectal cancer, because of consistently weak associations and lack of any apparent biological gradient, the available evidence does not support the hypothesis that asbestos exposure is a cause.

The report “Asbestos: Selected Cancers” published by the National Academy of Sciences (NAS) in 2006 was an

assessment, among other things, of the hypothesis of a causal relationship between asbestos and stomach cancer and between asbestos and colorectal cancer. Gamble completed his review before the NAS report was published and the NAS report did not refer to Gamble's work. Many of the studies analyzed by Gamble were also analyzed in the NAS review. The NAS committee concluded that the evidence is *suggestive but not sufficient* to infer a causal relationship between asbestos exposure and stomach cancer or between asbestos exposure and colorectal cancer. A comparison and synthesis of Gamble's methods and results with the methods and results of the NAS report may further illuminate the hypothesis of asbestos causality for digestive system cancers.

The next three papers in Session 5 address the health risk of exposure to non-asbestiform amphibole particles (cleavage fragments) that has been the subject of intense debate for more than 20 years. The papers in this session address three approaches for analyzing the disease-causing potential of non-asbestiform amphiboles: studies of worker cohorts; animal studies; and cellular studies. Each paper is a review of research completed through the first few years of the 21st century. Taken together the conclusions from these reviews indicate that exposure to non-asbestiform amphiboles is not associated with the same level of health risk as exposure to asbestiform amphiboles, and non-asbestiform amphiboles are an unlikely cause of asbestos-related cancer.

Notwithstanding the conclusions presented in the three review papers in this section, in February 2007 NIOSH published *Asbestos and Other Mineral Fibers: A Roadmap for Scientific Research*, which, among other things, revisits the cleavage fragment debate. NIOSH described the *Roadmap* as a first step in a science reappraisal effort, which includes NIOSH's current understanding of occupational exposure and toxicity issues concerning asbestos and other mineral fibers. The *Roadmap* outlines a research program intended to address three strategic goals including the development of "a broader understanding of the important determinants of toxicity for fibers and fiber-like cleavage fragments."

The three papers in this session were not publically available for review by NIOSH during the preparation of its *Roadmap*. However, the reference lists for the *Roadmap* and the three papers in this session contain a number of articles in common. It would be of some interest to understand the divergence of opinions; specifically NIOSH concluding that a broader understanding of the toxicity of cleavage fragments is needed and the authors contributing to the current session concluding that non-asbestiform amphiboles (cleavage fragments) are an unlikely cause of asbestos-related disease.

Paper 2: An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments, John F. Gamble and Graham W. Gibbs

This paper reports on an in-depth review conducted to assess whether amphibole cleavage fragments pose the same risk of lung cancer and mesothelioma characteristic of

amphibole asbestos fibers. The authors identified three groups of workers exposed to non-asbestiform amphiboles: two groups exposed to grunerite (Homestake gold miners and taconite miners) and one group exposed to industrial talc containing non-asbestiform tremolite and anthophyllite in St. Lawrence County, NY. Positive controls (cohorts exposed to asbestiform amphiboles) and negative controls (cohorts exposed to the mineral, e.g. talc that does not contain amphiboles) were employed to refine the analysis of exposure-response trends for the non-amphibole cohorts. The authors' analysis goes beyond simply relating the occurrence of lung cancer cases and mesothelioma cases to measures of exposure. They address and account for the effects of smoking among lung cancer cases and latency periods for mesothelioma cases. The authors reported that cohorts exposed to non-asbestiform amphiboles had no excesses of lung cancer or mesothelioma. Similar results were observed in the negative control groups in contrast to the excess risks of asbestos-related disease found in the asbestos cohorts. The authors conclude that the weight of evidence fully supports a finding that non-asbestiform amphiboles do not increase the risk of lung cancer or mesothelioma.

Paper 3: A review of carcinogenicity studies of asbestos and non-asbestos tremolite and other amphiboles, John Addison and Ernest E. McConnell

The authors have conducted a thorough review of published studies, including studies they conducted, that exposed animals to mineral particles. Their analysis of the studies addressed two questions: (1) to what extent is there support for the hypothesis that the carcinogenicity of fibers depends upon morphology; and (2) to what extent do short mineral fibers contribute to carcinogenicity in humans. The authors discuss the limitations of injection and implantation studies for projecting human health outcomes associated with inhalation of mineral particles. They conclude that there is very little evidence of carcinogenicity from exposure of animals to mineral fragments or short fibers formed from normal prismatic amphibole minerals. No positive carcinogenicity has been found with any experiment using non-asbestos amphibole dust. Furthermore, when genuinely short fiber amphibole asbestos has been used in inhalation or injection experiments they have also been shown to have no carcinogenic properties. Evidence from experiments with other mineral fibers suggests that fibers in excess of 20 μm and with diameters less than 1 μm are necessary to cause cancer. The authors assert that cleavage fragments of amphiboles rarely if ever are found with these critical dimensions.

Paper 4: Assessment of the pathogenic potential of asbestiform vs. non-asbestiform particulates (cleavage fragments) in *in vitro* (cell or organ culture) models and bioassays, Brooke T. Mossman, Ph.D

As an introduction, the paper explains that cleavage fragments of respirable dimensions have generally proven

nonpathogenic in animal studies. The author explains, therefore, that little data exists on assessing well-characterized preparations of cleavage fragments in *in vitro* models. *In vitro* studies have been used historically to compare the effects of different types of minerals on cells or organ (explant) cultures. Regardless of cell type, asbestos fibers, in comparison to a variety of other nonpathogenic, synthetic or naturally occurring fibers (glass, cellulose, etc.) or particles, have been most biologically active in these models. *In vitro* studies have shed light on the complex features of bioreactive minerals that may be important in reactions with cells and their ability to cause disease. Because they are much more inexpensive than animal testing, cell and or-

gan culture models have been suggested as screening tools for new synthetic fibers. However, uncertainties associated with *in vitro* work and minerals exist; these uncertainties are presented and discussed in the paper.

The paper describes research and results, including studies conducted by the author, involving three models: tracheal explant cultures; cell types of lung or pleural origin; and non-respiratory cells. The author states that the results represent a large body of work showing that non-asbestiform minerals are less potent than asbestos fibers in a number of *in vitro* bioassays. In most assays, these cleavage fragments or non-fibrous minerals are virtually inactive.

Identification and enumeration of asbestos fibers in the mining environment: Mission and modification to the Federal Asbestos Standard

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Abstract

Since the promulgation of the first Federal Asbestos Standard by the Occupational Safety and Health Administration in 1972, other federal agencies have modified the standard to better carry on their own unique missions. The instruments used to identify and measure asbestos, the sampling protocol, and the criteria used to define asbestos, have been modified to some degree. The Mine Safety and Health Administration regulates and controls asbestos dust in the mining and mineral commodity industries. However, crushed stone and processed ores contain mineral fragments that are frequently difficult to distinguish from asbestos. Mineral nomenclature, instruments for particle analysis, and sampling strategy must be accommodated to some degree to make asbestos control workable and meaningful. Precedent in other agencies has made consideration of these changes possible. Newly identified amphibole asbestos minerals have further complicated the agency's regulatory charge. Changes in its Asbestos Standard are now being considered. Crushed taconite ore in the Eastern Mesabi highlights many of these issues.

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Keywords: Amosite; Grunerite asbestos; Crocidolite; Riebeckite asbestos; Tremolite asbestos; Actinolite asbestos; Winchite asbestos; Richterite asbestos; Arfvedsonite asbestos; Fluor-edenite asbestos; Asbestos defects; Cleavage fragment; Mineral habit; Mesabi amphiboles

1. Introduction

The first national Asbestos Standard in the United States was promulgated through the Occupational Safety and Health Administration in 1972. The permanent standard, which superseded the initial emergency standard, was set at 5 fibers per milliliter of air (as a time-weighted average) in concert with a “hierarchy of controls”. Exposure excursions were permitted as well. The membrane filter technique was introduced as a means of dust collection and asbestos was defined as one of six minerals (one serpentine mineral, and five amphibole minerals) that exhibited specific morphological characteristics. A fiber was

defined on the basis of particle length (greater than 5 μm , less than 100 μm) exhibiting an aspect ratio (length-to-width) of 3:1 or greater. The instrument for asbestos assay was the phase-contrast light optical microscope employed at 430 $\times$ magnification.

For mines, mills, fabrication plants, and places where asbestos-containing products were known to be present, handled, processed, or manipulated, the protocol and prescribed counting strategy in the standard could be successfully employed. Long, thin, objects were assumed to be asbestos without requiring further habit characterization or more positive mineral identification.

The Food and Drug Administration (FDA) followed OSHA's technique and protocol in their studies of “asbestos” in talc but found the identification criteria and assay instrumentation oversimplified and flawed. The issue

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central to their problems was the nature of the mineral itself. Were the recognized amphibole particles asbestiform or the result of crushing, i.e., cleavage fragments? The agency hosted a conference in 1976 in Pennsylvania State University where analytical issues and protocols were described and discussed. [It is noted that the resulting publication carried many non-government laboratory protocols for talc analysis, e.g., Langer et al., 1977]. The Environmental Protection Agency (EPA) in their asbestos pollution studies of the outdoor ambient air found the OSHA instrumental protocol limited for their purposes. This agency concluded that transmission electron microscopy (TEM) was required. Modification of their Asbestos Standard followed and TEM became the analytical instrument in the agency's indoor air pollution studies as well.

Mine Safety and Health Administration (MSHA) especially experienced difficulties in the application of the OSHA Asbestos Standard. The mining and mineral-processing environments were replete with fragments of minerals, especially fragments of minerals with the same amphibole name that appeared in the Federal Asbestos Standard. These difficulties were articulated in the MSHA proposed rule changes governing their asbestos exposure limit and instrumentation in 2005. Nowhere has this problem been highlighted better than along the Eastern Mesabi Range where the nature of the amphiboles in the taconite iron-ores has been an issue for more than 35 years. MSHA has proposed modifications to their existing asbestos protocol, including instrumentation change from light to analytical electron microscopy.

2. Early Asbestos Standard

The Occupational Safety and Health Act of 1970 established both the National Institute for Occupational Safety and Health (NIOSH) and the Occupational Safety and Health Administration (OSHA) (Sunstein, 2002). The organizations were to collaborate in developing regulations regarding control of biologically active agents (toxic substances) in the workplace. The standards were to be based on existing science (NIOSH), epidemiological findings concerning the health experience of exposed workers (NIOSH), and available exposure data (OSHA). Asbestos was at the top of the OSHA "to be regulated" list. Data from consuming industries indicated hazards existed beyond those included in historical data sets (i.e., asbestosis). Of special concern were malignancies, which were occurring in numbers greater than those expected among the working populations studied. With asbestos applications on the rise, the size of the exposed populations increased correspondingly.

At the time of OSHA's creation, there were approximately 5 million workplaces in the United States employing about 90 million workers. OSHA replaced the authority covered under existing federal and state legislation. The entire US workforce at that time experienced about 2 million injuries per year resulting in lost time, with about 14 thousand deaths. The figure for workers developing

chronic disease was placed at about 100 thousand per year (Froines, 1996). The Asbestos Standard was to be devised to protect against pneumoconiosis (asbestosis), not malignancies. The issue facing OSHA was daunting.

Prior to this time, in the 1960s, the USPHS began to refocus on workplace exposure to asbestos. Its industrial hygiene group in Cincinnati was evaluating the British protocol for fiber assay. The United States at that time was using the midget impinger collection device and measuring total visible particulates in a dust cloud with bright field light optical microscopy. The British Occupational Hygiene Society's position was that asbestosis was caused by the inhalation of asbestos fiber and not total dust (fiber plus particulates). The membrane filter protocol was beginning to be used for work place assay and came to be adopted in the US following a period of evaluation (read the membrane filter evaluation in the UK in Holmes, 1965 and US protocol in Edwards and Lynch, 1968). An overview concerning asbestos exposure, measured indices, and their biological relationships are outlined in Lynch et al. (1970).

Based on information provided by the BOHS, and the British asbestos industry, the USPHS agreed that the most convenient and practical exposure index was the greater than 5 μm fiber length. The asbestos-containing dust cloud was collected on a membrane filter and the phase-contrast optical microscope employed at a magnification of 430 $\times$ was the recommended analytical tool for fiber count (Edwards and Lynch, 1968). The experience of the British industrial hygiene community, beginning in 1931, provided both the technical protocol and its rationale (Addingley, 1965; Addingley, 1966). The dust cloud was noted to vary among the asbestos consuming industries; included among the variables were fibers with differing length and width distributions, fiber number per mass unit of dust, and a variable ratio of fiber to particulate. The OSHA assay protocol, like all others, provided only an index of exposure.

The measurement of solid particles dispersed in a stable aerosol has always been an issue within the industrial hygiene community (Glenn and Craft, 1987). Drilling and blasting in mines, and crushing and grinding in mills, produce particulates that are visible to submicroscopic in size. Instruments for assay must necessarily vary.

The OSHA efforts regarding the development of a new Asbestos Standard replaced the provisions in the Walsh-Healey Public Contracts Act of 1960, the McNamara-O'Hara Act of 1966, and the Construction Safety Act of 1969. These regulatory attempts required employers engaged in business with the Federal Government to comply with "safety and health standards" developed by the Bureau of Labor Standards in the US Department of Labor (US DOL) (Froines, 1996). As Froines pointed out, these efforts were fragmented and, in retrospect, largely inadequate. Importantly, these acts did not specifically cover coal, metal and non-metal mines, railroads, or atomic energy installations.

OSHA supplanted the right of states to follow their own Asbestos Standard if they allowed higher exposures than

permitted in the Federal Standard. The states themselves had dissimilar standards. Dreessen et al.'s (1938) tentative standard of 5 million particles per cubic foot (mppcf) of air was adopted by many states but South Carolina's standard was 15 mppcf of air during this same time period. Some might regard this as ironic as both Drs. Lynch and Smith, pathologists in the state medical school in Charleston, were the first pathologists in the US to report primary carcinoma of the lung (found during routine autopsy) in two "asbestos-silicosis" cases who had worked in a Charleston South Carolina asbestos textile plant (Lynch and Smith, 1935). Their case report was prescient as lung cancer was to become the most prevalent malignancy found in excess among asbestos-exposed workers.

The OSHA emergency Asbestos Standard of 1971 was set at 12 fibers per milliliter of air based on data provided by the ACGIH. The data came from the US American Conference of Governmental Industrial Hygienists (ACGIH), the organization that focused on a permissible asbestos exposure level (then called a threshold limit value or TLV) for general industry in the United States since 1946 (Selikoff, 1980; Brownson, 1998). [Parenthetically, the ACGIH never had regulatory authority or enforcement power for any of its recommendations during the time period 1946–1972.] An overview of the mechanisms required for the establishment of a new standard or the modification of an existing standard was outlined by NIOSH (1976).

Changes in major provisions within the Asbestos Standard occurred over more than 35 years (Selikoff and Lee, 1978). Among the important modifications was the lowering of the permissible exposure level (PEL) over time. Other than the recognition of the differences in degree of hazard of cleavage fragments and their asbestiform analogues in the Asbestos Standard in 1994, the *minerals* regulated since 1971 have remained the same. The mineral names are given in Table 1. The instrument used for environmental assay has remained the same as well, i.e., the phase-contrast optical microscope (PCOM). However, other federal agencies, through necessity, have changed many of the analytical details of the Asbestos Standard to fit their unique charges and responsibilities.

3. The nature of asbestos

Assume that the name asbestos confers upon a mineral a specific set of physical properties (Speil and Leineweber, 1969; Ampian, 1976; Virta, 2001). Assume further that the six minerals cited in the OSHA Asbestos Standard usually display these specific properties to greater or lesser degree:

- They occur in nature as fibers. They require no unique processing or manipulation to produce fiber. Milling separates fiber from host rock, increases the concentration of fiber downstream in the process, and opens fiber bundles.
- The fibers are all polyfilamentous (they are composed of bundles of smaller, more narrow units called fibrils).

Table 1
Minerals regulated as asbestos in the United States

Asbestos name in the OSHA Asbestos Standard	Mineral as defined by crystal structure	Asbestos name in mineral literature
Chrysotile	Serpentine	Chrysotile
Actinolite ^a	Amphibole	Actinolite asbestos
Amosite	Amphibole	Grunerite asbestos
Anthophyllite ^a	Amphibole	Anthophyllite asbestos
Crocidolite	Amphibole	Riebeckite asbestos
Tremolite ^a	Amphibole	Tremolite asbestos

The earliest regulatory nomenclature did not reference specific mineral habit ("asbestos") for actinolite, anthophyllite or tremolite. The minerals with separate names were grunerite asbestos (*amosite*) and riebeckite asbestos (*crocidolite*). OSHA specifically identifies six minerals as asbestos as these six were recognized as commercial asbestos fibers by the USBM since the 1930s (see Bowles, 1937).

Two additional amphibole asbestos minerals have been found in ore deposits in the United States, asbestiform winchite and asbestiform richterite. Both have been identified in association with vermiculite ore in Libby, Montana and both are thought to be present in some talc deposits in the Death Valley region of California. They have never been, nor are they now, listed in any US Agency Asbestos Standard.

^a These minerals are not distinguished on the basis of habit. It is inferred by their appearance on the OSHA asbestos list that they are asbestos in habit.

- Fiber bundles may be broken open (disaggregated) upon mechanical manipulation.
- Fibers removed from an ore seam often display splayed, unraveled, fiber ends.
- Most fibers are flexible to some degree (depending on the fiber type); some fibers may be woven into a mineral fabric.
- All fibers display high tensile strength that is diameter dependent.
- All fiber types possess stability in extreme chemical and thermal environments (stability in acidic or alkaline environments depends on fiber type as well).

Many of these properties are described in Speil and Leineweber (1969) and Virta (2001). The US Bureau of Mines (USBM) (Campbell et al., 1980) further characterized properties of commercial asbestos and non-fibrous tremolite. The USBM materials were prepared and characterized for use by the National Toxicology Program in its bioassay systems. The above "properties" are gross descriptives. However, the asbestos minerals possess a set of crystallographic anomalies, most recently described in Verkoeteren and Wylie (2002), which impart the mineral fiber with anomalous properties. These are produced by an abundance of crystal defects that are useful in distinguishing asbestos from non-asbestos mineral analogues. They are also important in explaining the biological properties of the asbestos dust cloud.

The six minerals that appeared in the 1972 standard were enumerated in early USBM documents, e.g., in Bowles' (1937) report on asbestos. Interestingly, Bowles listed additional amphibole mineral names in the asbestos listing but were not considered commercially important, but as

“mineral curiosities”. Hornblende asbestos was among them. Today, the hornblende asbestos might be one of several newly described amphibole asbestos types, among them fluor-edenite asbestos, winchite asbestos, and richterite asbestos.

Based on the crystallographic properties that define asbestos, i.e., high frequency of closely spaced twinning and Wadsley defect structures involving chain dimensions (Chisholm, 1973; Hutchison et al., 1975; Champness et al., 1976; Franco et al., 1977; Harlow et al., 1985), fault offsets between adjacent twin planes (Seshan and Wenk, 1976; Crawford, 1980), disorientation of unit fibrils parallel to the long fiber axis (Franco et al., 1977), the amphibole asbestos minerals form thin fibrils within the fiber's composite bundle, with the fibrils randomly oriented around the *c*-axis. These features are summarized in Dorling and Zussman (1987) and Langer et al. (1991).

The non-asbestiform analogues also have twin plane defects as well as chain-width errors (Veblen et al., 1977). However, the frequency of occurrence of the defects is less and distances over which they repeat are far greater, as found by Harlow et al.'s (1985) study for amosite. But as noted in Verkouteren and Wylie, a fibrous particle lying on a twin plane can occur in non-asbestiform amphiboles as well.

The asbestos minerals that are mechanically manipulated generate dust particles that are longer and thinner and disproportionately higher in particle number as compared to non-asbestos minerals manipulated in the same way. This is especially true when comparing the non-asbestos analogues of the same mineral (Harlow et al., 1985; Wylie, 1988). Compare the mineral populations in Figs. 1 and 2. Consider for comparison a 1- μ m diameter orthorhombic prism and a 0.125- μ m diameter orthorhombic fibril with their *c*-crystallographic axes the same length. The same mass of mineral in the 1- μ m prism would crush to yield 64 particles with 32 times greater surface area (chemical potential) if reduced to the sizes cited above.

Are these size differences biologically important? The smaller fibril diameter would form a more stable aerosol, would possess greater inhalation potential, could penetrate the pulmonary architecture to the pleura more easily, and could “hit” many more cell targets. The state of aggregation of dust controls its biological potential (Langer and Nolan, 1986).

Because of their unusual crystallographic properties, the asbestos minerals may be distinguished from their non-asbestiform analogues based on their anomalous optical behavior in polarized light (Wylie, 1979, 1988). Verkouteren and Wylie cautioned that the application of these characteristics would depend on the crystal symmetry of the particle, the size of the unit fibrils, and their crystallographic orientation with respect to the optical axis of the instrument. The physical behavior of these materials, and their resulting population following crushing, is therefore useful in assisting the analyst in distinguishing asbestiform from non-asbestiform mineral populations. It is when sin-

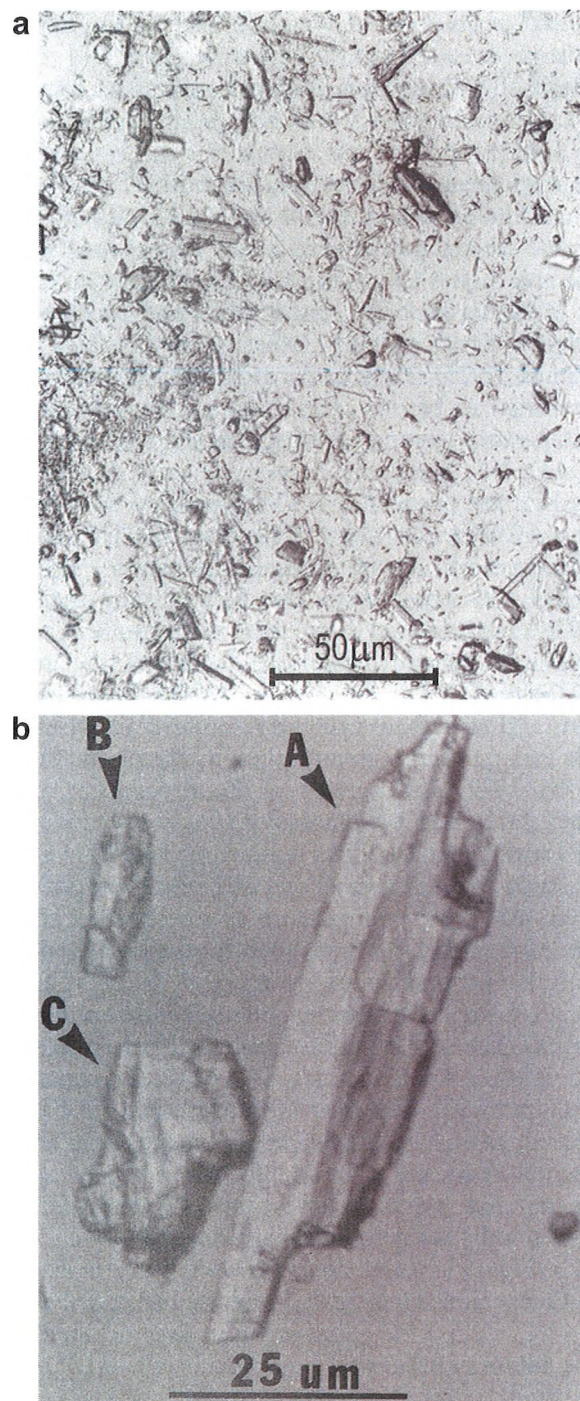


Fig. 1. (a) Tremolite fragments in crushed industrial grade talc. X-ray diffraction analysis of the “talc” specimen in (a) indicated that it was composed of ~35% tremolite. This photomicrograph was obtained in plane-polarized light (PLM). Particles of tremolite are cleavage fragments with aspect ratios varying from less than 3:1 to 20:1. The habit of tremolite is non-fibrous (non-asbestiform). Note some high aspect ratio fibers present as well, with optical properties consistent with talc and talc-anthophyllite intergrowths. Magnification marked. (b) Tremolite separated from crushed carbonate (marble) sand. The photomicrograph was obtained with Hoffman optics. The image is of three tremolite fragments, two (fragments A and B) displaying prismatic cleavage surfaces characteristic of the amphibole mineral group. The habit of tremolite is non-fibrous (non-asbestiform). Magnification marked. From Langer et al. (1991).

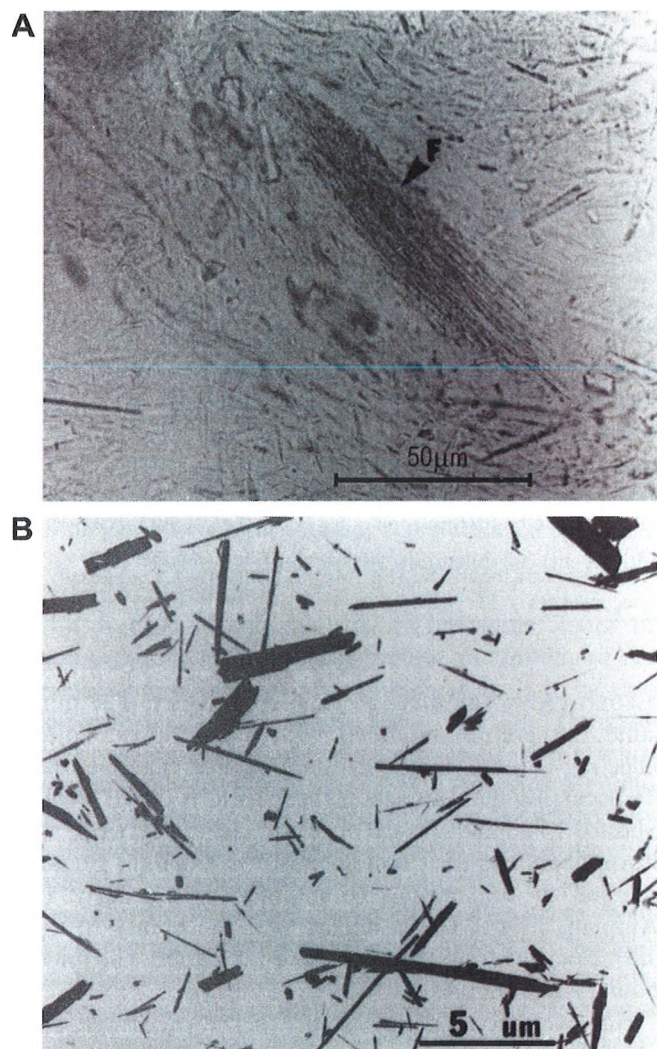


Fig. 2. (A) Tremolite asbestos fiber from a Mediterranean whitewash (stucco). Tremolite asbestos fiber bundle as seen in plane-polarized light (PLM). The fiber bundle is approximately 110 μm in length. From Langer et al. (1991). Some tremolite cleavage fragments are visible in the field as well. (B) Tremolite asbestos fibrils disaggregated from a fiber bundle by ultrasound as seen by transmission electron microscopy. Population of particles dominated by high aspect ratio amphibole fibrils.

gle isolated particles appear on a filter, or in a sample obtained in environments in which asbestos is not expected or thought to occur, that identification uncertainty increases.

4. Examples of Asbestos Standard accommodations

The US Environmental Protection Agency (EPA) required an assay instrument capable of resolving small airborne particulates in the ambient environment whose size was for the most part well beyond the resolution of the light microscope. The instrument of choice was found to be the transmission electron microscope (TEM). With time the TEM necessarily became an analytical instrument with chemistry and crystallographic data incorporated into the identification protocol. The diagnostics for single isolated

particles were initially described in Langer and Pooley (1973).

The EPA eventually modified its counting protocol for the indoor air environment of schools so that fibers greater than 0.5 μm in length were included in the assay count with the length-to-width aspect ratio of the fibers increased from 3:1 to 5:1 and greater. It was noted at that time that these changes had limited biological relevance.

Historically, the EPA required a modified collection technique for airborne particulates. The initial studies of the asbestos content of ambient air in large urban areas required collection of particulates from very large volumes of air (many cubic meters) onto membrane filters. The first high volume filters were glass fiber pads that on consideration were deemed inappropriate for a fiber assay. The collection filters, made of methyl cellulose ester (MCE), were found overloaded with combustion products that obscured any asbestos that might be present. The direct technique for filter preparation (used in the workplace setting) was abandoned through necessity and the indirect filter preparation technique was introduced for environmental assay. The modified protocol required ashing or burning off of organic matter, re-dispersion of the heat-resistant residual particulate load into a material capable of forming a support film substrate for the particulates, sizing fiber length on the TEM screen, TEM identification of single, isolated particles, and assay based on conversion of fiber dimensions to mass. Fiber concentrations were expressed as mass units, nanograms of mineral per cubic meter of air. The fiber found in virtually every instance was chrysotile that exhibited a reasonably constant fibril diameter rendering mass calculation relatively straight forward (Nicholson and Pundsack, 1973). The rationale used by the investigators at that time (to report mass rather than fiber number and concentration) was based on concern that the manipulation of the filter load introduced fiber number artifact, and to a lesser extent fiber size artifact. Conversion to fiber units from units defining millions of particles per cubic foot of air was attempted in a range of occupational and environmental settings later in time (NIOSH, 1976).

5. Work hazards in mines and mills pre MSHA

Concern regarding mining hazards in the United States evolved in the latter part of the nineteenth century. Important legislation by Congress followed the Monongah Coal Mine disaster of 1907 in which 362 miners were killed in an explosion. That year no less than 20 mine disasters were reported with the loss of 4192 lives. Accidents, fires, explosions and other agents and factors accounted for the loss of life. Mining for mineral commodities and metals, other than coal, claimed many lives as well. That year, Congress established the US Bureau of Mines charged with mine safety.

The Federal Coal Mine Safety Act (1952) followed the Centralia disaster in Illinois and important legislative modifications to the Act was passed in 1969, spurred by the

MSHA on the national level, and state authorities on the local level). Low-temperature iron silicate minerals that characterized the Biwabik Iron-Formation southwest of the Virginia bend had been transformed (“destroyed”) through contact and regional metamorphism with the Duluth Gabbro into high temperature assemblages that included amphiboles.

The taconite iron ore in the eastern Mesabi is principally magnetite and quartz, which is admixed with grunerite (grunerite-cummingtonite), actinolite, hornblende, riebeckite and a sodium hornblende. Amphibole intergrowths are common as well. These minerals are not homogeneously distributed through the stratigraphic members that define the Biwabik, but range in concentration outward with distance from the thermal and metasomatic effects of the gabbro body. These minerals have elemental compositions that are similar making it difficult to distinguish actinolite from some common forms of iron-rich hornblende (Gundersen and Schwartz, 1962). There are also issues involved in distinguishing between thin, acicular, grunerite cleavage fragments and grunerite asbestos (amosite). Descriptions of these mineral assemblages and characterization issues are in Gundersen and Schwartz (1962) and French (1968).

Matters changed dramatically in 1973. Crushed taconite ore examined by industrial hygienists was found to contain amphibole minerals a fraction of which were morphologically fibrous. Some argued that these particulates conformed to the then existing Federal definition of asbestos. In particular grunerite and actinolite fibers were present with morphological traits that OSHA used to define asbestos—greater than 5 μm in length with an aspect ratio of 3:1 or greater. These fragments were eventually dumped as tailings (in slurry form) into a containment dam in Lake Superior following iron mineral extraction in a wet-magnetic process in Silver Bay, Minnesota (Langer et al., 1979). Questions arose as to whether these objects were actually asbestos and whether they constituted a health threat to those who breathed the air in Silver Bay or drank the water drawn from Lake Superior.

Analyses performed in the ESL-Mt. Sinai in New York were eventually published as several reports. The last of these reports, based on particle analysis by analytical electron microscopy (Langer et al., 1979), concluded that the number of particles of grunerite that were indistinguishable from amosite constituted only a very small fraction of the total amphibole particle population. Many of the papers presented at this symposium outline some of the difficulties involving mineral characterization encountered by analysts in their efforts to distinguish between asbestos fiber and cleavage fragment.

9. MSHA and its current Asbestos Standard

Based on the health outcome among the mine and mill workers at Libby Montana, MSHA has proposed changes to its existing Asbestos Standard. [Many of these same

issues were observed during EPA’s investigation into the contamination of Lake Superior with taconite tailings in the early 1970’s (Langer et al., 1979).] In 2005, MSHA proposed that its PEL be lowered from 2.0 f/ml of air to the current OSHA level of 0.1 f/ml of air, its excursion level lowered to 1.0 f/ml of air over a 30 min time period, and the instrument of assay, to improve mineral identification, would be the analytical transmission electron microscope. If followed, the ability to distinguish amphibole asbestos fibrils from cleavage fragments would be greatly improved.

As if the MSHA community did not have enough to consider, there has been a spate of new “asbestos” minerals found in places both inside and outside of the United States that have been implicated as possible agents of disease. Fibrous balangeroite and fibrous carlosturanite have been identified within the chrysotile deposits of the Piedmont in Italy where they are considered agents of disease causation (mesothelioma) rather than the chrysotile itself (Astolfi et al., 1991). Fluor-edenite asbestos (Bruni et al., 2006) and arfvedsonite asbestos (Shcherbakov et al., 2001), both minerals with amphibole structures, have been described. Arfvedsonite asbestos was mined and exploited in Russia in the northern Urals. The fluor-edenite occurs in a volcanic aggregate in Sicily and its fibers have been found in the lung tissue study of a person who died of pleural mesothelioma in the local town. The arfvedsonite asbestos is suspected as an agent in mesothelioma causation in the Urals (Shcherbakov et al., 2001). Winchite asbestos and richterite asbestos have been identified in ore deposits in the United States.

10. Conclusions and recommendations

Among its many responsibilities, MSHA is concerned with protecting the mineral industry workforce from the hazards associated with asbestos exposure. The agency recognizes that some amphiboles that are common rock forming minerals may, under special geological circumstances, form asbestos deposits. The agency also recognizes that when the massive non-asbestiform varieties of these common minerals are crushed during mining and milling a portion of the mineral particle population closely resembles asbestos. These are cleavage fragments and they have been found to possess far less biological activity than their asbestiform analogues. [OSHA removed cleavage fragments from their Asbestos Standard in 1994.] MSHA has grappled with this problem since its inception and analytical and counting strategies were modified to assist in distinguishing between habits of the same mineral.

Polarized light microscopy has occasionally been substituted for PCM in that it yields information regarding habit. Single crystal fragments (cleavage fragments) may be easily distinguished from polyfilamentous fiber bundles (asbestos) (Wylie, 1979). The PLM, when used with immersion oils, is a powerful analytical tool in the hands of an experienced microscopist (Crane, 1992). The anomalous optical behavior of amphibole asbestos, as compared to its non-asbestos

analogues, was described in Wylie (1979). The crystallographic defects of the amphibole asbestos minerals, and the random orientation of the fibrils in the ab plane, impart parallel to sub parallel extinction to fibers and only two indices of refraction parallel to and across fiber length.

Single isolated fragments with widths or thicknesses greater than 1 μm are probably cleavage fragments (see the population data in Wylie, 1988). If the sample is amphibole asbestos, the population of particles will invariably contain fibrils with thicknesses much less than this value (Table 3). Langer et al.'s data (1974) obtained on the UICC Reference Asbestos standards also highlighted this characteristic of the asbestos minerals.

The MSHA assay for asbestos has in the past included X-ray diffraction analysis. In the continuous scan mode, with a high intensity X-ray source, minor concentrations of minerals may be detected, identified and quantified. This technique has been used in the Salt Lake City laboratory. Mineral identification is obtainable but morphological habit is not. The technique is rapid and assisted with powder diffraction file search programs.

MSHA proposed in 2005 that the analytical transmission electron microscopy (ATEM) be used as an assay tool. The microscopist would count only phase-contrast equivalent fibers, i.e., those greater than 0.2 μm in diameter. Mineral identification would be greatly improved with acquisition of structural data by means of electron diffraction studies.

Although the issue has been informally discussed, the chemistry of some amphiboles may be used to distinguish amphibole asbestos fibrils from thin diameter cleavage fragments. The aluminum content of some amphiboles has been considered important in this regard (Verkouteren and Wylie, 2002; Ross et al., 2008). An issue that has emerged is whether or not energy dispersive spectrometry can resolve the chemical differences as well as the standard probe crystal spectrometry technique.

The use of an analytical transmission electron microscope allows the assay for fibers that cannot be visualized by any light microscopy method (lying below the constraints imposed by physical nature of light, i.e., Abbe's Law).

ATEM also provides information regarding principal planes of separation of the amphibole particles. The ability of the analyst to obtain an interpretable diffraction pattern on an amphibole fragment requires a sufficiently thin plate that will allow passage of the diffracted electrons through the crystal (Whittaker, 1979; Dorling and Zussman, 1987). Thin twin planes, which lie on the (100) twin plane surface, are frequently expressed by amphibole asbestos fibrils. Diffraction nets and the planes on which fragments of minerals lie have been used to distinguish amphibole asbestos fibrils from cleavage fragments (Langer et al., 1991).

It might well be that each and every mineral deposit, processing mill, and aggregate quarry in the United States will require investigation for the presence or absence of

asbestos. This was suggested by Walter Banks' report to the USBM (1980). The USEPA had also become involved in these issues because of asbestos fiber entering the general environmental. [It is important to note that the precursor organization to the US EPA initiated the studies concerning asbestos air pollution in major urban centers well before this time. The National Air Pollution Control Administration (NAPCA) held international conferences pertaining to air pollutants in the environment and their health effects. This writer presented a paper, co-authored with Dr. Selikoff, concerning chrysotile air pollution in New York City, chrysotile asbestos in the lungs of NYC residents (Langer and Selikoff, 1971).] With the Federal Asbestos Standard as a guide, the mining and mineral communities will continue to make modifications to its own standard.

MSHA might explore the implementation of a tier-system of analysis. Investigations have found that the study of asbestos begins with the determination of its presence or absence on a field inspection scale. The ATEM is not a universal solution to the identification problem. It is important to note that the number of laboratories equipped with ATEMs is limited, the personnel with the expertise required for the interpretation of diffraction data are small, the ability of real-time workplace assay (based on acquisition of all three particle diagnostics) for worker protection does not exist. Consider the time required for specimen preparation and analysis.

The report by Van Gosen et al. (2004) concerning the talc deposits in the Death Valley region of California found that the presence of amphibole minerals could be predicted on the basis of the geological process and rock type. Field survey by a member of MSHA's geology staff appears a reasonable first step. Is serpentine present? Are amphiboles present? The determination of mineral habit is a separate issue.

Conflict of Interest

The author declares that he has no conflict of interest.

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References

- Addingley, C.G., 1965. Dust measurement and monitoring in the asbestos industry. *Ann NY Acad Scis.* 132, 298–305.
- Addingley, C.F., 1966. Asbestos dust and its measurement. *Ann. Occup. Hyg.* 9, 73–82.
- Ampian, S.G., 1976. Asbestos minerals and their nonasbestos analogues. In: Asher, I.M., McGrath, P.P. (Eds.), *FDA Symposium on Electron Microscopy of Microfibers*. Pennsylvania State University, 23–25 August 1976. US Government Printing Office, Washington, DC, pp. 12–27.
- Astolfi, A., Fubini, B., Giamello, E., Volante, M., Belluso, E., Ferrais, G., 1991. Asbestiform minerals associated with chrysotile from the western

- Alps (Piedmont–Italy): chemical characteristics and possible related toxicity. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanisms of Fibre Carcinogenesis*. NATO ASI Series. Life Sciences, vol. 223, pp. 269–283.
- Banks, W., 1980. Asbestiform and/or Fibrous Minerals in Mines, Mills and Quarries. US Department of Labor, US Bureau of Mines, Information Report IR1111, pp. 1–25.
- Bandli, B.R., Gunter, M.E., Twamley, B., Foit Jr., F.F., Cornelius, S.B., 2003. Optical, compositional, morphological, and x-ray data on eleven particles of amphibole from Libby, Montana, USA. *Can. Mineral.* 41, 1241–1253.
- Bowles, O., 1937. Asbestos. United States Bureau of Mines Bulletin, vol. 403. US Government Printing Office, pp. 1–92.
- Brownson, R.D., 1998. Current and historical American asbestos regulations. *Monaldi Arch. Chest Dis.* 53 (2), 181–185.
- Bruni, B.M., Pacella, A., Mazziotti Tagliani, S., Gianfagna, A., Paoletti, L., 2006. Nature and extent of the exposure to fibrous amphiboles in Biancavilla. *Sci. Total Environ.* 370, 9–16.
- Campbell, W.J., Blake, R.L., Brown, L.L., Cather, E.E., Sjöberg, J.J., 1977. Selected silicate minerals and their asbestiform varieties. Mineralogical definitions and identification characterization. Information Circular 8751. USBM, US Department of the Interior. 56 p.
- Campbell, W.J., Huggins, C.W., Wylie, A.G., 1980. Chemical and physical characterization of amosite, chrysotile, crocidolite and non-fibrous tremolite for oral ingestion studies by the National Institute of Environmental Health Sciences. US Department of the Interior, US Bureau of Mines, Report of Investigations RI 8452, pp.1–63.
- Champness, P.E., Cliff, G., Lorimer, G.W., 1976. The identification of asbestos. *J. Microsc.* 108, 231–249.
- Chisholm, J.E., 1973. Planar defects in fibrous amphiboles. *J. Mater. Sci.* 8, 475–483.
- Crane, D.T., 1992. Polarized light microscopy of asbestos. OSHA Sampling and Analytical Methods ID-191, 21 October 1992, pp. 1–31.
- Crawford, D., 1980. Electron microscopy applied to studies of the biological significance of defects in crocidolite asbestos. *J. Microscopy* 120, 181–192.
- Dorling, M., Zussman, J., 1987. Characteristics of asbestiform and non-asbestiform calcic amphiboles. *Lithos* 20, 469–489.
- Dreessen, W.C., Dallavalle, J.M., Edwards, T.I., Miller, J.W., Sayers, R.R., 1938. A study of asbestosis in the asbestos textile industry. USPHS Public Health Bulletin No. 241, August 1938.
- Edwards, G.H., Lynch, J.R., 1968. The method used by the US Public Health Service for enumeration of asbestos dust on membrane filters. *Ann. Occup. Hyg.* 11, 1–6.
- Federal Register, 1992. OSHA Hearings. The Federal Asbestos Standard: 57 (10) June 8 1992, p. 24310.
- Franco, M.A., Hutchison, J.L., Jefferson, D.A., Thomas, J.M., 1977. Structural imperfection and morphology of crocidolite (blue asbestos). *Nature* 266, 520–521.
- French, B.M., 1968. Progressive Contact Metamorphism of the Biwabik Iron Formation, Mesabi Range, Minnesota. *Minn. Geol. Survey Bulletin* 45. University of Minnesota Press, Minneapolis, pp. 1–93.
- Froines, J.R., 1996. Occupational regulatory approaches. In: Harber, P., Schenker, M.B., Balmes, J.R. (Eds.), *Occupational and Respiratory Disease*. Mosby Pub., NY, pp. 899–921.
- Glenn, R.E., Craft, B.F., 1987. Air sampling for particulates. In: Mechant, J.A., Boehlecke, B.A., Taylor, G., Pickett-Harner, M. (Eds.), *Occupational Respiratory Diseases*. DHHS—OSHA, pp. 69–82.
- Gundersen, J.N., Schwartz, G.M., 1962. The geology of the metamorphosed Biwabik Iron-Formation, eastern Mesabi District, Minnesota. *Minn Geol Survey Bulletin* 43. University of Minnesota Press, Minneapolis, pp. 1–139.
- Harlow, G.E., Kimball, M.R., Dowty, E., Langer, A.M., 1985. Observations on amosite/grunerite dusts. In: Park, W.C., Hausen, D.M., Hagni, R.D. (Eds.), *Proc. 2nd Int. Congress Applied Mineralogy in the Minerals Industry*. The Metallurgical Soc. of AIME, pp. 1147–1157.
- Holmes, S., 1965. Developments in dust sampling and counting techniques in the asbestos industry. In: *Biological Effects of Asbestos*. Ann. NY Acad. Sci. 132, 288–297.
- Hutchison, J.L., Irusteta, M.C., Whittaker, E.J.W., 1975. High-resolution electron microscopy and diffraction studies of fibrous amphiboles. *Acta Crystallogr.* A31, 794–801.
- Langer, A.M., Selikoff, I. J., 1971. Chrysotile asbestos in lungs in residents of New York City. In: Englund, H.M., Beery, W.T. (Eds.), 2nd International Clean Air Congress, Washington, DC. Academic Press, New York, pp. 161–165.
- Langer, A.M., Pooley, F.D., 1973. Identification of single asbestos fibers in human tissues: IARC Sci. Publ. No. 8. In: Bogovski, P., Gilson, J., Timbrell, V., Wagner, J.C. (Eds.), *International Agency for Research on Cancer*, Lyon, France, pp. 119–125.
- Langer, A.M., Mackler, A.D., Pooley, F.D., 1974. Electron microscopical investigation of asbestos fibers. *Environ. Health Perspect.* 9, 63–80.
- Langer, A.M., Rohl, A.N., Wolff, M.S., Klimentidis, R., Shirey, S.B., 1977. Review of current techniques for the analysis of fibers in talc. In: Asher, I.M., McGrath, P.P. (Eds.), *Electron Microscopy of Microfibers*. FDA Symposium Pennsylvania State University. US Government Printing Office, Washington, DC, pp. 28–33.
- Langer, A.M., Maggiore, C.M., Nicholson, W.J., Rohl, A.N., Rubin, I.B., Selikoff, I.J., 1979. The contamination of Lake Superior with amphibole gangue minerals. *Ann. NY Acad. Sci.* 330, 549–572.
- Langer, A.M., Nolan, R.P., 1986. The properties of chrysotile asbestos as determinants of biological activity. In: Wagner, J.C. (Ed.), *Accomplishments in Oncology* 1(2), 30–51.
- Langer, A.M., Nolan, R.P., Addison, J., 1991. Physico-chemical properties of asbestos as determinants of biological potential. In: Liddell, D., Miller, K. (Eds.), *Mineral Fibers and Health*. CRC Press, Boca Raton, Florida, pp. 211–228.
- Leake, B.E., Woolley, A.R., Arps, C.E.S., Birch, W.D., Gilbert, M.C., Grice, J.D., Hawthorne, F.C., Kato, A., Kisch, H.J., Krivovichev, V.G., Linthout, K., Laird, J., Mandarino, J.A., Maresch, W.V., Nickel, E.H., Rock, N.M.S., Schumacher, J.C., Smith, D.C., Stephenson, N.C.N., Ungaretti, L., Whittaker, E.J.W., Youzhi, G., 1998. Nomenclature of amphiboles. *Mineralogical Association of Canada. Can. Mineral.* 36, 49–76.
- Lynch, J.M., Smith, W.A., 1935. Pulmonary asbestosis: carcinoma of the lung in asbestos-silicosis. *Am. J. Cancer* 24, 56–64.
- Lynch, J.R., Ayer, H.E., Johnson, D.L., 1970. The interrelationships of selected asbestos exposure indices. *Am. Ind. Hyg. Assoc. J.*, 598–604.
- Meeker, G.P., Bern, A.M., Brownfield, I.K., Lowers, H.A., Sutley, S.J., Hoepen, T.M., Vance, J.S., 2003. The composition and morphology of amphibole from the Rainy Creek Complex, near Libby, Montana. *Am. Mineral.* 88, 1955–1969.
- Nicholson, W.J., Pundsack, F.L., 1973. Asbestos in the environment. In: Bogovski, P., Gilson, J., Timbrell, V., Wagner, J.C. (Eds.), *Biological Effects of Asbestos*. IARC Sci. Publ. No. 8, International Agency for Research on Cancer, Lyon, France, pp. 126–131.
- NIOSH, 1976. Revised Recommended Asbestos Standard. US DHEW PHS CDC. US Govt. Printing Office, Washington, DC, pp. 96.
- Ronov, A.B., Yaroshevsky, A.A., 1969. Chemical composition of the earth's crust. In: Hart, P.J. (Ed.), *The Earth's Crust and Upper Mantle*. Geophys. Monogr., vol. 13. American Geophys. Union, Washington, DC, pp. 37–57.
- Ross, M., Langer, A.M., Nord, G.L., Nolan, R.P., Lee, R.J., Van Orden, D., Addison, J., 2008. The mineral nature of asbestos. *Regul. Toxicol. Pharmacol.* 52, S26–S30.
- Selikoff, I.J., Lee, D.H.K., 1978. *Asbestos and Disease*. Academic Press, New York, pp. 1–549.
- Selikoff, I.J., 1980. Occupational respiratory diseases. In: Last, J.M. (Ed.), *Public Health and Preventive Medicine*, Maxcy-Rosenau Eleventh Edition. Appleton-Century-Crofts, NY, pp. 568–598.
- Seshan, K., Wenk, H.R., 1976. Identification of faults in asbestos minerals and application to pollution studies. In: Bailey, G.W. (Ed.), *Proc. Electron Microscope Soc. America, 34th Ann. Meeting*. Claitors Publ., Baton Rouge, Louisiana, pp. 616–617.

- Shcherbakov, S.V., Kashansky, S., Domnin, S.G., Kogan, F.M., Kozlov, V., Kochelayev, V.A., Nolan, R.P., 2001. The health effects of mining and milling chrysotile: the Russian experience. In: *The Health Effects of Chrysotile Asbestos: Contribution of Science to Risk-Management Decisions*. Can. Mineral., Spec. Publ. 5, 187–198.
- Speil, S., Leineweber, J.P., 1969. Asbestos minerals in modern technology. *Environ. Res.* 2, 166–208.
- Sunstein, C.R., 2002. *Risk and Reason. Safety, Law, and the Environment*. Cambridge University Press, New York, pp. 1–342.
- Van Gosen, B.S., Lowers, H.A., Sutley, S.J., Gent, C.A., 2004. Using the geologic setting of talc deposits as an indicator of amphibole asbestos content. *Environ. Geol.* 45, 920–939.
- Veblen, D.R., Buseck, P.R., Burnham, C.W., 1977. Asbestiform chain silicates: new minerals and structural groups. *Science* 198, 359–366.
- Verkouteren, J.R., Wylie, A.G., 2002. Anomalous optical properties of fibrous tremolite, actinolite, and ferro-actinolite. *Am. Mineral.* 87, 1090–1095.
- Virta, R.L., 2001. Some facts about asbestos. US Geological Survey Fact Sheet FS-012-01, March 2001. US Government Printing Office, Washington, DC, pp. 1–4.
- Whittaker, E.J.W., 1979. Mineralogy, chemistry and crystallography of amphibole asbestos. In: Ledoux, R.C. (Ed.), *Short Course in Mineralogical Techniques of Asbestos Determination*. Mineralogical Association of Canada, pp. 1–34.
- Wylie, A.G., 1979. Optical properties of the fibrous amphiboles. In: *Health Hazards of Asbestos Exposure*. Ann. NY Acad. Sci., 330, 611–619.
- Wylie, A.G., 1988. Discriminating amphibole cleavage fragments from asbestos: rationale and methodology. In: *Proceedings VIIth International Pneumoconiosis Conference*, Pittsburgh, pp. 1065–1069.

An overview of the risk of lung cancer in relation to exposure to asbestos and of taconite miners

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Abstract

Exposure–response relationships between the relative risk of lung cancer and quantitative measures of exposure to asbestos are available from a number of epidemiological studies. Meta-analyses of these relationships have been published by Lash et al. (1997) [Lash, T.L., Crouch, E.A.C., Green, L.C., 1997. A meta-analysis of the relation between cumulative exposure to asbestos and relative risk of lung cancer. *Occup. Environ. Med.* 54, 254–263] and Hodgson and Darnton (2000) [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]. In this paper, the risks derived in these meta-analyses have been compared. Lash et al., concentrated on process and found that the risk of lung cancer increased as the asbestos is refined by processing. Hodgson and Darnton concentrated on fibre type and found that the risk was highest for exposure to amphibole asbestos (crocidolite and amosite), lowest for chrysotile and intermediate for mixed exposure. Some of the differences between the conclusions from the two meta-analyses are a consequence of the choice of studies included. The range of asbestos types included in the studies in the analysis of Hodgson and Darnton was wider than that in Lash et al., enabling differences between fibre types to be analyzed more readily. There are situations where occupational exposure to chrysotile asbestos has shown no detectable increase in risk of lung cancer. Taconite miners have shown no increased risk of mortality due to lung cancer.

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Keywords: Mesothelioma; Amosite; Grunerite; Taconite; Crocidolite; Tremolite; Anthophyllite; Winchite; Risk assessment; Etiology

1. Introduction

The association of lung cancer with exposure to asbestos has been beyond dispute for more than 50 years following the epidemiological study of asbestos textile workers reported by Doll (1955). In the following decades there have been many studies of particular situations reported, and in some quantitative data on exposure have been available allowing consideration of exposure–response relationships. The more recent work on quantitative exposure–response relationships has enabled risk estimates to be derived including estimates due to environmental exposure

based on direct study in addition to extrapolation from occupational situations.

2. Meta-analyses and measures of effect

Meta-analyses of exposure–response relationships between the relative risk (RR) of lung cancer and cumulative exposure to asbestos (d) have been published by Lash et al. (1997) and by Hodgson and Darnton (2000). Lash et al. included 15 cohorts, and fitted the linear dose–response model within each cohort:

$$RR = A(1 + kd)$$

where A is an intercept term, that is the relative risk for zero exposure, k is the slope, or increase in relative risk

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per unit of exposure, and d is the cumulative exposure (fibres/ml years).

Hodgson and Darnton included 17 cohort studies in their analysis and fitted the average dose–response effect estimated for each cohort. They defined an average effect as

$$R_L = 100 * (SMR - 1) / X,$$

where SMR is the ratio of observed to expected lung cancer deaths for the whole cohort, and X is the mean exposure (fibres/ml years) of the cohort. R_L is the percentage excess risk per unit of exposure and was taken as the slope of the relationship

$$RR = 1 + R_L d / 100.$$

The intercept, relative risk for zero exposure, was taken as 1.

The relationships used in the two meta-analyses were similar, but a difference was that since Lash et al. fitted exposure–response relationships within each study, they were able to estimate the intercept, as well as the slope, of the relationship. In contrast Hodgson and Darnton included studies where only the average exposure was available and thus were forced to assume that the intercept was unity in order to estimate the slope. Although this seems a reasonable choice, since zero exposure clearly gives no associated increase in risk, the intercept is not necessarily equal to unity because the reference population, from which death rates are taken for the calculation of expected deaths, may not correspond exactly to that of the workers in a study due to differences in other local factors or in smoking levels (Liddell and Hanley, 1985).

The relationship between the slopes used in the two meta-analyses is

$$R_L = 100k$$

Another way of expressing the slope is by its inverse which gives the cumulative exposure at which the relative risk is doubled

$$D(RR = 2) = 100 / R_L = 1 / k.$$

Lash et al. (1997) concentrated their analysis on process (Table 1) and concluded that the risk of lung cancer increases as the asbestos is refined by processing (mining/milling—cement products—textiles/manufacturing). They found that adding a multiplicative term for predominantly chrysotile use added no significant information. The estimate of the multiplicative term was 0.19 (95% confidence interval 0.02–1.6).

Table 1

Estimates of k (increase in relative risk per fibre/ml year of exposure) by industry from the meta-analysis of Lash et al. (1997)

	k	$D(RR = 2)$
All studies	0.0026	385
Mining and milling	0.00025	4000
Cement products	0.0034	294
Manufacturing/textiles	0.0077	130

Table 2

Values of R_L (the percentage excess risk per fibre/ml year of exposure) by fibre type from the meta-analysis of Hodgson and Darnton (2000)

	R_L	$D(RR = 2)$
Crocidolite	4.2	24
Amosite	5.2	19
Mixed (amphibole/chrysotile)	0.47	213
Chrysotile	0.062	1613

Hodgson and Darnton (2000) concentrated on fibre type (Table 2) and found the highest risk for the amphiboles, crocidolite and amosite, a much lower risk for chrysotile, and an intermediate risk for exposure to mixed amphibole and chrysotile.

3. Comparison of “Lash et al.” and “Hodgson and Darnton”

There were 11 studies in common to the two meta-analyses so that the values may be compared:

1. Paterson insulation factory processing amosite (Seidman et al., 1986);
2. Ontario asbestos cement plant using chrysotile and crocidolite (Finkelstein, 1984);
3. Pennsylvania textile factory processing mainly chrysotile and amosite (McDonald et al., 1983);
4. Vöcklabruck asbestos cement factory using chrysotile and crocidolite (Neuberger and Kundi, 1990);
5. Rochdale male textile factory workers processing mainly chrysotile but with some crocidolite (Peto et al., 1995);
6. Johns Manville retirees working in production or maintenance with mixed exposures to chrysotile, crocidolite and amosite (to 1980, Enterline et al., 1987; to 1973, Henderson and Enterline, 1979);
7. New Orleans asbestos cement (plant 1) using mainly chrysotile, small amounts of amosite and later crocidolite irregularly (Hughes et al., 1987);
8. South Carolina male textile factory workers using chrysotile (Dement et al., 1994);
9. Connecticut friction products plant processing chrysotile (McDonald et al., 1984);
10. Quebec chrysotile miners and millers (to 1992, Liddell et al., 1997; to 1989, McDonald et al., 1993);
11. Balengero chrysotile miners (Piolatto et al., 1990).

The values of R_L from both meta-analyses are given in Table 3 and Fig. 1. Excluding those studies with a zero value of R_L in either analysis, the range of values is of over two orders of magnitude. For six of the studies the two meta-analyses give fairly similar values. For Paterson (study 1) and Ontario (study 2), Hodgson and Darnton give a value about 7 times higher than Lash et al. For both of these studies Lash et al. estimated the value of A as over 3, that is, they found a high rate of lung cancer for zero exposure. The opposite occurred for Pennsylvania (study

Table 3

Values of R_L (the percentage excess risk per fibre/ml year of exposure) from the meta-analyses of Hodgson and Darnton and Lash et al. for the 11 cohort studies in common to the two analyses

		Value of R_L	
		H&D	Lash et al.
1	Paterson insulation factory	5.8	0.88
2	Ontario asbestos cement plant	5.2	0.69
3	Pennsylvania textile factory	0.8	3.6
4	Vöcklabruck asbestos cement factory	0.45	0
5	Rochdale textile factory (men)	0.37	0.41
6	Johns Manville retirees	0.21	0.25
7	New Orleans asbestos cement (plant 1)	0	0.066
8	South Carolina textile factory (men)	4.6	2.4
9	Connecticut friction products plant	0.8	0
10	Quebec chrysotile miners and millers	0.06	0.02
11	Balengero chrysotile miners	0.03	0.02

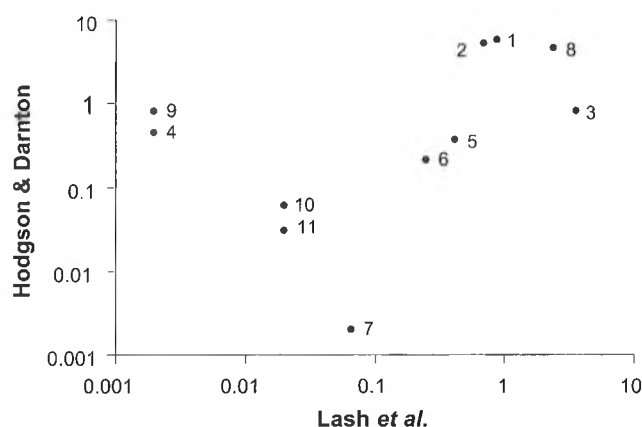


Fig. 1. Values of R_L (the percentage excess risk per fibre/ml year of exposure) from the meta-analyses of Hodgson and Darnton and Lash et al. for the 11 cohort studies in common to the two analyses. The points are labelled by the study number (text and Table 3). (To facilitate plotting on the log scales, the three zero values have been plotted at 0.002.)

3), where Lash et al. give a value over 4 times higher than Hodgson and Darnton, and the value of A was only 0.5. For Connecticut (study 9) and Vöckalbruck (study 4), Hodgson and Darnton give moderate values of R_L whilst Lash et al. give zero. Again for both of these Lash et al. found a high lung cancer rate for zero exposure (1.6 and 2.1). For New Orleans (study 7) Hodgson and Darnton found no excess risk overall but Lash et al. found an exposure–response relationship within the study.

For the Ontario study there were only 21 lung cancer deaths and examination of the plot of the exposure–response data shows no clear pattern of effect. No reliable exposure–response relationship may be fitted (the 95% confidence interval given by Lash et al. for R_L is from 0 to 25) and it is not surprising that the two methods differ.

Some of the differences between the conclusions from the two meta-analyses are a consequence of the choice of studies included. Lash et al. included two mining populations, both chrysotile mining. Consequently once the industry was taken into account there was no possibility of

Table 4

Mortality due to lung cancer at Ferodo friction products factory (Newhouse and Sullivan, 1989)

	Lung cancer deaths		
	Observed	Expected	SMR
Men	229	221.4	103
Women	12	21.1	57
Total	241	242.5	99

finding a fibre type effect within this industry. In contrast Hodgson and Darnton included the two chrysotile mines but also crocidolite mines in Australia and South Africa, and an amosite mine in South Africa. Of the 19 sub-groups analysed by Hodgson and Darnton there were 3 with exposure to crocidolite, 2 to amosite, 5 to chrysotile, and 9 with mixed exposure to chrysotile and amphibole. Lash et al. included 15 cohorts but for two an exposure–response relationship could not be fitted and another was of a vermiculite mine with tremolite in the ore. Of the other 12, 1 involved exposure to amosite, 4 to chrysotile, and 7 mixed exposure to chrysotile and amphibole, of which 5 were predominantly to chrysotile. There was less variation in fibre type between the studies included by Lash et al., compared with those included by Hodgson and Darnton, and consequentially there was less opportunity to explore differences in effect between fibre types.

Chrysotile has been processed with no detectable increase in lung cancer, as shown by the study of workers manufacturing friction products at the Ferodo factory in the north of England (Table 4) (Newhouse and Sullivan, 1989).

4. Problems in estimating exposure

There are uncertainties in the measurements of exposure, arising from changes in instrumentation, problems in conversion of results obtained using old types of instruments to modern methods, a lack of systematic sampling in early years, and consequentially the use of “guestimates” of early exposure (Rogers, 2001). A consequence of this is that exposure–response relationships which may be qualitatively valid within a study because relative exposure levels are reasonable, can be invalid outside the study because absolute exposure levels are incorrect.

5. Taconite and cummingtonite–grunerite

A cohort study of miners at the Reserve Mining Company was reported by Higgins et al. (1983). Five thousand seven hundred and fifty-one workers employed for a year or more between 1952 and 1976 were followed up until 1976 (a maximum of 24 years). For all causes of death there were 298 deaths, compared with an expected number of 344 (SMR = 87). For mortality due to respiratory cancer, there were 15 observed deaths, compared with an expected num-

ber of 18 (SMR = 84). These include deaths soon after exposure, and after 15 years latency, there were 103 deaths (expected 115, SMR = 90) including 8 respiratory cancer deaths (expected 7.9, SMR = 102). There were no apparent exposure–response trends.

Another cohort study of Minnesota taconite miners and millers was reported by Cooper et al. (1988, 1992), in which the mortality experience of 3431 men employed for 3 months or more between 1947 and 1958 in either the Erie or Minntac operations was compared with both US and Minnesota white males death rates. The Minnesota death rates are less than the US rates for all causes and for respiratory cancer. The observed and expected mortality to 1983 and 1988 for deaths due to all causes and respiratory cancer, compared with expected numbers calculated using Minnesota rates, are shown in Table 5.

Mortality due to respiratory cancer was analysed by time since first exposure (Table 6). There was clearly no excess mortality due to respiratory cancer after a 10-year latency period.

Three studies of miners exposed to cummingtonite–grunerite at the Homestake mine in South Dakota have been reported. These studies overlap so that the results are not independent. The first study was of 440 men employed for at least 5 years underground by 1960 (Gillam et al., 1976). Observed mortality was compared with expected mortality calculated using the death rates for South Dakota. In the period 1960–1973, there were 71 deaths due to all causes (expected 53, SMR 134), and 10 deaths due to respiratory cancer (expected 2.7, SMR 370). Analysing mortality due to respiratory cancer with respect to time since first exposure, the SMR was greater in the first 20 years than later.

The second study was of 1321 men employed for at least 21 years by 1973 (McDonald et al., 1978). Expected deaths were calculated using South Dakota rates. Between 1937 and 1973, there had been 631 deaths (expected 550, SMR 115). For respiratory cancer there were 17 deaths (expected

16.5, SMR 103). The results were examined in terms of exposure–response relationships. Clear relationships were found for pneumoconiosis and respiratory tuberculosis, but not for respiratory cancer.

The third study was 3328 men employed underground for at least a year during 1940–1964 (Brown et al., 1986). Deaths occurring in the period 1941–1977 were analysed, with expected deaths calculated using US rates. There were 861 from all causes (expected 769, SMR 112). After 15 years latency there were 41 deaths due to lung cancer (expected 40, SMR 102). Restricting this analysis to those with 10 or more years of exposure there were 21 deaths due to lung cancer (expected 18.2, SMR 115).

Taking all these studies there is no convincing evidence of an increase in deaths due to lung cancer in the Homestake miners. The excess reported by Gillam et al. (1976) is not supported by the other two studies, and attributing this excess to the exposure in the mine is questionable given that the relative risk was higher within the first 20 years since first exposure than later. The results have been reviewed by Ross et al. (1993).

6. Environmental exposure

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 fibres/ml years, with a plausible range from 5 to 125 fibres/ml years, equivalent to 105 fibres/ml working years, after converting to the measure used for occupational exposure over 40 h a week.

There had been 71 deaths due to lung cancer, compared with 71.4 expected from rates in unexposed areas. Predictions based on an EPA model ($RR = 1 + 0.01 \text{ cumexp}$) gave a relative risk of 2.05 and 146 lung cancer deaths (excess of 75). Clearly the EPA model was inappropriate. Using the risk estimate for Quebec mining and milling from Hodgson and Darnton ($RR = 1 + 0.0006 \text{ cumexp}$) gives a relative risk of 1.06 predicting 76 lung cancer deaths (excess of 5). The risk estimate for this industry from Lash et al. is $RR = 1 + 0.00025 \text{ cumexp}$ which gives a relative risk of 1.025 predicting 73 lung cancer deaths (excess of 2). Thus, both these estimates are in accord with the observed number of 71 when taking account of chance variation. However, for such a low relative risk, whether there is any actual excess or not, is not detectable.

7. Risk at low exposure

A linear dose–response relationship between relative risk of lung cancer and exposure is often used (“a widely accepted and scientifically reasonable compromise rather than an established scientific principle” (HEI, 1991)). Non-linearity and/or the existence of a threshold at low levels of exposure are very difficult, perhaps impossible, to detect from epidemiological data (Liddell, 2001). Depending on the potency of the agent low exposures

Table 5

Mortality of taconite miners and millers at the Erie and Minntac operations in Minnesota, compared with Minnesota death rates (Cooper et al., 1988, 1992)

	All causes			Respiratory cancer		
	Observed	Expected	SMR	Observed	Expected	SMR
To 1983	801	820	98	41	48	85
To 1988	1058	1165	91	65	67	97

Table 6

Mortality due to respiratory cancer of taconite miners and millers at the Erie and Minntac operations in Minnesota, compared with Minnesota death rates by time since first exposure (Cooper et al., 1992)

Time since first exposure	Observed	SMR
–10 years	7	145
10–19 years	12	75
20+ years	46	99

can result in risks that are so low that they are undetectable from epidemiological studies.

8. Summary

Asbestos exposure increases lung cancer incidence. There are situations where occupational exposure to chrysotile asbestos has shown no detectable increase in risk. Taconite miners have shown no increased risk of mortality due to lung cancer.

Conflict of Interest

Dr Berry has given opinions in asbestos-related disease compensation cases. Dr Gibbs has appeared as an expert witness in asbestos-related litigation cases. Several years ago Dr Gibbs provided consultation services to an organization representing the Taconite Industry.

References

- 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.F., Winn, D.M., Shy, C.M. (Eds.), *Silica, Silicosis, and Cancer*. Praeger, New York, pp. 335–350.
- Camus, M., Siemiatycki, J., Meek, B., 1998. Nonoccupational exposure to chrysotile asbestos and the risk of lung cancer. *N. Engl. J. Med.* 338, 1565–1571.
- 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.
- 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.
- Dement, J.M., Brown, D.P., Okun, A., 1994. Follow-up study of chrysotile asbestos textile workers: cohort mortality and case-control analyses. *Am. J. Ind. Med.* 26, 431–447.
- Doll, R., 1955. Mortality from lung cancer in asbestos workers. *Br. J. Ind. Med.* 12, 81–86.
- Enterline, P.E., Hartley, J., Henderson, V., 1987. Asbestos and cancer: a cohort followed up to death. *Br. J. Ind. Med.* 44, 396–401.
- Finkelstein, M.M., 1984. Mortality among employees of an Ontario asbestos-cement factory. *Am. Rev. Respir. Dis.* 129, 754–761.
- Gillam, J.D., Dement, J.M., Lemen, R.A., Wagoner, J.K., Archer, V.E., Blejer, H.P., 1976. Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. *Ann. NY Acad. Sci.* 271, 336–344.
- HEI, 1991. Asbestos in public and commercial buildings: a literature review and synthesis of current knowledge. Health Effects Institute–Asbestos Research, Cambridge, MA, pp. 6–31.
- Henderson, V.L., Enterline, P.E., 1979. Asbestos exposure: factors associated with excess cancer and respiratory disease mortality. *Ann. NY Acad. Sci.* 330, 117–126.
- Higgins, I.T.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., Weill, H., Hammad, Y.Y., 1987. Mortality of workers employed in two asbestos cement manufacturing plants. *Br. J. Ind. Med.* 44, 161–174.
- Lash, T.L., Crouch, E.A.C., Green, L.C., 1997. A meta-analysis of the relation between cumulative exposure to asbestos and relative risk of lung cancer. *Occup. Environ. Med.* 54, 254–263.
- Liddell, D., 2001. The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure (letter to editor). *Ann. Occup. Hyg.* 45, 329–335.
- Liddell, F.D.K., Hanley, J.A., 1985. Relations between asbestos exposure and lung cancer SMRs in occupational cohort studies. *Br. J. Ind. Med.* 42, 389–396.
- Liddell, F.D.K., McDonald, A.D., McDonald, J.C., 1997. The 1891–1920 cohort of Quebec chrysotile miners and millers: development from 1904 and mortality to 1992. *Ann. Occup. Hyg.* 41, 13–36.
- McDonald, A.D., Fry, J.S., Woolley, A.J., McDonald, J.C., 1983. Dust exposure and mortality in an American factory using chrysotile, amosite, and crocidolite in mainly textile manufacture. *Br. J. Ind. Med.* 40, 368–374.
- 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, J.C., Gibbs, G.W., Liddell, F.D.K., McDonald, A.D., 1978. Mortality after long exposure to cummington-grunerite. *Am. Rev. Respir. Dis.* 118, 271–277.
- McDonald, J.C., Liddell, F.D.K., Dufresne, A., McDonald, A.D., 1993. The 1891–1920 birth cohort of Quebec chrysotile miners and millers: mortality 1976–88. *Br. J. Ind. Med.* 50, 1073–1081.
- Neuberger, M., Kundi, M., 1990. Individual asbestos exposure: smoking and mortality—a cohort study in the asbestos cement industry. *Br. J. Ind. Med.* 47, 615–620.
- Newhouse, M.L., Sullivan, K.R., 1989. A mortality study of workers manufacturing friction materials: 1941–86. *Br. J. Ind. Med.* 46, 176–179.
- Peto, J., Doll, R., Hermon, C., Binns, W., Clayton, R., Goffe, T., 1995. Relationship of mortality to measures of environmental asbestos pollution in an asbestos textile factory. *Ann. Occup. Hyg.* 29, 305–355.
- Piolatto, G., Negri, E., La Vecchia, C., Pira, E., Decarli, A., Peto, J., 1990. An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. *Br. J. Ind. Med.* 47, 810–814.
- Rogers, A., 2001. An evaluation of the exposure criteria and lung fibre burden associated with the Helsinki Criteria and its applicability to Australia. Dust Diseases Board of New South Wales Research Report, November 2001.
- Ross, M., Nolan, R.P., Langer, A.M., Cooper, W.C., 1993. Health effects of mineral dusts other than asbestos. In: Guthrie, G., Mossman, B.T. (Eds.), *Health Effects of Mineral Dusts*. Mineralogical Society of America, Washington, DC, pp. 361–407.
- 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.

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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Keywords: Mesothelioma; Amosite; Grunerite; Taconite; Crocidolite; Tremolite; Anthophyllite; Winchite; Risk estimation; Etiology

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 Thetford 5041 Asbestos 4031 Factory 708	8009 (81.9%) 4125 3331 553	38 (0.47%) 25 (0.61%) 8 (0.2%) 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

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). Yarborough (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.

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
Wittenoom	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)!	0.0130
Balangero!	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.

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 midjet 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 (Malaker 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 (Spirtas 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 tremolite 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

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

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-

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.

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 Wittenoom, 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 fluorooedenite 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, Medichem 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., Mackawa, 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.
- Malter, H.S., McLaughlin, J.K., Malter, 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 cumingtonite–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., Bufler, 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., Lillis, 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.
- Spiras, 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.

Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore

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Abstract

In the early 1970s, it became a concern that exposure to the mineral fibers associated taconite ore processed in Silver Bay, Minnesota would cause asbestos-related disease including gastrointestinal cancer. At that time data gaps existed which have now been significantly reduced by further research. To further our understanding of the types of airborne fibers in Silver Bay we undertook a geological survey of their source the Peter Mitchell Pit, and found that there are no primary asbestos minerals at a detectable level. However we identified two non-asbestos types of fibrous minerals in very limited geological locales. Air sampling useful for risk assessment was done to determine the type, concentrations and size distribution of the population of airborne fibers around Silver Bay. Approximately 80% of the airborne fibers have elemental compositions consistent with cummingtonite-grunerite and the remaining 20% have elemental compositions in the tremolite-actinolite series. The mean airborne concentration of both fiber types is less than 0.00014 fibers per milliliter that is within the background level reported by the World Health Organization. We calculate the risk of asbestos-related mesothelioma and lung cancer using a variety of different pessimistic assumptions. (i) that all the non-asbestos fibers are as potent as asbestos fibers used in the EPA-IRIS listing for asbestos; with a calculated risk of asbestos-related cancer for environmental exposure at Silver Bay of 1 excess cancer in 28,500 lifetimes (or 35 excess cancers per 1,000,000 lifetimes) and secondly that taconite associated fibers are as potent as chrysotile the least potent form of asbestos. The calculated risk is *less than* 0.77 excess cancer case in 1,000,000 lifetimes. Finally, we briefly review the epidemiology studies of grunerite asbestos (amosite) focusing on the exposure conditions associated with increased risk of human mesothelioma.

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1. Introduction

A risk assessment for the effects of fibrous particles in taconite ore is simultaneously very simple and somewhat complex. It is simple because there have been good epidemiological studies of the health of miners, workers, and nearby residents, that have been exposed to such particulates at historically higher concentrations than exist today

(Ross et al., 1993; Brunner et al., 2008; Gamble and Gibbs, 2008). No statistically significant increase in cancer risk has been found due to fibrous particulates commonly associated with taconite ore. Although sufficient time has passed to allow for the long latency commonly associated with human cancer. In the intervening years dust concentrations both in air and water have been much reduced—perhaps by a factor of 50. Since adverse effects are expected to be reduced at least as much as the concentrations although zero divided by 50 is still zero, one can estimate thereby that there will be no directly measurable risk.

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But this simple argument, while correct, is inadequate to satisfy legitimate concerns of public health authorities and of public emotions. This we see as follows. An epidemiological study of a new agent has never been accepted as sole evidence that this agent causes adverse health effects unless the probability of an adverse outcome is at least doubled. Technically this means that the Risk Ratio, or RR, must be greater than 2, if an agent has already been accepted as the cause of adverse effects at higher concentrations, then a RR as low as 1.3 has sometimes been accepted as evidence of increased risk. For example, $RR > 1.3$ has been accepted as evidence that second-hand cigarette smoke causes cancer since it is well known that cigarette smoking causes cancer. EPA has accepted a much smaller RR of 1.05 as evidence for an effect of air pollution since we know, for example, that in December 1952, over 4000 people died in London with $RR > 2$. A $RR > 1.3$ is accepted that X-rays in pregnancy can cause childhood leukemia since radiation is known to be dangerous.

But few would accept a Risk Ratio of 1.05 as evidence by itself of adverse effects. Below we estimate for residents of Silver Bay a much smaller RR of 1.0005, (risk of 4×10^{-5}) which obviously cannot be measured by direct epidemiological evidence. Yet in 1975, when risks from the taconite mines was first being seriously discussed, the US EPA was trying to regulate risks at a one in a million per lifetime level, pessimistically calculated. For lung cancer that was a Risk Ratio of 1.000013.

2. Origin of the problem

Concern about exposure to fibrous minerals at Northshore Mining Company originated when Reserve Mining Company began an effort to commercially process the taconite iron ore from the Peter Mitchell Pit. Northshore's operation is located in the eastern part of Minnesota's Mesabi Iron Range which contains vast quantities of taconite ore. Processing the ore to pellets suitable for commercial sale required more water for the wet magnetic separation than was available at the mine site and so Reserve Mining decided to move the iron ore by rail to the shore of Lake Superior and develop a processing facility at that site, i.e., Silver Bay, Minnesota. In 1948 the Army Corp of Engineers issued the required permit to Reserve Mining for disposal of the waste rock generated from the processing facility in a deep trough (900 feet) in Lake Superior off-shore from Silver Bay (Bartlett, 1980). The Northshore Mining Company began operating the Silver Bay facility and Peter Mitchell Pit in 1994.

Lake Superior supplied all of the water the facility required and the iron ore product could then be transported by ship. The initial plan called for disposing of the waste rock into Lake Superior, which would eventually reach 67,000 tons/day. Concern initially focused on the possibility that the waste rock would have long-term adverse effects on the ecology of the lake (Bastow, 1986). Also of concern was the light scattering from the fine par-

ticles suspended in the water which caused surface clouding and discoloration sometimes appearing as green water caused by the movement of the particle plume. Analysis by X-ray diffraction and transmission electron microscopy of these suspended particulates revealed the presence of particles suspended in the lake water a percentage of which were reported to be asbestiform amphiboles (Cook et al., 1974). The predominant fibrous amphibole in the water was reported to be in the same cummingtonite-grunerite series as we found in the air samples collected about 25 years later. However, we did not find the population of fibers to have morphological characteristics consistent with grunerite asbestos or any other type of amphibole asbestos. Cook et al., 1974 reported that analysis by X-ray diffraction revealed about 23% of the suspended particles in the lake were amphiboles but the type of amphibole and the percentage that were asbestiform are not reported. These early studies did not include a geological survey of the mine to identify the origin of the asbestiform fibers. Generally air and water samples from other locations were used as negative controls to determine if the levels fibers in Silver Bay were increased.

The taconite ore contains approximately 30% amphibole minerals which are a group of silicates commonly found in the earth's crust. In addition to quartz, three types of amphiboles were identified as predominantly present—hornblende, cummingtonite-grunerite and tremolite-actinolite. Amosite is the commercial name given to grunerite asbestos. Analysis of airborne fibrous particles by analytical transmission electron microscopy indicated elemental compositions indistinguishable from two amphibole minerals that can occur as asbestos, cummingtonite-grunerite and tremolite-actinolite were present meriting further consideration. At the time attention was focused on the cummingtonite-grunerite fibers and if exposures to them particularly in potable water present a risk similar to amosite asbestos where exposure to airborne dust for just one year increased the rate of gastrointestinal cancer (Selikoff et al., 1972). Whether or not the health hazards of these two types of amphiboles were the same as those of asbestos fibers was not clearly established. Of less concern was the presence of tremolite-actinolite fibers at that time little evidence of health effects existed and of least concern was hornblende which can form fibers but rarely, if ever, forms asbestos and other minerals commonly found in ambient air (Langer et al., 1979; Veblen and Wylie, 1993).

During this same time period in the early 1970s, workers with heavy occupational exposure to commercial asbestos, were found by epidemiological studies to have more gastrointestinal cancer than would normally be expected (Selikoff et al., 1972; Selikoff and Hammond, 1979). These important findings stimulated questions about the potential for the fibrous amphiboles discarded into Lake Superior to increase the risk of gastrointestinal cancer. As several communities used unfiltered water from Lake Superior for drinking, there was concern that *ingesting* fibrous particles associated with taconite could increase the risk of develop-

ing gastrointestinal cancer in the same way that the asbestos workers had increased risk from exposure to similar mineral fibers by *inhalation* (Hills, 1979). Studies indicate that the potential ingestion of these fibers did not pose the same level of risk that was affecting asbestos workers (Moore, 1978).

The grunerite asbestos workers were exposed to markedly higher concentrations airborne fiber than the workforce at Reserve Mining (Nolan et al., 1999; Ribak and Ribak, 2008). In addition the gastrointestinal tract of asbestos insulation workers had been exposed by inhalation either by directly swallowing airborne fibers or by coughing up and swallowing inhaled asbestos fibers leading to an increased risk of gastrointestinal cancer. The exposure from Lake Superior would be primarily from drinking water containing mineral fibers although concern was also expressed about the potential of inhalation exposures from the re-entrainment of fibers remaining on the floor after the water from Lake Superior used to wash them evaporated. Inhalation is a more common route of asbestos exposure and the health effects are better understood and might produce asbestos-related disease in the general population (Mason et al., 1974; Levy et al., 1976; Sigurdson et al., 1981; Sigurdson, 1983).

The findings of Selikoff (1974) properly raised the public health concern about asbestos. Workers with occupational asbestos exposures could be experiencing up to 25% excess mortality from asbestos-related diseases (Selikoff et al., 1979). Two points learned in these studies underscored the concern about the exposures in Silver Bay. Firstly, the asbestos-related cancers have a very long latency period with little, if any, disease occurring less than 20 years after first being exposed. Therefore any disease which might be associated with disposing of the waste rock in the lake would not be observable for a considerable period of time. The second concern was the build-up of fibers in the lake water that could turn out to be a human carcinogen. If the concentration of fibers in the lake water increased with time so that in 20 years—when the increased risk of gastrointestinal cancer would be expected to become observable—fewer options would be available to reduce the risk of fiber related gastrointestinal cancer in the already exposed population.

The Eighth Circuit Court of Appeals rendered its decision in the Reserve Case on March 14, 1975 (Reserve Mining, 1975). At that time it was decided to monitor the airborne and waterborne fibers in Silver Bay using an indirect sample preparation technique and analytical transmission electron microscopy (ATEM). In 1975 there was no standard in the scientific or medical literature worldwide to evaluate the non-occupational cancer risks which might be associated with exposure to the various types of fibrous minerals being found in and around Silver Bay (National Research Council, 1984). The measurements of the airborne fibers in the non-occupational environment were unreliable and no risk assessment models existed to predict the risk of asbestos-related cancer related to any exposure measured (Peters and Doerfler, 1978).

Ultimately the solution for the Silver Bay facility was to end the practice of discharging the waste rock into the lake and dispose of the material in a facility on land. Duluth's drinking water was filtered by November, 1976 and the disposal of the waste rock in Lake Superior ended by July, 1980. To limit the exposure to the fibers present in the waste rock by inhalation, they were to be placed under water in a large in land disposal basin. Clear evidence of a public health problem did not drive the steps taken at that time, but rather the decisions were made based on extrapolation, judgment and a desire to do no harm (Schaumburg, 1976; Bartlett, 1980; Bastow, 1986). This would now be called the Precautionary Principle. It can be satisfied by an open and effective use of evidence based risk assessment (Richter and Laster, 2004).

Occupational exposures were monitored by phase-contrast light microscopy counting the number of fibers equal to or greater than 5 μm in length with a length to width ratio of 3:1 or greater, reporting the number of such fibers per milliliter of air (Langer et al., 1991). Occupational exposure to asbestos is controlled using an index of exposure not by measuring the total number of fibers to which a worker is exposed. In 1971, the asbestos standard was 12 f/mL and the initial goal of the standard was to eliminate the development of asbestosis. By 1994 the standard had been lowered on four occasions to the current standard of 0.1 f/mL mainly to reduce the risk of asbestos-related cancer (Fig. 1).

The decision in the Reserve Mining Case ordered St. Paul to be used as a control city to assess Silver Bay exposures. The theory was that if the airborne concentrations of fibrous mineral (of all lengths) in Silver Bay were below those for airborne asbestos in St. Paul, then the levels would be presumed to be safe and further steps to reduce the concentration of airborne fibers in Silver Bay would not be necessary. This control city protocol was not benchmarked to the risk of asbestos-related cancer, the levels of airborne asbestos in St. Paul were simply assumed to be safe.

The air samples collected and analyzed to comply with the 1975 court decision, which continue to this day, are prepared using the indirect method and uses analytical transmission electron microscopy as instrument of choice. The airborne particles were collected on membrane filters, the filters were then dissolved and the fibers dispersed in water. An aliquot of the suspension is then filtered onto a new filter at a lower particle loading. As the air monitoring program began to compare the airborne fiber levels in the two locations—those in Silver Bay (0.0048 f/mL, $N = 155$) were consistently ~ 5 -fold lower than in St. Paul (0.023 f/mL, $N = 35$) (Fig. 1). The airborne fibers in St. Paul were predominantly chrysotile asbestos while in Silver Bay fibrous particle associated with taconite predominated. Eventually the air sampling in St. Paul was discontinued and the ongoing air monitoring in Silver Bay is now only compared to the airborne concentrations of fibers already determined historically in St. Paul and Silver Bay. In March of 2006 the Minnesota Pollution Control Agency

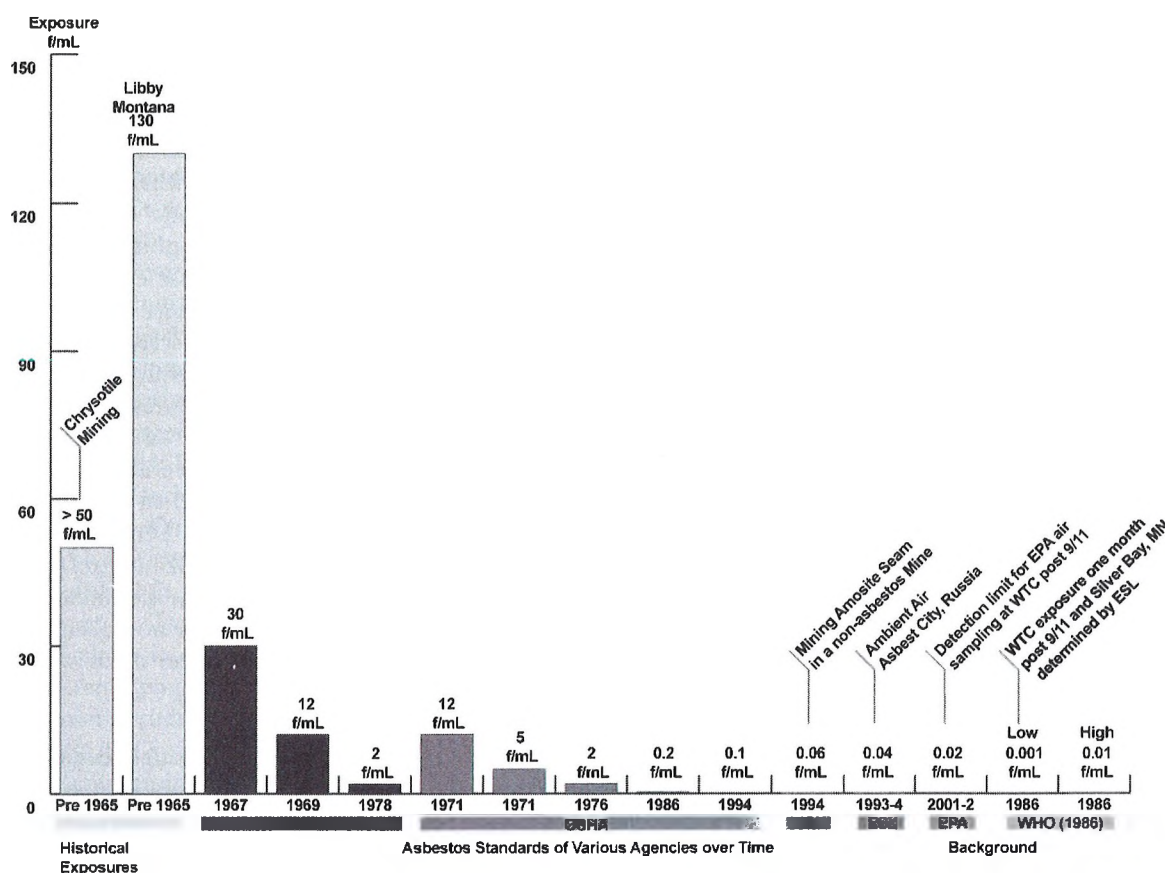


Fig. 1. The airborne concentration of taconite associated fibers greater than 5 μm in length is less than 0.00014 f/mL in Silver Bay, Minnesota which is at the low-end of background for airborne asbestos concentration and orders of magnitude less than the historically high occupationally exposed of the past.

has started to collect air samples in St. Paul again. Indirect sample preparation has been largely abandoned although the analytical transmission electron microscopy remains the instrument of choice for monitoring the non-occupational environment for asbestos.

For comparison, occupational exposure to airborne asbestos in 1975 was held below 5 f/mL by regulation, as determined by phase-contrast optical microscopy (PCOM) using a direct transfer sample preparation method and counting only fibers greater than or equal to 5 μm (Fig. 1). Thus, even if the fibers from Silver Bay were asbestos, the levels monitored in Silver Bay are at least 700 times lower than the current permissible exposure level for asbestos.

Ambient air in all natural settings contains airborne particulates, among them asbestos, and Silver Bay is no exception. Airborne asbestos has been found on small isolated Pacific Islands without naturally occurring asbestos and in 10,000-year-old ice samples from Antarctica indicating airborne asbestos pre-dates its industrial use (Kohyama, 1989). Bowes et al., 1977 report asbestos to be present in the Greenland ice cap indicating airborne asbestos was present in both hemispheres prior to industrial use. Of all the particles in the air only a small percentage are fibers and generally a sub-population of these are asbestos. Since the air in Silver Bay contained very few fibers it was necessary to sample large volumes of air to determine if there

was any asbestos present. The air samples, required by the court decision, were continuously collected over three days of sampling the air at 16.7 l of air per minute (Axten and Foster, 2008).

After this long period of air sampling, the filters on which the particles deposited are too heavily loaded for direct examination of the small number of the fibers collected. The particles collected on the filter, the filter was dissolved using chemicals or low-temperature ashed and re-dispersed in water. An aliquot was then filtered onto a new membrane filter at a lower particle density for counting purposes. By selecting aliquots of various volumes the loading can be adjusted to an optimum for fiber counting. The use of the second membrane is called indirect sample preparation and can alter the particle number and size distribution. The transfer to the second filter to reduce the fiber density changes the fiber size distribution and counting fibers of all lengths rather than only those greater than or equal to 5 μm cause the indirect sample preparation method not to use when air sampling for the purpose of asbestos risk assessment.

3. Changes in the state of knowledge regarding asbestos and other fibers

It is now more than 30 years since the 1975 court decision ruling the Reserve discharge into Lake Superior posed

a potential health threat. Additional information about the health effects of asbestos and other fibers has become available relevant to the decision in the Reserve case. Even among those with high-occupational exposure to asbestos there is no consistent increase in the risk of gastrointestinal cancer (Gamble, 1994; Weiss, 1995; Gamble and Gibbs, 2008) and therefore no risk assessment model exists. Drinking potable water carried in asbestos cement pipes or drinking water from a source high in naturally occurring asbestos was suspected of causing increased risk of gastrointestinal cancer. However, recent comprehensive reviews of the epidemiology does not show any increased risk of gastrointestinal cancer or any other asbestos-related disease from drinking water contaminated with fibrous particles (Kanarek, 1989; Hillerdal, 1999; Browne et al., 2005; Gamble and Gibbs, 2008).

The preponderance of evidence from experimental animal studies with rats and hamsters living a lifetime with asbestos in their food have shown little or no increased risk of gastrointestinal cancer or any other disease of the gastrointestinal tract (Moore, 1978; McConnell et al., 1983a,b). Nor have experimental animals exposed to asbestos by inhalation developed such diseases. The lack of evidence for the ingestion or inhalation of asbestos causing gastrointestinal cancer in experimental animals leads to questions about causality in those ecological studies of asbestos ingestion where a small effect is shown (Doll, 1989). Gastrointestinal cancer involves cancer at a number of sites the most common of which is stomach cancer. Markedly different incidence rates of this disease exist between different regions of the world and between different races living in the same city (Higginson et al., 1992). Although on the decline it remains the most frequently occurring human cancer in the world and we have no idea of the cause(s) so it is difficult to understand the reasons for fluctuation in the incidence rates. Similarly the World Health Organization and other national and international health organization emphasized the extremely low-risk of health effects from asbestos in water (WHO, 1986, 1989, 1999). On the basis of current knowledge no epidemiological study support a claim of adverse health effects from disposing of waste rock in the lake.

When President Ronald Reagan signed the Asbestos Hazard Emergency Response Act (AHERA) into law in 1986, interest again began to focus on monitoring asbestos levels in indoor air post-asbestos abatement. A direct preparation technique was adopted for the preparation of the air samples and analytical transmission electron microscopy (ATEM) would be used for the fiber analysis (ISO, 1995). ATEM is useful when a significant percentage of the airborne fibers present are not asbestos and it is important to know the concentration of very short and/or thin fibers. AHERA air sampling strategy requires the direct counting of fibers greater than or equal to 0.5 μm in length (one tenth of the OSHA exposure index fiber) and a slightly higher value for the length to diameter ratio of 5:1 or greater. The air was sampled at approximately 16 l of air

per minute but only for 4–6 h rather than the 72 h used in Silver Bay.

In 1986, the United States Environmental Protection Agency published the *Airborne Asbestos Health Assessment Update*. The risk assessment is derived from the increased incidence of lung cancer and mesothelioma among cohorts occupationally exposed to asbestos. The assessment uses the occupational exposure index noted above. It assumes linear (no threshold) dose–response curve. The risk calculated using the *Airborne Asbestos Health Assessment Update* would be accurate if one were to assume the fiber exposures in Silver Bay were all equivalent to the average asbestos potency derived from the results of epidemiology studies of asbestos-exposed cohort of workers. This assessment is also the basis for the overall risk coefficient for asbestos-related cancer risk listed in the Integrated Risk Information System (IRIS) (see United States Environmental Protection Agency (IRIS) <http://www.epa.gov/iris/subst/0371.htm>) which became available in 1988. Neither the air sampling protocols for non-occupational exposure nor the asbestos-related cancer models were available at the time of the Reserve Mining Case.

4. United states consumer product safety commission and the occupational safety and health administration address cleavage fragments

The most interesting development since 1975 has been the results of a geological survey showing that the North-shore fibers associated with taconite ore are an assortment of cleavage fragments and alteration products and not asbestos (Ross et al., 2008a,b). Associated with this is the determination that such cleavage fragments are less potent in producing human cancer as well as cancer in experimental animals (Davis et al., 1991; Nolan et al., 1991; Federal Register, 1992; Ilgren, 2004; Gamble and Gibbs, 2008).

The definition used for the regulation of asbestos has been an issue at least since 1971 (Federal Register, 1971). The morphological counting criteria that accompanies the definition of asbestos used in the OSHA regulations has been incorrectly as including certain types of rock fragments occurring in a fibrous form commonly called cleavage fragments and alteration products as if these fiber were asbestos (Langer et al., 1991). The fibers had to be one of the six regulated asbestos minerals, visible by phase-contrast microscopy, greater than or equal to 5 μm in length and have a length to width (or aspect ratio) of 3:1 or greater. Several different types of mines (including St. Lawrence tremolitic talcs in New York State, vermiculite from Enoree, South Carolina and taconite) had fibers meeting morphological counting criteria, which were not asbestos. Some in public health researchers became concerned that exposures to potentially dangerous fibers would be ignored due to the arcane mineralogical criteria defining asbestos, which were not relevant to any health hazard evaluation (Health Effects of Tremolite, 1990; Nolan et al., 1991; Federal Register, 1992). This position

was in part rationalized by the results of experimental animal studies by Stanton et al. (1981) showing the importance of morphology.

The new scientific evidence since 1971 has weakened the rationale for regulating non-asbestos amphibole fibers under the asbestos standard. The new evidence has been obtained from high-resolution transmission electron microscopy examination revealing unique structural properties of asbestos, experimental animal studies showing much lower risk for non-asbestos amphibole fibers compared with amphibole asbestos and epidemiological studies showing little or no increase in asbestos-related diseases among workers occupationally exposed to non-asbestos amphibole fibers (Langer et al., 1991; Nolan et al., 1991; Veblen and Wylie, 1993; Ross et al., 1993; Ross and Nolan, 2003; Ilgren, 2004; Gamble and Gibbs, 2008).

At various times OSHA had administrative orders, which limited the impact of asbestos regulation on non-asbestos fibers, although these could be reversed at the discretion of the agency. This loose end of the asbestos regulations led to a claim in 1986 that tremolite asbestos was present in children's play sand. This issue was addressed by the Consumer Product Safety Commission (CPSC) (Germine, 1986, 1987; Langer and Nolan, 1987). The CPSC found that tremolite in the play sand *was not* asbestos but rather cleavage fragments. Of the 2–4% tremolite asbestos originally claimed in the New England Journal of Medicine to be present approximately 0.01% of the tremolite was in the form of fibers with size distributions similar to asbestos. Once these two types of fibers are recognized to be different and the health effects of the non-asbestos fibers are separated those of asbestos the non-asbestos fibers are clearly less active than asbestos therefore should not be regulated using the asbestos permissible exposure limit (Langer et al., 1991; Nolan et al., 1991). After careful review and public hearing both CPSC and OSHA found insufficient cause to regulate non-asbestos fibers (Federal Register, 1992). In the public hearings, Terence Scanlon, the Chairman of the CPSC at the time, likened calling cleavage fragments asbestos to hollering fire in a crowded theater.

The disharmony between these two federal regulatory agencies concerning the types of fiber that should be regulated as asbestos put further pressure on OSHA to re-evaluate this long-standing matter and render some type of final decision. Public hearings were conducted by OSHA to gather information concerning the matter as well as written comments and documents submitted to the rulemaking docket. After a careful review, of over two years, the agency's final rule appeared in the Federal Register on June 8th, 1992 (Federal Register, 1992). The non-asbestos amphibole minerals were not to be regulated as asbestos. National Institute of Safety and Health (NIOSH) had recommended that "... for regulatory purposes that cleavage fragments of the appropriate aspect ratio and length from the non-asbestiform mineral should be considered as hazardous as fibers from the asbestiform minerals" OSHA dis-

agreed with NIOSH's recommendation and stated "... OSHA does not believe the current record provides an evidentiary basis to determine "the appropriate aspect ratio and length" for determining pathogenicity." OSHA concluded "... the discussion indicates that populations of fiber and populations of cleavage fragments can be distinguished from one another when viewed as a whole. For example, one can look at the distribution of aspect ratios or even widths for a population of particles as being asbestiform or non-asbestiform. However when one looks at individual particles (e.g., particles from air sampling filters) sometimes these mineralogical distinctions are not clear." Later in our report we will show Northshore fibers have population characteristics which are not consistent with asbestos, but are consistent with a population of non-asbestos fibers.

OSHA also concluded "... for most mineral deposits, asbestos and non-asbestiform habits are distinguishable." "OSHA has determined that non-asbestiform ATA and asbestos anthophyllite, tremolite and actinolite should be defined separately for regulatory purposes to conform to common mineralogic usage." The rule making focused on only three of the five amphibole asbestos minerals regulated under the asbestos standard. The reason for this is that the commercially less important anthophyllite, tremolite and actinolite asbestos but not have specific have specific commercial asbestos names. Therefore grunerite asbestos and riebeckite asbestos known commercially, respectively, as amosite and crocidolite were not included in the rulemaking. Although logically the non-asbestos fibers formed by any of the five amphiboles should not be regulated as asbestos.

OSHA concluded that mineral fibers should be regulated based on using mineralogical criteria to define them rejecting the similarity in morphology as an acceptable criteria for inclusion in the asbestos standard. This regulatory action eliminated any justification for claiming a federal definition for asbestos that differs from the mineralogical definition described by Ross et al., 1984, 2008b. The OSHA ruling eliminated any justification for claiming a federal fiber definition.

OSHA concluded that, "...currently available evidence is not sufficiently adequate for OSHA to conclude that these mineral types pose a health risk similar to asbestos." Although the non-asbestos amphibole fibers were not shown to be non-carcinogenic the evidence available was adequate to demonstrate their carcinogenic potency was clearly less than that of asbestos. OSHA recognized that a small percentage of populations of cleavage fragments and asbestos would be indistinguishable but accepted that each is a unique mineral with different potential for causing a health hazard. One critical point is that it is difficult to find environments where a high-concentration of non-asbestos amphibole fibers is present in the air. This is consistent with the information available for fibers released at the Northshore facility in Silver Bay, Minnesota.

Based on the information that became available after the 1975 decision in the Reserve Mining case we decided to take the following steps to fill in the data gaps which existed at that time:

1. We undertook a geological survey of the Peter Mitchell Pit, near Babbitt, Minnesota focused on determining if asbestos and/or other fibrous minerals are present. A summary of the geological survey will be presented here the details are in Ross et al. (2008a).
2. Conduct environmental air sampling in Silver Bay, Minnesota to determine the concentration and type of airborne fibers that were greater than or equal to 5 μm in length.
3. Compare the airborne concentration of fiber in Silver Bay to the background ambient airborne levels of asbestos fiber worldwide as reported by the World Health Organization.
4. Determine the size distribution of airborne fibers in Silver Bay and compare the size distribution to respirable grunerite asbestos (amosite). Using the criteria OSHA described in 1992 that on a population basis cleavage fragments have a size distribution different from respirable airborne asbestos (Federal Register, 1992).
5. The risk assessment model used here to evaluate the risk of asbestos-related disease in Silver Bay, Minnesota is a simple linear relationship between dose and response. Several alternate risk coefficients for this relationship were considered. First a coefficient derived from EPA's Integrated Risk Information System (IRIS). Then we used the coefficients suggested by Hodgson and Darn-ton (2000) to evaluate each type of asbestos-related cancer separately and specifically for the type of asbestos most similar in elemental composition to the airborne fibers at Silver Bay, Minnesota and for the least active of the asbestos fiber types—chrysotile asbestos. The assumptions are described in detail below.
6. Critically review the epidemiological and non-human primate studies designed to determine if grunerite asbestos (amosite) causes mesothelioma at exposures below the historical occupational exposures.

5. Geological survey of the peter mitchell pit

As noted above, asbestos is a mineralogical and economic geology term which is used to describe a highly fibrous group of commercial minerals (Ross et al., 1984, 2008a). These minerals form in rather high-concentrations as seams in dilated rock. These seams can vary from approximately 1 mm to several centimeters in width. Before measuring the airborne fiber concentrations in Silver Bay, 49 bulk samples were collected from the Peter Mitchell Pit near Babbitt, Minnesota to survey for asbestos in the ore. A priority was given to examining areas in the pit where there appeared to be geological faults and shear zones looking for slip fibers along limbs of tight folds.

Asbestos can form in these areas and in addition the amphibole minerals within these types of rock are particularly susceptible to a geological process called weathering which occurs via low-temperature alterations due to the infusion of rain water coupled with oxidation and rock shearing. Two types of alteration of amphiboles minerals were noted:

1. The Type I samples contained the amphibole ferroactinolite that has partially altered to very fibrous crystallites, red-brown in color indicative of a hydrous iron oxide mineral. The fibrous crystallites usually form as a mass of fiber bundles. In the incompletely altered material, amphibole grain areas can be seen within the fiber bundles where the ferroactinolite is green in color, non-fibrous and pristine. It is suggested that rain water moving through the shear zones altered and oxidized the original amphibole to a red-brown acicular product. Where the alteration is incomplete, some of the pristine amphibole remains. It also appears that some iron was removed from the amphibole grains during this weathering process to recrystallize as iron oxide, probably in the form of goethite $[\text{FeO}(\text{OH})]$ which can form on grunerite asbestos (amosite) too, and appears as brown masses associated with the weathered fibrous material. Examination by analytical transmission electron microscopy of two samples representative of Type I reveal fibers similar to those of the ferroactinolite used by the EPA in experimental animal studies (Coffin et al., 1983). After injection of the ferroactinolite into the experimental animals the fiber number increased with time by separating along the altered zones producing mesothelioma in the rat.
2. The Type 2 samples contained ferroactinolite amphibole that is much more altered than Type I. The amphibole crystals have been degraded to a ropy to platy mass with only a small amount of the original material left. The platy mass gives X-ray diffraction lines that suggest the amphibole is altered to ferrosiepiolite or hydrobiotite. Examination of two Type 2 samples by analytical transmission electron microscopy reveal highly fibrous minerals with an elemental composition similar to sepiolite and unlike any regulated asbestos mineral.

The conclusion of the fiber survey is that only a tiny fraction of less than 1% of the total rock mass in the Peter Mitchell Pit is fibrous. The fibrous ferroactinolite is a low-temperature alteration product of non-fibrous amphiboles; it does not occur in the manner of common commercial asbestos, which crystallizes as a primary mineral from hydrothermal solution into open veins within deformed rock. There was no evidence of a geological process of alteration for cummingtonite-grunerite forming fibers similar to the ferroactinolite. No primary asbestos minerals were found in the Peter Mitchell Pit (Ross et al., 2008a).

6. Risk assessment for asbestos

6.1. General comments

If the distribution of the asbestos fiber types and morphology were the same in the Northshore environmental samples as in the various occupational asbestos exposures from which the risk coefficients were derived, the risk assessment would be relatively straightforward. But that is not the case (Gamble, 2008; Nolan et al., 2008). The risk coefficients are indexed to the fibers greater than or equal to 5 μm in length having length to width ratios of 3:1 or greater and short-fibers are not counted. All of the coefficients in the risk assessment models for asbestos-related cancer are derived from occupational exposure to airborne asbestos where only fibers equal to or greater than 5 μm in length are counted. EPA takes an average value for the various types of asbestos fiber and does not in the risk assessment model address the question of whether some asbestos fibers types have different potency nor do they address the potency of non-asbestos amphibole fibers. Hodgson and Darnton (2000) reanalyze the data (including several new epidemiology reports particularly on amphibole asbestos-exposed cohorts) and conclude there are large differences between the various commercial asbestos fiber types that should be considered. However they do not address cleavage fragments or other types of non-asbestos fibers. Our analyses of Northshore fibers indicate that on a population basis their size distribution is consistent with non-asbestos amphibole fibers rather than asbestos. Because these are still issues being discussed (and may therefore be considered controversial) we estimate the risk by using several different risk coefficients to illustrate how fiber type impacts the outcome. We note that under all reasonable possibilities the risk of asbestos-related cancer from environmental exposure is small. There should be no controversy about this statement.

6.2. EPA-IRIS aggregate risk coefficient

We calculate an aggregate lifetime risk using the EPA-IRIS system, noted earlier, that provides a summed risk for two asbestos-related cancers. The risk is an average of the risk to a standard US population. This uses an “absolute risk” model for mesothelioma and a “relative risk” model for lung cancer. It is conservative (or one might say pessimistic) in that the model assumes a linear no threshold (LNT) increase in cancer risk.

According to the LNT model any exposure, no matter how small, increases the aggregate cancer risk and the model assumes continuous exposure over a 70-year lifetime. As the model is linear very small increases in exposure correspond to very small increases in the cancer risk. The model predicts an average risk for exposure based on asbestos-related cancer among workers occupationally exposed to the three principal commercial asbestos fiber types—chrysotile, riebeckite asbestos (crocidolite) and grunerite asbestos (amosite) and indexes the relative risks

to fibers greater than or equal to 5 μm . Asbestos fibers less than 5 μm are not included in the exposure index. The EPA-IRIS model uses the following equation:

Screening value = Target cancer risk/Inhalation unit risk

- Screening value (SV) is the exposure to fibers equal to or greater than 5 μm in length given as f/mL, at which the Risk equals the Target cancer risk.
- Target cancer risk (TR) is the lifetime cancer risk for example, 1 asbestos-related cancer death in 10,000 lifetimes is reported as a frequency of how often it occurs—0.0001 or 10^{-4} .
- Inhalation unit risk (IUR) is the upper bound excess lifetime cancer risk estimated to result from continuous lifetime exposure to asbestos given in the EPA-IRIS as 0.23 mL/f.

$$\text{SV} = \text{TR}/\text{IUR} = 0.0001/0.23 = 0.0004 \text{ f/mL}$$

Using the EPA-IRIS risk coefficient we predict one asbestos-related cancer death over the lifetimes of 10,000 people exposed continuously for 70 years to an average daily asbestos exposure of 0.0004 f/mL. It is important to realize that it could never be proven directly that a risk of this small magnitude exists.

7. Exposures to fibrous minerals in Silver Bay, MN

The EPA-IRIS aggregate risk coefficient assumes that the exposure is estimated from the concentration of fibers greater than 5 μm with an aspect ratio of 3:1 or greater. This exposure had not previously been determined for the residents of Silver Bay as the air sampling mandated by the court case counted fibers with lengths less than 5 μm and is therefore not useful for risk assessment. To determine the concentration and exposure we selected the air sampling station closest to the residential area because it would be most representative of the level of exposure the residents would experience. Twelve air samples were collected between October 24 and December 9, 1998. Three of the air samples were collected in duplicate therefore nine values of the average fiber concentration greater than or equal to 5 μm over a 24-hour period were determined. Each of the air samples was prepared by the direct transfer technique for examination by analytical transmission electron microscopy using the protocol described in ISO, 1995. The grid openings were scanned directly on the screen at 20,000 $\times$ magnification. Any object, which had a length three times greater than its width was considered a fiber. Energy dispersive X-ray spectra were obtained for each fiber and a digital image was recorded. The fibers were sized from the printout of the digital image. Only two fiber types having an elemental composition similar to any of the asbestos minerals were found and used for the exposure estimates. These were cummingtonite-grunerite (79%, $N = 15$) and tremolite-actinolite (21% $N = 4$). The results of this analysis are shown in Tables 1 and 2.

The concentration on average was 0.00014 f/mL. This is about 35% of the level IRIS predicts will cause one cancer

Table 1
Results of the analysis of site N° seven air samples by analytical transmission

Date	ID N°	Volume of air (in liters)	N° of fields examined	Grid area examined (in mm) ²	N° of fields detected length		Cummingtonite- grunerite length		Tremolite actinolite length		Volume of air scanned (mL)	Total airborne fiber concentration F/mL all lengths	Total airborne fiber concentration F/mL with length >5 µm
					>5 µm	<5 µm	>5 µm	<5 µm	>5 µm	<5 µm			
Electron microscopy in the area of the Northshore pellet plant													
10/24/98	F7-1	24,157	53	0.641	3	3	2	1	1	2	11,729	0.00051	0.00026
	F7(T)-1	24,352	60	0.726	3	8	2	5	1	3	13,391	0.00082	0.00022
Sub-total		48,509	113	1.673	6	11	4	6	2	5	25,110	0.00067	0.00024
10/28/98	T7-1	24,727	61	0.738	4	7	4	6	0	1	13,823	0.0008	0.00029
10/30/98	T7	24,744	60	0.726	0	0	0	0	0	0	13,607	<0.00073	<0.00073
11/05/98	T7	25,839	60	0.726	4	10	4	3	8	1	14,209	0.00099	0.00028
11/10/98	F7	24,818	60	0.726	0	3	0	0	2	0	13,647	0.00022	<0.00073
	T7	24,298	61	0.738	0	2	0	1	0	1	13,582	0.00015	<0.00074
Sub-total		49,116	121	1.464	0	5	0	3	0	2	27,229	0.00019	<0.00074
11/17/98	T7	25,548	120	1.456	1	3	4	1	3	0	28,097	0.00014	0.00035
11/21/98	T7	25,488	60	0.726	0	5	0	5	0	0	14,016	0.00036	<0.00071
12/03/98	T7	24,656	60	0.726	1	0	1	0	0	0	13,558	0.00007	0.00007
12/09/98	F7	26,258	60	0.726	0	1	0	1	0	0	14,439	0.000069	<0.00069
	T7	25,712	60	0.726	3	0	3	0	1	0	14,139	0.00021	0.00021
Sub-total		51,970	120	1.452	3	1	4	2	1	0	28,578	0.00014	0.00011
												Mean	<0.00014 (n = 9)

death in 10,000 lifetimes (Table 2). We assume that the residents of Silver Bay will be exposed to this concentration for their lifetimes. According to the linear no threshold dose–response relationship the lower exposure determined here will be associated with 1 excess asbestos-related cancer death in about 28,500 lifetimes (or 35 asbestos-related cancer deaths in 1,000,000 lifetimes). Considering the population of Silver Bay is about 2500 the pessimistic conservative model predicts that at worst one excess cancer death related to fiber exposure in more than 10 lifetimes of the entire Silver Bay population. Since about 22% of the US population die of cancer by age 70 about 6240 cancer deaths from all types of cancer would be expected in this time period, including about 10 background mesothelioma cases not related to asbestos exposure (Price and Ware, 2004) and 627 lung cancer cases. The lung cancer deaths assume 2.2% lung cancer mortality among residents of Silver Bay.

The IRIS asbestos-related cancer risks are based on exposure to asbestos fibers. The air sampling protocol used in Silver Bay determined the airborne fiber concentration, which is predominantly *non-asbestos* fibers, is at the low-end of background measurements for *asbestos* fibers in other communities. If present in Silver Bay, asbestos fibers would be at an even lower concentration. On the basis of the geological survey of the Peter Mitchell Pit we doubt whether any significant fraction of airborne fiber is asbestos. The fibrous ferroactinolite associated with the alteration products found in the geological survey occur at small concentration in the pit and only about 20% of the Northshore fibers in the air samples have elemental compositions consistent with ferroactinolite and only a sub-population of these have morphology consistent with the alteration products. The concentration of airborne fibers in Silver Bay is at what World Health Organization reports as the low-end of background for airborne asbestos (WHO, 1986, see Fig. 1).

To further examine the type of airborne fiber in Silver Bay we looked at the size distribution of 387 fibers of all lengths found in the ambient air in and around Silver Bay and compared the size distribution with 288 fibers of respirable grunerite asbestos (amosite) lofted for experimental animal studies (Hesterberg et al., 1999; McConnell et al., 1999). We choose grunerite asbestos (amosite) for comparison because approximately 80% of the airborne fibers at Silver Bay had elemental compositions consistent with cummingtonite-grunerite (Tables 1 and 2). The Northshore fibers increase in diameter, to a significantly greater extent than asbestos, as the fiber length increases. We conclude from this observation that the airborne fibers in Silver Bay are predominantly non-asbestos fibers (Table 3).

8. Comparison with EPA led task force working group doing risk assessment for asbestos exposure world trade center post-9/11

We now compare our approach to that of the EPA for the World Trade Center post-9/11. The initial air sampling

Table 2
Summary of the results of the air sampling at station N° seven for risk assessment

Air sample	Weather	N° of fibers detected length >5 µm	Fiber type		Volume of air scanned (in mL)	Total airborne fiber concentration f/mL with length >5 µm
			Cummingtonite/ grunerite	Tremolite/ actinolite		
1	No precipitation	6	4	2	25,110	0.00024
2	No precipitation	4	4	0	13,823	0.00029
3	0.06" Precipitation	0	0	0	13,607	<0.000073
4	No precipitation	4	3	1	14,209	0.00028
5	1.96" Precipitation	0	0	0	27,229	<0.000074
6	No precipitation	1	1	0	28,097	0.000035
7	No precipitation	0	0	0	14,016	<0.000071
8	No precipitation	1	1	0	13,558	0.00007
9	No precipitation	3	2	1	28,578	0.00011
Mean <0.00014 ± 0.001						

Table 3
Comparison of the length distribution of grunerite (Amosite) asbestos and the 387 airborne fibers of cummingtonite-grunerite and tremolite-actinolite collected at the perimeter of the Northshore pellet plant

Samples	Fibers sized	N° of % in each length range			
		<5 µm	>5 to <10 µm	≥10 to <20 µm	≥20 µm
<i>Grunerite (Amosite) asbestos</i> ^a	288	47.2	23.6	15.6	13.5
Average diameter	288	0.27 ± 0.17 µm	0.39 ± 0.30 µm	0.37 ± 0.29 µm	0.70 ± 0.75 µm
Average aspect ratio	288	15 ± 12	27 ± 22	57 ± 40	120 ± 116
<i>Northshore fibers</i>	387	65.9	23.5	9.6	1.0
Average diameter		0.60 ± 0.27 µm	1.13 ± 0.56 µm	2.12 ± 1.02 µm	3.65 ± 2.63 µm
Average aspect ratio		6.2 ± 3.7	9.1 ± 10.9	8.4 ± 7.1	10 ± 5

The aspect ratios of the Northshore fibers are independent of length while the aspect ratio of a population of grunerite (amosite) asbestos fibers increases with length. This difference is the morphological basis for differentiating asbestos and cleavage fragments.

^a Determine from photographs and digital images obtained by transmission electron microscopy.

^a The grunerite (amosite) asbestos used for comparison is a respirable sample lofted for the studies by Hesterberg et al., 1999; McConnell et al., 1999.

undertaken by a multi-agency Task Force focused on outdoor air (World Trade Center, 2003). Measurements of airborne asbestos concentrations in Lower Manhattan post-9/11 were evaluated against a 70 structures per millimeter-squared standard, which corresponds to 0.021 f/mL counting all fibers greater than 0.5 µm with aspect ratios of 5:1 (Office of Inspector General, 2003). Once asbestos exposures were below this level EPA recommended that residents be allowed to return to their homes in Lower Manhattan. The outdoor concentrations of asbestos fibers considered acceptable in Lower Manhattan were 58-fold higher than the mean for the *predominantly non-asbestos* concentrations of fibrous particle of all lengths associated with taconite that were measured in Silver Bay (Table 1). The EPA value is not based on lifetime asbestos-related cancer risk but rather it was derived from the background contamination on the membrane filters used to collect the air samples. Values up to 0.021 f/mL could be simply contamination on the filter and do not represent the airborne asbestos level. Concern about the high-background contamination on the membrane filters date to the period of the AHERA Act in 1986, our controls indicate contamination is much lower and generally chrysotile asbestos (Nolan and Langer, 2001). If the concentration of asbestos in the ambient air in Lower Manhattan was below this level it

could be considered acceptable based on the fact that the debris removal would only last a year and the consequent exposure would be acceptable for that period of time. Exposure to a concentration of 0.021 f/mL for one year gives the same cumulative exposure as exposure to 0.0003 f/mL for a 70-year lifetime. Not all structures are fibers and the fiber counting criteria use a length of 0.5 µm or greater therefore the exposure is more protective than 1 asbestos-related cancer death in 10,000 lifetimes.

After 9/11 the EPA decided to assist residents in cleaning of their apartments in Lower Manhattan. The agency used the IRIS model to set a health-based benchmark for when the apartments would be cleaned to an acceptable standard (World Trade Center, 2003). The Task Force decided that 1 excess asbestos-related cancer in 10,000 lifetimes would be the Target Cancer Risk (TR) corresponding to a Screening value (SV) of 0.00043 f/mL for asbestos fibers with a length greater than or equal to 5 microns. The Task Force further concluded that the arithmetic mean background concentration was between 0.00003 and 0.0060 f/mL and decided a residence would be clean and acceptable for re-occupation if some form of aggressive air sampling demonstrated the airborne concentration of asbestos to be less than 0.0009 f/mL (accepting a concentration of airborne asbestos about 6-fold higher in Lower

Manhattan apartments than ambient airborne fibers in Silver Bay). This Lower Manhattan exposure corresponds to 1 excess asbestos-related cancer in 10,000 lifetime for 35 years of continuous exposure rather than the 70 years corresponding to a Screening value (SV) 0.00043 f/mL having a length greater than is equal to 5 μm .

Therefore the upper limit of predominantly *non*-asbestos fiber concentrations in Silver Bay is *six times lower* than the post-asbestos clean up level for asbestos fibers EPA used for residents near the World Trade Center.

9. Hodgson and Darnton (2000) asbestos fiber type specific risk coefficients for each asbestos-related disease

Approximately 80% of the airborne Northshore fibers in Silver Bay have elemental compositions in the cummingtonite-grunerite series. The remaining fibers are in the tremolite-actinolite series. For the Hodgson and Darnton (2000) risk assessment we will make two alternate assumptions that we did not need to make for the IRIS model. Initially we will assume that all the airborne fibers in Silver Bay are as potent in producing asbestos-related cancer as the asbestos fiber type with the same elemental composition. Then we will calculate the asbestos-related cancer risk assuming the Northshore (non-asbestos) fibers are only as potent as the least dangerous form of commercial asbestos which is chrysotile asbestos. This last assumption seems consistent with the conclusion by CPSC and OSHA that the non-asbestos fibers are less active than asbestos.

First, we will assume the Northshore fibers are *all* grunerite asbestos (amosite) as approximate 80% of Northshore have elemental compositions in the cummingtonite-grunerite series and there is no risk assessment model yet available for tremolite-actinolite asbestos. For this we use Hodgson and Darnton's coefficient for grunerite asbestos (amosite). We would argue that this assumption seriously over estimates the risk for asbestos-related disease among the long-term residents of Silver Bay. It was the default assumption during the period of the Reserve Mining controversy and represents the upper limit of an asbestos-related cancer risk. Our second assumption is that the Northshore fibers are no more active than *the least active asbestos fiber types*. We make this assumption consistent with OSHA's conclusion that non-asbestos fibers are less active than asbestos (Federal Register, 1992). At this time we will not make any statement as to how much less the Northshore fibers are than the least potent asbestos fiber type. Accordingly we calculate two alternate values for the mesothelioma risk the total expected mesothelioma mortality (R_M) expressed in fiber/mL $\times$ years. We choose the total value for amosite cohorts to predict the mesothelioma incidence if the Northshore fiber were all grunerite asbestos(amosite) ($R_M = 0.1$ fiber/mL $\times$ years) (alternate 1) and the total chrysotile excluding South Carolina textile workers assuming Northshore fibers to be equivalent to the least potent asbestos fiber type ($R_M = 0.001$ fiber/mL $\times$ years) (alternate 2).

The number of asbestos-related mesothelioma cases (O_M) depends on the type of asbestos to which one is exposed, the cumulative exposure and the age at which exposure first occurs (Hodgson and Darnton, 2000) and can be calculated by:

$$O_M = \frac{R_M \times E_{CA} \times T_{pop}}{100}$$

Where:

- R_M —Risk of mesothelioma as a percentage of the total expected mortality per (f/mL) year. The R_M used, 0.1, is obtained from Hodgson and Darnton, 2000 (entry "Total amosite cohort" in their Table 1) (adjusted to 30 years of age at first exposure) the value of R_M is specific for grunerite asbestos (amosite). This is derived from occupational exposure, assumed to be 8 h/day for 250 days per year.
- E_{CA} —The environmental concentration of grunerite asbestos (amosite) is 0.00014 f/mL and needs to be converted to an occupational concentration from which the risk coefficients are derived. We assume an 8 h/day for 250 days per year. This is done by taking the environmental concentration (0.00014 f/mL) and multiplying by 4.38 to the equivalent occupational concentration of 0.00061 f/mL. We assume this exposure goes on for 40 years so we multiply 0.00061 f/mL by 40 to obtain the cumulative concentration of 0.0245 f/mL $\times$ years.
- T_{pop} —Adjusted total exposed population for Silver Bay. The total population is 2500 residents.

This equation is basically the same equation as in Hodgson and Darnton, 2000, page 566 but there X is used in place of E_{ca} and E_{adj} is the total expected deaths from all causes which we here set equal to the total population T_{pop} on the plausible assumption that everyone will die sometime. It is similar but with different notation to the equation used with the EPA-IRIS risk coefficients.

By solving for O_M we find that 0.061 mesothelioma cases among the 2500 residents of Silver Bay (or 24 mesothelioma cases per 1,000,000) might be caused by the total fiber exposures. This assumes that the Northshore fibers are all as potent in producing cancer as grunerite asbestos (amosite) from which we derived the lifetime risk of 24 mesothelioma cases in 1,000,000 lifetimes (alternate 1). Assuming, however, that the Northshore fibers are only as active in producing mesothelioma as the least potent asbestos fiber type which is chrysotile asbestos this estimate is reduced to 0.24 mesothelioma cases in 1,000,000 (alternate 2). This can be compared to the background rate of mesothelioma not related to asbestos exposure which has recently been estimated to be 350 cases in 1,000,000 lifetimes (Price and Ware, 2004).

Again we select two values this time for the lung cancer risk (R_L) the percentage expected lung cancer mortality expressed as fiber/mL $\times$ years. We chose the total value for amphibole asbestos [exposure to riebeckite asbestos (crocidolite) and/or grunerite asbestos(amosite)] cohorts

[excluding Republic of South Africa (SA) miners] to predict the percentage increase in lung cancer assuming the Northshore fiber were as potent as amphibole asbestos ($R_L = 5.1 \text{ fiber/mL} \times \text{years}$) (alternate 3) and the best estimate of the lung cancer risk for chrysotile asbestos assuming Northshore fiber to be equivalent to the least potent asbestos fiber type ($R_L = 0.1 \text{ fiber/mL} \times \text{years}$) (alternate 4).

For a given cumulative asbestos exposure, the risk of developing lung cancer will increase as a percentage of the existing lung cancer risk in the population. We will assume that on average 8% of cigarette smokers develop lung cancer, 90% of the lung cancers are found in smokers, and 25% of the residents of Silver Bay smoke. Lung cancer mortality in Silver Bay would be 2.2%. The risk of lung cancer increases linearly with cumulative asbestos exposure following the relationship:

$$\text{Obs}_L = \text{Exp}_L + \frac{R_L \times E_{CA} \times \text{Exp}_L}{100}$$

$$2.2025\% = 2.20000\% + 0.0025\%$$

We calculate the increase in the observed number of asbestos-related lung cancers (Obs_L) assuming exposure to Northshore fibers is as potent as asbestos.

- R_L —Risk of lung cancer expressed as a percentage of lung cancer deaths per f/mL $\times$ years of asbestos exposure. The R_L used is 5.1 obtained from Hodgson and Darnton, 2000 (entry “ex. SA amosite” in their Table 2) and although an average is specific for amphibole asbestos.
- E_{CA} —The cumulative chrysotile asbestos environmental concentration (assumed to be continuous) $0.00014 \text{ f/mL} \times \text{years}$ is converted to the equivalent occupational concentration of $0.00061 \text{ f/mL} \times \text{years}$. Assuming 40 years of exposure the E_{CA} is $0.0245 \text{ f/mL} \times \text{years}$.
- Exp_L —Expected background of lung cancer deaths, 55.5, among the 2500 residents of Silver Bay. This background rate is determined by solving equations that reflect the relationship between the percentage of smokers who get lung cancer and the percentage of lung cancers that occur in smokers. Specifically, $0.9 \times (N^\circ \text{ of lung cancers}) = 0.08 \times (\text{Silver Bay Population}) = 0.08 \times 0.25 \times 2500/0.9 = 55.5$.

Using these values $\text{Obs}_L = 55.5$ lung cancers expected plus 0.069 of a case increase from assuming Northshore fibers are as potent as amphibole asbestos. The increase is equivalent to 27 lung cancer cases per 1,000,000 lifetimes (alternate 3). The lung cancer risk falls to 0.53 cases per 1,000,000 assuming the Northshore fibers are as potent as the least active form of asbestos (chrysotile with a $R_L = 0.1 \text{ fiber/mL} \times \text{years}$) (alternate 4).

10. Conclusions

The total risk for the asbestos-related cancers assuming the Northshore fibers have a potency equivalent to that of

grunerite asbestos (amosite) and the least active asbestos fiber type—chrysotile asbestos—is, respectively, 51 or 0.77 asbestos-related cancers per 1,000,000 lifetimes according to Hodgson and Darnton (2000) or 1 asbestos-related cancer in 28,500 lifetimes according to EPA’s IRIS an average for all the asbestos fiber types which corresponds to 35 asbestos-related cancers in 1,000,000 lifetimes.

However we believe, as did the Consumer Product Safety Commission and the Occupational Safety and Health Administration, that the potency of non-asbestos fibers to induce cancer is far less than the potency of asbestos to do so. Comparison of the size distribution of airborne Northshore fibers with respirable grunerite asbestos (amosite) indicate the Silver Bay exposures are predominantly non-asbestos fibers and not asbestos. Even in South Africa where grunerite asbestos (amosite) was commercially mined for more than 70 years no environmental mesotheliomas are known to occur and mesothelioma among the large mining population has been and remains a rare disease (Murray and Nelson, 2008).

There is only one epidemiology report in the world medical literature whose goal was to determine if asbestos-related diseases were developing from neighborhood exposure to grunerite (amosite) asbestos.

We have established that the airborne fiber levels in Silver Bay are at the low-end of background for asbestos worldwide (Fig. 1). Although the EPA-IRIS provides useful information and allows us to compare the fiber associated cancer risks in Silver Bay with EPA’s recent approach to asbestos post-9/11 in Lower Manhattan, it does not allow us to fully explore the issues about asbestos fiber type that are critical to understanding cancer risk from Northshore fibers in Silver Bay (Nolan et al., 1999, 2005). As asbestos risk assessments specific for fiber type are now available (Hodgson and Darnton, 2000) we selected the least potent form of asbestos for the upper limit of the mesothelioma and lung cancer risk and found it to be less than 0.77 cases per 1,000,000 lifetimes from exposure to Northshore fibers in Silver Bay, Minnesota.

We further conclude that the steps to dispose of the waste rock on land were sufficient to reduce the risk of cancer from fiber exposure among the general population around the Silver Bay facility to a combined excess risk of lung cancer and mesothelioma of approximately 1/1000 of the background risk (Price and Ware, 2004). The disposal method selected for the waste rock is highly likely to prevent the build-up of fibers in the environment. Nothing has occurred to indicate that additional steps need to be taken to further reduce the health hazards in Silver Bay related to exposure to Northshore fibers.

We emphasize that the conclusions are based upon using a model that has a linear dose–response relationship. However many scientists believe that there is a threshold exposure below which asbestos fibers do not cause cancer. If we were to believe such a threshold model and the exposures in Silver Bay below threshold, the predicted effects would approximately zero and our conclusions correspondingly enhanced.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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References

- Axten, C.W., Foster, D., 2008. Analysis of airborne and waterborne particles around a taconite ore processing facility. *Reg. Tox. Pharm.* 52, S66–S72.
- Barlett, Robert V., 1980. *The Reserve Mining Controversy: Science, Technology and Environmental Quality*. Indiana University Press, Bloomington and London (pp. 1–293).
- Bastow, T.F., 1986. *This Vast Pollution, "United States of America V. Reserve Mining Company"*. Green Fields Books, Washington, DC (pp. 1–208).
- Bowes, D.R., Langer, A.M., Rohl, A.N., 1977. Nature and range of mineral dusts in the environment. *Phil. Trans. R. Soc. Lond. A* 186, 593–610.
- Browne, M.L., Varadarajulu, D., Lewis-Michl, E.L., Fitzgerald, E.F., 2005. Cancer incidence and asbestos in drinking water, Town of Woodstock, NY 1980–1998. *Environ. Res.* 98, 224–232.
- Brunner, W.M., William, A.N., Bender, A.P., 2008. Investigation of exposures to commercial asbestos in northeastern Minnesota iron miners who developed mesothelioma. *Reg. Tox. Pharm.* 52, S116–S120.
- Coffin, D.L., Palekar, L.D., Cook, P.M., 1983. Correlation of *in vitro* and *in vivo* methods by mean of mass dose and fiber distribution for amosite and fibrous ferroactinolite. *Environ. Health Perspect.* 51, 49–53.
- Cook, P.M., Glass, G.E., Tucker, J.H., 1974. Asbestiform amphibole minerals: detection and measurement of high concentrations in municipal water supplies. *Science* 185, 853–855.
- Davis, J.M.G., Addison, J., Bolton, R.E., Donaldson, K., Jones, A.D., Miller, B.G., 1991. Variations in the carcinogenicity of tremolite dust samples of differing morphology. In: Landrigan, P.J., Kazemi, H. (Eds.), *The Proceedings of the Third Wave of Asbestos: Exposure to Asbestos in Public Places*. Public Health Control. Annals of the NY Academy of Sciences 643, pp. 3–490.
- Doll, R., 1989. Mineral fibres in the non-occupational environment: concluding remarks. In: Bignon, J., Peto, J., Saracci, R., (Eds.), *Non-Occupational Exposures to Mineral Fibres*. International Agency for Research on Cancer, N° 90, pp. 511–518.
- Federal Register 36: 23207, December 7, 1971.
- Federal Register 57: 24310, June 8, 1992.
- Gamble, J.F., 1994. Asbestos and colon cancer: a weight-of-the-evidence review. *Environ. Health Perspect.* 102, 1038–1050.
- Gamble, J.F., 2008. Risk of gastrointestinal cancers from inhalation and ingestion of asbestos. *Reg. Tox. Pharm.* 52, S124–S153.
- Gamble, J.F., Gibbs, G.W., 2008. An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragment. *Reg. Tox. Pharm.* 52, S154–S186.
- Germine, M., 1986. Asbestos in play sand. *N. Eng. J. Med.* 315, 891.
- Germine, M., 1987. Asbestos in play sand. *N. Eng. J. Med.* 316, 882.
- Health Effects of Tremolite, 1990. *Am. Rev. Respir. Dis.* 142, 1453–1458.
- Hesterberg, T.W., Axten, C., McConnell, E.E., Hart, G.A., Müller, W., Chevalier, J., Everitt, J., Thevenaz, P., Oberdorster, G., 1999. Studies on the inhalation toxicology of two fibreglasses and amosite asbestos in the Syrian golden hamster. Part I. results of a subchronic study and dose selection for a chronic study. *Inhal. Toxicol.* 11, 747–784.
- Higginson, J., Muir, C.S., Munoz, N., 1992. Stomach. In: *Human Cancer: Epidemiology and Environmental Causes*. Cambridge University Press, Cambridge, United Kingdom, pp. 273–82.
- Hills, J.P., 1979. Asbestos in public water supplies discussion of future problems. *Ann. N Y Acad. Sci.* 330, 573–577.
- Hillerdal, G., 1999. Mesothelioma: cases associated with non-occupational and low dose exposures. *Occup. Environ. Med.* 56, 505–513.
- Hodgson, J.T., Darnton, A., 2000. The quantitative risk of mesothelioma and lung cancer in relation to asbestos exposure. *Ann. Occup. Hyg.* 44, 564–601.
- Ilgren, E.B., 2004. The biology of cleavage fragments: a brief synthesis and analysis of current knowledge. *Indoor Built Environ.* 13, 343–356.
- ISO, 1995. 10312 (First Edition 1995-05-01) International Standard Ambient Air-determination of asbestos fibres—Direct-transfer transmission electron microscopy method, pp. 1–51.
- Kanarek, M.S., 1989. Epidemiological studies on ingested mineral fibres: gastric and other cancers. In: Bignon, J., Peto, J., Saracci, R., (Eds.), *Non-occupational Exposures to Mineral Fibres*. International Agency for Research on Cancer, N° 90, pp. 428–437.
- Kohyama, N., 1989. Airborne asbestos levels non-occupational environments in Japan. In: Bignon, J., Peto, J., Saracci, R. (Eds.), *Non-occupational Exposures to Mineral Fibres*. International Agency for Research on Cancer, N° 90, pp. 262–276.
- Langer, A.M., Maggiore, C.M., Nicholson, W.J., Rohl, A.N., Rubin, I.B., Selikoff, I.J., 1979. The contamination of lake Superior with amphibole gangue minerals. *Ann. N Y Acad. Sci.* 330, 549–572.
- Langer, A.M., Nolan, R.P., 1987. Asbestos in play sand. *N. Engl. J. Med.* 316, 882.
- Langer, A.M., Nolan, R.P., Addison, J., 1991. Distinguishing between amphibole asbestos fibers and elongate cleavage fragments of their non-asbestos analogues. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanism Fibre Carcinogenesis*. Plenum, New York, pp. 253–267.
- Levy, B.S., Sigurdson, E., Mandel, J., Laudon, E., Pearson, J., 1976. Investigating possible effects of asbestos on city water: surveillance of gastrointestinal in Duluth, Minnesota. *Am. J. Epidemiol.* 103, 362–368.
- Mason, T.J., McKay, E.W., Miller, R.W., 1974. Asbestos-like fibers in Duluth water supply: relation to cancer mortality. *J. Am. Med. Assoc.* 228, 1019.
- McConnell, E.E., Rutter, H.A., Ulland, B.M., Moore, J.A., 1983a. Chronic effects of dietary exposure to amosite asbestos and tremolite in F344 rats. *Environ. Health Perspect.* 53, 27–44.
- McConnell, E.E., Shefner, A.M., Rust, J.M., Moore, J.A., 1983b. Chronic effects of dietary exposure to amosite and chrysotile asbestos in Syrian golden hamsters. *Environ. Health Perspect.* 53, 11–25.
- McConnell, E.E., Axten, C., Hesterberg, T.W., Chevalier, J., Müller, W.C., Everitt, J., Oberdorster, G., Chase, G.R., Thevenaz, P., Kotin, P., 1999. Studies on the inhalation toxicology of two fibreglasses and amosite asbestos in the syrian golden hamster. Part II. Results of chronic exposure. *Inhal. Toxicol.* 11, 785–835.
- Moore, J.A., 1978. NIEHS oral asbestos studies. National bureau of standards special publication 506. *Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods*, pp. 153–61.
- Murray, J., Nelson, G., 2008. Health effects of amosite mining and milling in South Africa. *Reg. Tox. Pharm.* 52, S75–S81.
- National Research Council, 1984. *Asbestiform Fibers: Non-occupation Health Risks*, National Academy Press, Washington DC, pp. 1–334.
- Nolan, R.P., Langer, A.M., Oechsle, G.W., Addison, J., Colflesh, D.E., 1991. Association of tremolite habit with biological potential: preliminary report. In: Brown, R.C., Hoskins, J.A., Johnson, N.F. (Eds.), *Mechanism of Fibre Carcinogenesis*. Plenum, New York, pp. 213–251.
- Nolan, R.P., Langer, A.M., 2001. Concentration and type of asbestos fibers in air inside buildings. In: *The Health Effects of Chrysotile*

- Asbestos: Contribution of Science to Risk Management Decisions. Canadian Mineralogist Special Publication 5, 39–51.
- Nolan, R.P., Langer, A.M., Wilson, R., 1999. A risk assessment for exposure to grunerite asbestos (Amosite) in an iron ore mine. *PNAS USA* 96 (7), 3412–3419.
- Nolan, R.P., Ross, M., Nord, G.L., Axten, C.W., Osleeb, J.P., Domnin, S.G., Price, B., Wilson, R., 2005. Risk assessment for asbestos-related cancer from the 9/11 attack on the world trade center. *J. Occupa. Environ. Med.* 47, 817–825.
- Nolan, R.P., Langer, A.M., Ross, M., Addison, J., Gee, J.B.L. 2008. Non-occupational exposure to commercial amphibole asbestos and asbestos-related disease. Is there a Role for Grunerite Asbestos (Amosite) Proceedings of the Geologists' Association 118, 117–127.
- Office of Inspector General. Evaluation Report on EPA's Response to the World Trade Center Collapse: Challenges, Successes and Areas of Improvement. Report N° 2003-P-00012, August 21, 2003. Available from: URL: <<http://www.epa.gov/oigearth/index.htm>>.
- Peters, E.T., Doerfler, T.E., 1978. Amphibole mineral fiber analysis by electron microscopy: comparison of sample preparation procedures. In: Russell, P.A., Hutchings, A.E. (Eds.), *Electron Microscopy and X-ray Application to Environmental and Occupational Problems*. Ann Arbor Science, Ann Arbor, Michigan, pp. 189–203.
- Price, B., Ware, A., 2004. Mesothelioma trends in the United States: an update based on SEER data for 1973 through 2003. *Amer. J. Epidem.* 159, 107–112.
- Reserve Mining v United States 514F. 2d 492, March 14, 1975, US App on Petition for Review under Section 509 (b) (1) of the Federal Water Pollution Control Act. Appeal from United States District Court for the District of Minnesota.
- Ribak, J., Ribak, G., 2008. Human Health Effects Associated with the Commercial Use of Grunerite asbestos (amosite): Paterson, NJ; Tyler, TX, Uxbridge, UK. *Reg.Tox. Pharm.* 52, S82–S90.
- Richter, E.D., Laster, R., 2004. The precautionary principle, epidemiology and the ethics of delay. *Int. J. Occ. Med. Ind. Health* 17, 9–16.
- Ross, M., Kuntze, R.A., Clifton, R.A., 1984. Definition of Asbestos. Special Technical Publication 834 (Am. Soc. Testing Mat., Philadelphia), pp. 139–147.
- Ross, M., Nolan, R.P., Langer, A.M. Cooper, W.C., 1993. Health Effects of Mineral Fibers other than Asbestos. In: *Health Effects of Mineral Dust*. Guthrie, G.D., Mossman, B.T. (Eds.), Reviews in Mineralogy vol. 28, Mineralogical Society of America, Washington, DC, pp. 361–407.
- Ross, M., Langer, A.M., Nord, G.L., Nolan, R.P., Lee, R.J., Van Orden, D., Addison, J., 2008a. The mineral nature of asbestos. *Reg. Tox. Pharm.* 52, S26–S30.
- Ross, M., Langer, A.M., Nord, G.L., 2008b. The Search for Fibrous Minerals within the Peter Mitchell Taconite Mine, near Babbitt, Minnesota. *Reg. Tox. Pharm.*, 52, S43–S50.
- Ross, M., Nolan, R.P., 2003. History of discovery and use and asbestos-related disease in context with the occurrence of asbestos within ophiolite complexes. In: Dilek, Y., Newcomb, S. (Eds.), *Ophiolite concept and the evolution of geological thought*. GSA Special Paper 373, pp. 447–470.
- Schaumburg, F.D., 1976. Judgment Reserved: A Landmark Environmental Case. Reston Publishing, Reston, VA (pp. 1–265).
- Selikoff, I.J., 1974. Epidemiology of gastrointestinal cancer. *Environ. Health Perspect.* 9, 299–305.
- Selikoff, I.J., Hammond, E.C., Churg, J., 1972. Carcinogenicity of amosite asbestos. *Arch. Environ. Health.* 25, 183–208.
- Selikoff, I.J., Hammond, E.C., Seidman, H., 1979. Mortality experience of insulation workers in the United States and Canada, 1943–1976. *Ann. N Y Acad Sci.* 330, 91–116.
- Selikoff, I.J., Hammond, E.C., 1979. Health hazards of asbestos. *Ann. N Y Acad Sci.* 330, 1–814.
- Sigurdson, E.E., Levy, B.S., Mandel, J., McHugh, R., Michienzi, L.J., Jagger, H., Reason, J., 1981. Cancer morbidity investigations: lessons from the Duluth study of possible effects of asbestos in drinking water. *Environ. Res.* 25, 50–61.
- Sigurdson, E.E., 1983. Observations of cancer incidence in Duluth, Minnesota. *Environ. Health Perspect.* 53, 61–67.
- Stanton, M.F., Layard, M., Tegerig, A., Miller, A.E., May, M., Morgan, E., Smith, A., 1981. Relation of particle dimension to carcinogenesis of amphibole fibers and other fibrous materials. *J. Nat. Canc. Inst.* 67, 965–975.
- United States Environmental Protection Agency, 1986. Airborne Asbestos Health Assessment Update, EPA/600/8.84/003F, Washington, DC.
- United States Environmental Protection Agency (IRIS). Available from: <<http://www.epa.gov/iris/subst/0371.htm>>.
- Veblen, D.R., Wylie, A.G., 1993. Mineralogy of amphiboles and 1:1 layer silicates. In: Guthrie, G.D., Mossman, B.T. (Eds.), *Health Effects of Mineral Dust*. Reviews in Mineralogy, vol. 28. Mineralogical Society of America, Washington, DC, pp. 61–131.
- Weiss, W., 1995. The lack of causality between asbestos and colorectal cancer. *J. Occup. Environ. Med.* 37, 1364–1373.
- World Health Organization, 1986. International Programme on Chemical Safety (IPCS), Environmental Health Criteria 53. Asbestos and Other Natural Mineral Fibres, Geneva, pp. 1–194.
- World Health Organization, 1989. Occupational Exposure Limits for Asbestos WHO/OCH/89.1. Office of Occupational Health, World Health Organization, Geneva.
- World Health Organization 1999. International Programme on Chemical Safety (IPCS), Environmental Health Criteria 203. Chrysotile Asbestos. Available from: <http://www.who.int/pcs/docs/ehc_203.htm>.
- World Trade Center Indoor Environmental Assessment: Selecting Contaminates of Potential Concern Setting Health-Based Benchmarks. Task Force Working Group (EPA, Agency for Toxic Substances and Disease Registry, NYC Dept. of Health and Mental Hygiene and the Occupational Safety and Health Administration, May 2003.



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Rapporteur's Report Session 6: Risk assessment of asbestos and other fibrous mineral particulates: Robert P. Nolan & Arthur M. Langer

1. Paper 1—Identification and enumeration of asbestos fibers in the mining environment: mission and modification to the federal asbestos standard

Arthur M. Langer

Asbestos-related disease is increased with cumulative exposure (the concentration of asbestos in the air and duration of exposure). The maximum duration is assumed to be a working lifetime so federal agencies control cumulative exposure by limiting the airborne concentration of asbestos fibers equal to or greater than 5 μm in length. Air samples are collected in the environment of interest by entraining the airborne particulates including fibers on membrane filters and then counting the number of fibers using phase-contrast light microscopy. In addition to length, the fibers must have a length to width ratio of at least 3 to 1. This ratio is also referred to as the aspect ratio. Some counting strategies placed an upper limit on the fiber width restricting the counting to respirable fibers. Airborne asbestos is controlled by monitoring a sub-population of the airborne asbestos. No asbestos fibers shorter than 5 μm or fibers of any length having widths less than the resolution of the light optical method are counted. In the non-occupational environment, the Environmental Protection Agency requires the use of analytical transmission electron microscopy and fibers and counting fibers with lengths of 0.5 μm or greater and aspect ratios of 5 to 1 or greater are counted.

The permissible exposure limit for asbestos has been reduced by more than 120-fold since 1969, when the standard was 12 fiber/ml and the current monitoring methodology was developed. The manufacturing and mining worksites are regulated by two different federal agencies and the asbestos exposure limit was higher in the mining environment until recently (Mine Safety and Health Administration 30 CFR Part 56, 57, and 7, Federal Registry, February 29, 2008). Currently the permissible exposure limit (PEL) is the same in both types of workplace and it is 0.1 fibers per milliliter (fiber/ml) over an 8-h shift as a time-weighted average (TWA). A milliliter (ml) is equivalent to a cubic centimeter (cc) and sometimes this standard is reported as 0.1 f/cc. As the phase-contrast methodology was used to monitor lower exposures and environments, other fibrous mineral particulates were incorrectly characterized as asbestos. These occurred in talc deposits and taconite ores from the Eastern Mesabi Range.

The nature of asbestos is discussed and how it differs from other types of fibrous minerals that commonly form in other geological processes different from asbestos. Asbestos forms as a primary mineral in bundles of fibers making them polyfilamentous. The growth mechanism disorients the *a*–*b* plane causing monoclinic amphiboles to have anomalous optical properties. The unidirectional growth of asbestos imparts the mineral with unique physical

properties important in its commercial use and are described in the paper. Asbestos minerals have narrow distribution of widths because of how they grow so the width does not increase much as the fibers grow in length. Other types of mineral fiber form by cleavage and alteration from other primary minerals. Fibrous particulate formed by these processes tend not to have width as small as asbestos and widths increase significantly with length.

2. Paper 2—An overview of the risk of lung cancer in relationship to exposure to asbestos and of taconite miners

Geoffrey Berry, Graham W. Gibbs

The paper includes a review of meta-analyses of the relationship between cumulative exposure to asbestos and increased risk of lung cancer. The risk of lung cancer was found to increase as asbestos is processed into manufactured products compared to mining and milling. Also, the type of asbestos is an important factor with exposure to the amphibole asbestos minerals—crocidolite and amosite—having higher lung cancer risk than chrysotile. In most analyses, the exposure–response relationship is assumed to be linear and have no threshold. So every exposure no matter how small increases the risk of lung cancer. One should note that small exposures cause small increases in the lung cancer risk that often cannot be observed using epidemiology but can only be calculated using risk assessment.

The linear model was treated differently in the two important meta-analyses presented here. In one meta-analysis, it was assumed that where no exposure occurred the relative risk (RR) was similar to the general population and the intercept was set equal to 1 (number of observed cases equals the number of expected cases). In the other meta-analysis, the slope of the line and the intercept were both estimated for each study and interestingly for some studies, the intercepts were greater than 1. For these the fitted line indicated that for no asbestos exposure the RR of lung cancer was higher than the general population. One possible explanation for this is that smoking is more common among the asbestos exposed population than the reference population.

Cumulative asbestos exposures are quantified by multiplying the intensity of the exposure (in fiber/ml) by the duration of the exposure (in years). Working a lifetime (of 45 years) at the current asbestos exposure limit (0.1 fiber/ml) would correspond to a lifetime cumulative exposure of 4.5 fiber/ml $\times$ years. This can be compared to the cumulative exposure in the various asbestos cohorts that would double your risk of lung cancer for RR of 2. In chrysotile mining and milling, it takes a cumulative exposure of 4000 fiber/ml $\times$ years to double the lung cancer risk while in chrysotile manufacturing and textiles the same risk is acquired after a cumulative exposure of just 130 fiber/ml $\times$ years. The importance of asbestos fiber-type can be seen because exposure to 24 fiber/ml $\times$ years of

crocidolite doubled the lung cancer risk while for chrysotile it requires 1613 fiber/ml $\times$ years.

The United States Environmental Protection Agency developed a model to estimate increased risk of asbestos-related lung cancer. The model was parameterized using the high historical asbestos exposures. An effort to validate that model has been done using females in the asbestos mining towns of Quebec where environmental exposure to asbestos are estimated to be 105 fiber/ml $\times$ years. The EPA model predicted twice the number of lung cancer actually observed among the Quebec women.

The risk of lung cancer has been studied in three cohorts exposed to the fibrous particulates associated with taconite ore. The workers were miners and millers at Reserve Mining (currently called Northshore Mining), Erie or Minntac both in Minnesota and Homestake in South Dakota. No convincing evidence for an increase lung cancer risk has been identified among workers exposed to the fibrous mineral particulates found in taconite.

3. Paper 3—Mesothelioma and asbestos

Graham W. Gibbs, Geoffrey Berry

Mathematic models have been developed describing the relationship between mesothelioma and cumulative exposure to the three most important commercial asbestos fiber-types: crocidolite, amosite and chrysotile. Mesothelioma was first identified in 1960 among South Africans exposed to crocidolite. About 40% of the cases in this cluster had only environmental exposure. Few of these tumors were found among the South African amosite miners but were found to be far more common among the workers exposed while processing the amosite into products. Amosite was established as a cause mesothelioma in 1971, when an increased incidence of the disease was reported in a Paterson, New Jersey factory. Increased risk of mesothelioma among chrysotile-exposed workers is limited to miners and millers with significant occupational exposure.

The general causation argument for chrysotile causing mesothelioma is weak as this paper clearly points out. Mesothelioma causation relies almost exclusively on chrysotile miners and millers where all the mesotheliomas are pleural with no cases supporting a claim for peritoneal mesothelioma caused by chrysotile. There is considerable evidence supporting the claim that tremolite asbestos is an important confounder in these cases. While it is difficult to exclude a small effect there are important epidemiological studies indicating an effective threshold for chrysotile described in this paper. Such studies do not exist for the crocidolite and amosite.

Although anthophyllite mining in Finland started in 1918, it was not until 1994 that evidence-linking anthophyllite asbestos exposure to increased risk of mesothelioma was reported. It is common to read in the literature that amphibole asbestos is more mesotheliomagenic than chrysotile but the evidence for anthophyllite asbestos is not supportive of this statement. No mathematical model for anthophyllite asbestos causing mesothelioma has yet been developed due to the small number of cases, just four.

The vermiculite deposit near Libby, Montana contains fibrous minerals in the calcic amphibole group. Epidemiological studies of this cohort are often taken as evidence for the tremolite asbestos causing mesothelioma. Gibbs and Berry report the potency of this calcic amphibole as high based on McDonald et al. (2004) where 12 mesotheliomas occurred among 286 deaths or 4.2%. However, Sullivan (2007) recently reported a follow-up study where 767 deaths have occurred (an addition of 481 deaths) where only three new mesotheliomas occurred. Twelve mesotheliomas in the first 286 deaths with just three in the next

481 deaths the percentage of mesothelioma deaths decreased from 4.2% to 2% for the cohort. One peritoneal mesothelioma was reported among the three new cases, the other 14 were all pleural mesotheliomas.

Asbestos fiber-type	Cohort name		Total No. of mesotheliomas/deaths (%)
Tremolite–actinolite asbestos	Miners, Libby, MT	McDonald et al. (2004)	12/286 (4.2%)
		Sullivan (2007)	15/767 (2%)

McDonald, J.C., Harris, J., Armstrong, B., 2004. Mortality in a Cohort of Vermiculite Miners Exposed to Fibrous Amphiboles in Libby, Montana. *Occup. Environ. Med.* 61, 363–366.

Sullivan, P.A., 2007. Vermiculite, Respiratory Disease, and Asbestos Exposure in Libby, Montana: update of a Cohort mortality study. *Environ. Health Perspect.* 115, 579–585.

These results bring into question the claim that proportional mortality ratios increase sharply with increased length of follow-up. Exposures among the early deaths in the Libby cohort may have been higher and decreased with time making mesothelioma less common disease in the follow-up study.

Among the four major cohorts exposed to crocidolite during mining and manufacturing the mesothelioma mortality ranges from 2.3 to 17.8 (overall about 8.2) % or about 4-fold higher than the among the vermiculite workers based on the more recent follow-up data.

Gibbs and Berry present a convincing argument for the importance of asbestos-fiber-type in developing risk assessments for mesothelioma. The US EPA has long favored averaging the potency of the commercial asbestos fiber-types to develop risk assessment for asbestos-related cancer. This clearly over estimates the risk of chrysotile only exposures. Chrysotile specific risk assessments for mesothelioma predict values close to the observed numbers of cases, validating the fiber-type specific model.

There are four epidemiological studies of three cohorts exposed to the types of fibrous particulates associated with taconite ore. Among these workers, 2907 deaths have occurred with 2 of these deaths from mesothelioma making mesothelioma the cause of 0.07% of the deaths. Among males in the US general population 0.17% of the deaths are from mesothelioma. The workers in these three cohorts exposed to fibrous particulates associated with taconite experienced about half the mesothelioma risk of males in the general population.

4. Paper 4—Risk assessment due to environmental exposure to fibrous particulates associated with taconite ore

Richard Wilson, Ernest E. McConnell, Malcolm Ross, Charles W. Axten, Robert P. Nolan

The authors of this paper point out that the processing of taconite iron ore in the Silver Bay magnetic extraction mill has generated much public health interest since the early 1970s. This has stemmed from the early impressions concerning the nature of the mineral dust, i.e., that several of the amphibole minerals were in fact asbestiform. The Silver Bay facility, where milling and extraction takes place, is associated with release of fibrous gangue minerals, amphiboles of the cummingtonite–grunerite and tremolite–actinolite series. These mineral fibers have been found in the town air of Silver Bay.

The air of Silver Bay has been monitored for the past 35 years and much data have accumulated. The mean concentration of these suspect amphiboles has been found to be 0.00014 ml of air, which the authors point out are within the background level reported by the World Health Organization for asbestos in the

ambient air of urban environments. To place this level of dust in perspective, Wilson and colleagues state that the Silver Bay level was found to be consistently five-times lower than asbestos levels found in the air of the city of St. Paul. The public health community in Minnesota, placed their focus on the air of Silver Bay. The issue before Wilson and colleagues was “what is the risk of asbestos disease (mesothelioma and excess lung cancer) in Silver Bay resulting from these airborne fiber exposures?”

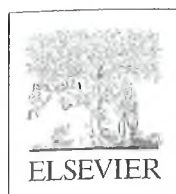
To calculate risk, Wilson and colleagues made several important assumptions: (1) the amphibole “fiber” monitored in the air of Silver Bay over time was as potent a carcinogen as asbestos. [Parenthetically, the authors comment that a recent mineralogical survey of the Peter Mitchell pit failed to find asbestos. Therefore the amphibole “fiber” was actually a population of non-asbestiform cleavage fragments.] The risk calculation is therefore a “worst-case”; (2) the average value of 0.00014 f/ml of air was representative of the concentration of these fibers over the entire time period of air monitoring; (3) the linear, no-threshold, models for asbestos and lung cancer and mesothelioma holds for low-level exposure to these fibrous particles; (4) exposure–response data exist for occupationally exposed groups of asbestos workers and may be used to calculate risk following these exposures as well; (5) An exposure to 0.00014 f/ml of air took place every day, 24 h a day (3×), three hundred sixty-five days a year, over a lifetime of 75 years. The cumulative lifetime exposure to fibrous particulates in the air in Silver Bay calculates to 0.0479 f/cc-years.

Using dose–response data available in the literature, and basing risk on cumulative dose over a 75-year lifetime, Wilson and col-

leagues calculated an excess cancer risk (lung and mesothelioma), based on an amphibole exposure, of one excess cancer in 28,500 lifetimes, or 35 excess cancers in one million lifetimes. Using the data available specifically for the chrysotile type of asbestos, the excess cancer risk drops to less than 0.77 excess cancer deaths in one million lifetimes.

How did these exposures impact the citizens of Silver Bay? The population of the town, given in the year 2000 (US Census data), was 2068. The risk of an excess cancer death of one in 28,500 lifetimes translates into a Silver Bay excess cancer death of one in almost 14 generations. This is a worst-case calculation based on the fibrous particles in air being asbestos. Using the chrysotile-exposed cohorts the risk is 45-fold lower. The calculable risk of observed cancer/expected cancer drops to values so low as to be impossible to distinguish by epidemiological study. Using a national figure of US lung cancer deaths of about one per 200 deaths, the Silver Bay Relative Risk for lung cancer calculates to: $RR = 1.007$.

The authors review the data for amosite asbestos and contrast the mortality differences between the mining and milling populations in the Transvaal amosite mines of South Africa and the mortality observed in manufacturing sites, especially in Paterson, New Jersey. The explanation for these different outcomes may lie in the final size distribution of the fibers subjected to vigorous manipulation during the manufacturing process. Manipulation decreases width dimension as the fibers are “opened” and thereby increases their biological potential.



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