Experience with Occupational and Environmental Asbestos Exposure

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In Vitro Solubility and In Vivo Biopersistence of Asbestos and Various Types of MVF in Lung

Fiber Class	Fiber type and use	K_{dis} at pH 7.4[a]	Time to dissolve, days[b]	WT ½ , days[c]
Asbestos	Amosite	<1	>5,000	~400
Asbestos	Crocidolite	<1	>5,000	~800
RCF	High temperature applications	3	~1,700	~50
Glass	MMVF 32 specialty applications	9	~550	~80
Rock	MMVF 21, building insulation	20	~250	~60

[a] Dissolution rate of fibers in vitro, k = ng/cm^2-hour.
[b] Time it would take a 1.0-μm-diameter fiber to dissolve completely.
[c] Weighted clearance half-time.

T.W. Hesterberg, et al. Toxicol Appl Pharmcol 151(2):262-275, 1998.
Review, National Research Council, #0-309-07093-7, 2000.

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Asbestos Exposure Indices

Disease	Relevant Exposure Index
Asbestosis *	Surface area of fibers with: Length >2 μm; diameter >0.15μm
Lung cancer **	Number of fibers with: Length >10 μm; diameter >0.15μm
Mesothelioma **	Number of fibers with: Length >5 μm; diameter <0.1μm

* total surface area of fibers within these dimensions
** number of fibers within these dimensions

M. Lippmann. Environ Res 46:86-106, 1988
T. Schneider and J. Skotte. Environ Res. 51:108-116, 1990

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Health and Safety Commission Report, London

Asbestosis: Review of data to early 1980 resulting in the following statement. "… the conclusion of the Ontario Royal Commission that 'lifetime occupational exposure to asbestos … in the range of 25 f/cc-years and below' cannot cause the fibrotic process to advance to the point of *clinical manifestation* is accepted."

Lung cancer: "One percent increase in the standard mortality ratio for lung cancer per year of exposure to one regulated fiber per ml is the best that can be suggested."

R. Doll and J. Peto. Asbestos Effects on Health of Exposure to Asbestos. Health and Safety Commission. London: Her Majesty's Stationery Office, 1985.

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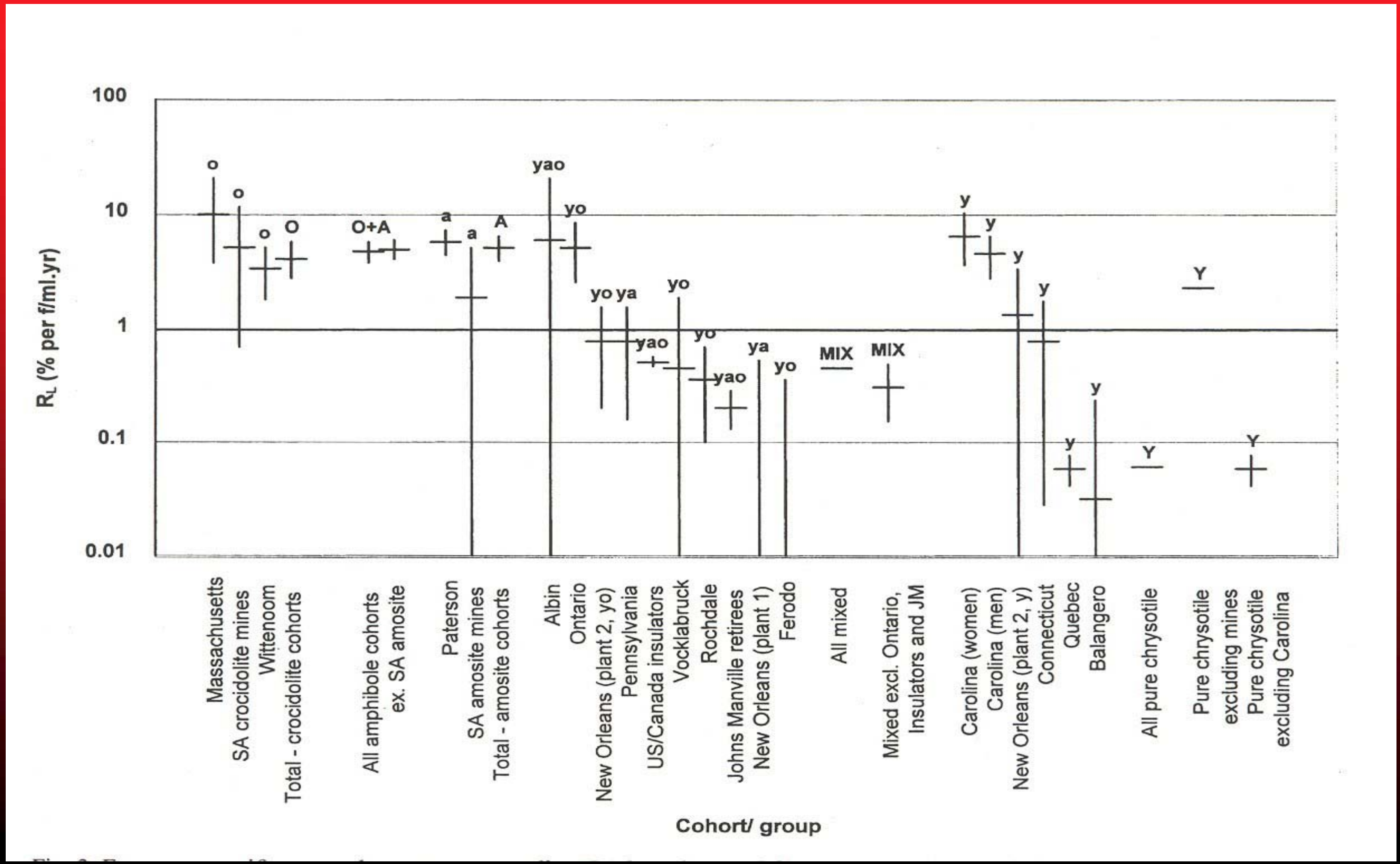
Exposure-Specific Excess Lung Cancer Mortality (R_L) by Cohort and Fiber Type



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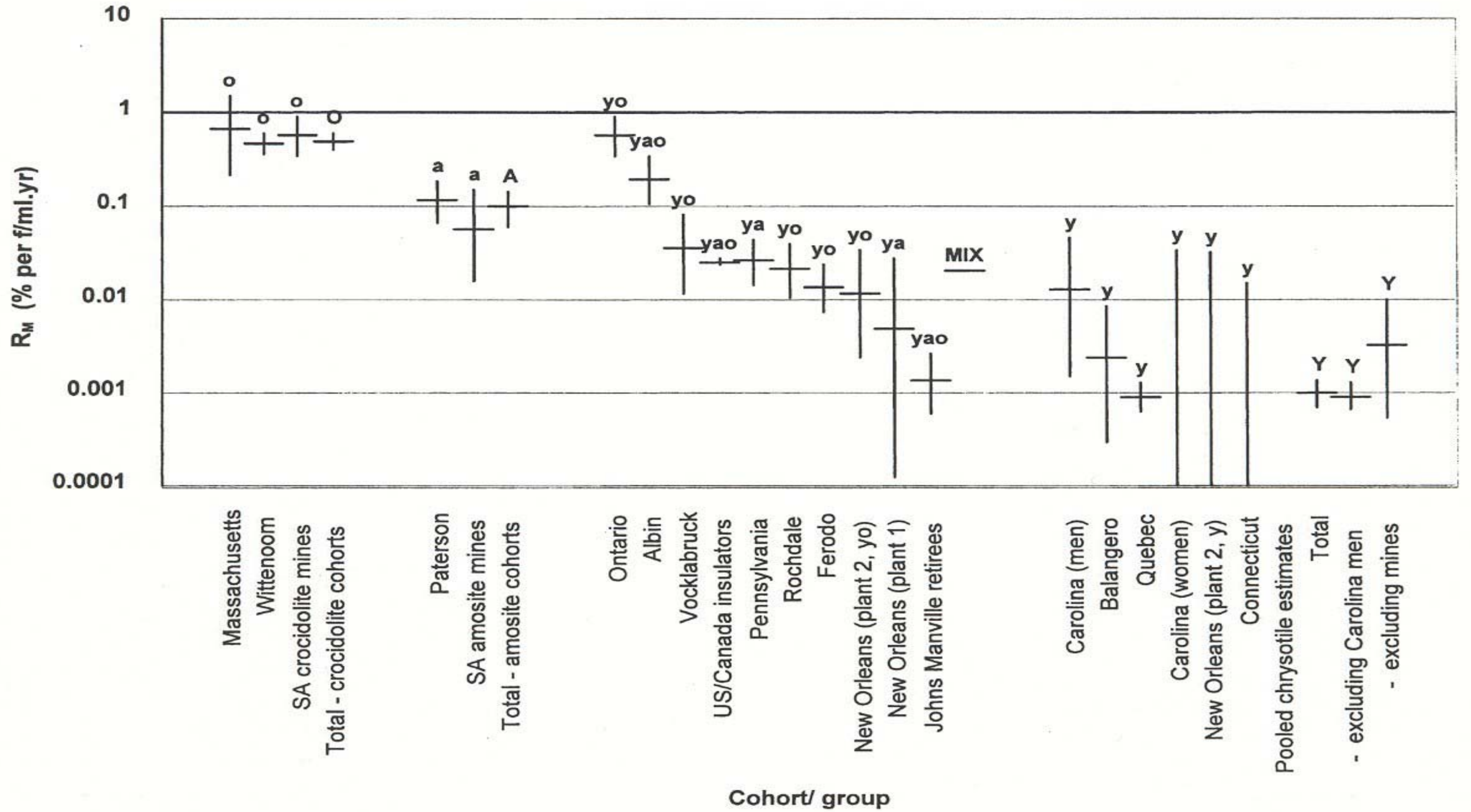
J.T. Hodgson and A. Darnton. Ann Occup Hyg 44:565-601, 2000.

Exposure-Specific Mesothelioma Mortality (R_M) by Cohort and Fiber Type



J.T. Hodgson and A. Darnton. Ann Occup Hyg 44:565-601, 2000.

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Risk summaries for cumulative exposure of 1 f/ml.yrs

Fibre	Mesothelioma	Lung Cancer
Crocidolite	Best estimate about 650 deaths per 100,000 exposed. Highest arguable estimate 1500, lowest 250	Best estimate about 85 (range 20 to 250) excess lung cancer deaths per 100,000 exposed.
Amosite	Best estimate about 90 deaths per 100,000 exposed. Highest arguable estimate 300, lowest 15.	
Chrysotile	Best estimate about 5 deaths per 100,000 exposed. Highest arguable estimate 20, lowest 1.	Best estimate about 2 excess lung cancer deaths per 100,000 exposed. Cautious estimate 30 per 100,000. In exceptional circumstances, it is arguable that an estimate of 100 per 100,000 might be justified. The case for a threshold, ie. zero, or at least very low risk - is arguable.*

* "exceptional circumstance" derived from the Carolina cohort

J.T. Hodgson and A. Darnton. Ann Occup Hyg 44:565-601, 2000.

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Fiber Induced Pleural Disease

- pleural plaques
- exudative pleural effusions
- diffuse pleural fibrosis
- rounded atelectasis
- malignant mesothelioma

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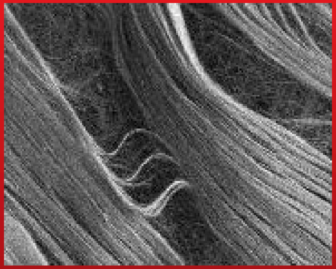
Mineralogical Terminology

Acicular

Equant

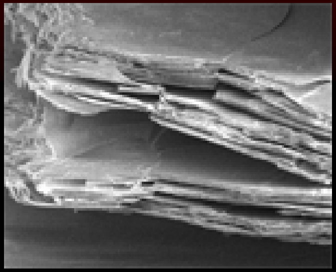


Fiber

Fibrous

Filiform

Prismatic



Platy

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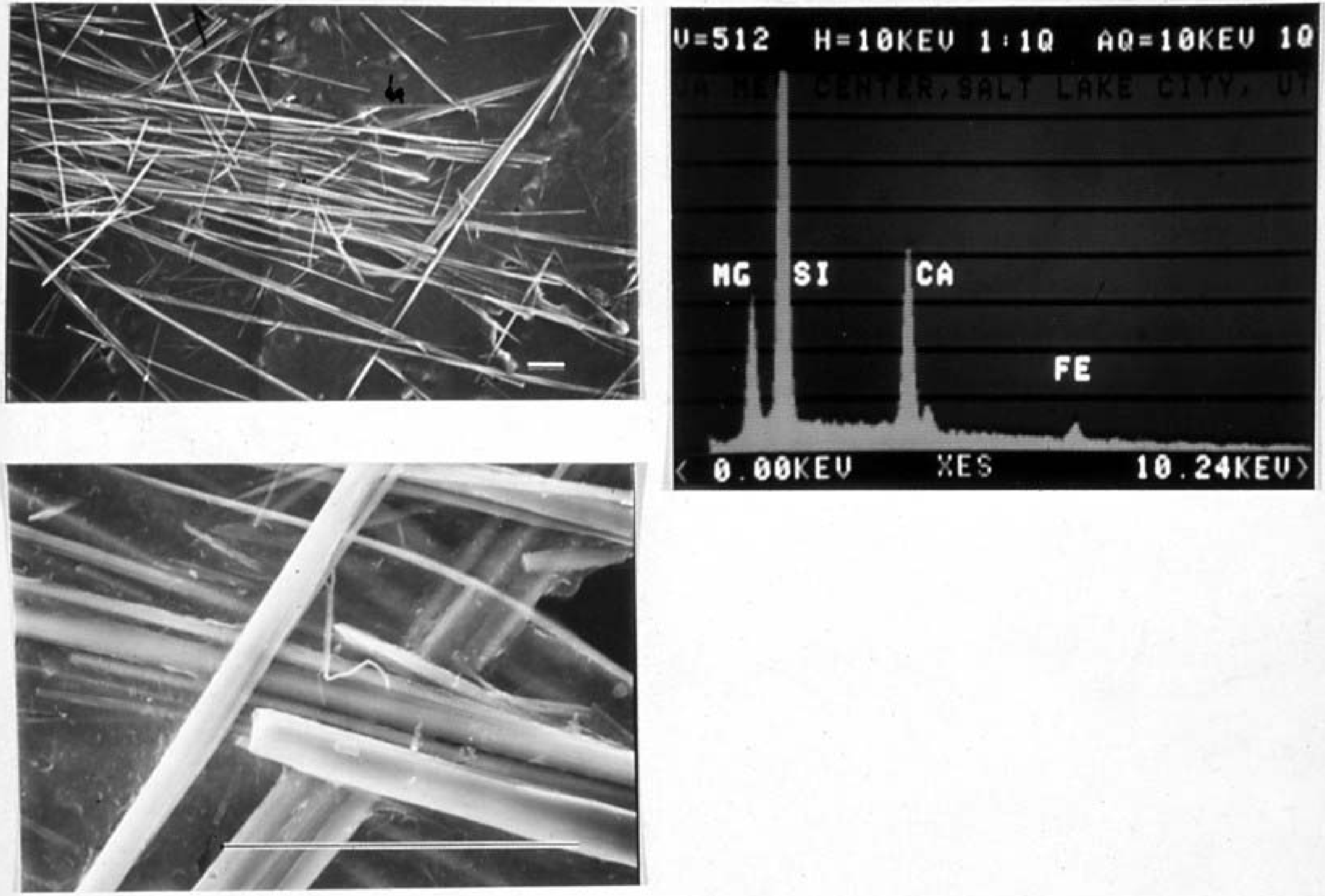

Scanning electron micrograph of fibrous tremolite with EDX analysis of the ore showing 25% magnesium, 56% silicon, 16% calcium, and 3% iron. The bars indicate 50 µm.

Dose-Response Relationship and Pleural Thickening and Pleural Calcification

Male Production Workers Thetford Mines

(standardized prevalence rates percent)

Radiographic Change	Age Groups						Total Dust Index *						Average Prevalence Rate
	36-	41-	46-	51-	56-	61-65	<10	10-	100-	200-	400-	800+	
Pleural thickening	2.8	4.2	7.1	8.0	7.9	11.5	2.4	4.6	6.5	5.8	8.3	10.5	6.4
Pleural Calcification	1.3	4.0	4.5	6.7	6.2	10.4	0.7	3.6	5.9	6.9	5.9	6.3	5.2

* Product of respirable dust level (mpcf) multiplied by the number of years worked at that level, corrected to a 40-hour working week.

C.E. Rossiter, et al. Arch Environ Health 24:388-400, 1972.

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Dose-Response Relationship and Pleural Thickening and Pleural Calcification

Male Production Workers from Asbestos

(standardized prevalence rates percent)

Radiographic Change	Age Groups						Total Dust Index *						Average Prevalence Rate
	36-	41-	46-	51-	56-	61-65	<10	10-	100-	200-	400-	800+	
Pleural thickening	0.7	1.7	4.1	3.6	4.6	7.6	2.9	2.6	3.0	3.0	4.7	5.8	3.2
Pleural Calcification	0.0	0.0	0.2	0.0	0.8	2.3	0.0	0.7	0.2	0.2	0.5	0.0	0.4

* Product of respirable dust level (mpcf) multiplied by the number of years worked at that level, corrected to a 40-hour working week.

C.E. Rossiter, et al. Arch Environ Health 24:388-400, 1972.

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Local deposits of mineral fibres (asbestos or erionite), incidence of plaques, and of malignant mesothelioma

Country or area	Type of fibre	Plaques %	Mesothelioma risk	Comment
Austria	tremolite	5.3	not increased	vineyard
Bulgaria	anthophyllite tremolite	2.8(F), 5.6(M)	not increased	tobacco growers
Corsica	tremolite	41(>50y.)	high	general population
Cyprus	tremolite		high	general population
Czechoslovakia	unknown	2.7-6.6	--	farmer
Finland	anthophyllite	6.5-9.0	not increased	
Metsovo (GR)	tremolite	46.9	high	ww houses*
SW Aridea (GR)		24.2(>40y)	high	
New Caledonia			high	ww houses*
South Africa	amosite crocidolite	2.5-6.6	high	population near mine
Turkey	tremolite erionite	1.2-25	high extremely high	farmers, ww houses
USSR	unknown		locally high	

* white-washing

G. Hillerdal. Indoor Built Environ. 6:86-95, 1997.

Biological Effects of Tremolite

Sample	Total No. of Fiber (x 10^4)	Number of Fibers > 8 μm (x10^3) and <1.5 μm
California flake-like talc deposit	5.1	1.7
Greenland	4.8	0
South Korea*	15.5	56.1

California	<6 μm length and <0.8 μm diameter
Greenland	<3 μm length and <1.2 μm diameter
South Korea*	majority <20 μm length and <0.4 μm diameter

* Mesothelioma 14/47 rats intrapleural injections.

J.C. Wagner, et al. Br J Cancer 45:352-360, 1982.

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Amosite Inhalation and Intraperitoneal Injection* Studies in Rats

Inhalation

- Short amosite: essentially no fibrosis and one peritoneal mesothelioma
- UICC amosite: relatively little pulmonary fibrosis and two adenoma
- Long amosite: widespread pulmonary fibrosis and pulmonary malignant tumors and mesothelioma

* Greater than 90% of animal developed mesotheliomas with long and UICC amosite vs. 4% with short amosite

J.M.G. Davis, et al. Br J Exp Path 67:415-430, 1986.

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Crocidolite and Erionite Intrapleural Inoculation Studies in Rats

Dust/Fiber	Mesothelioma	Non-mesothelioma
UICC Crocidolite	24	8
Shortened Crocidolite	1	31
Erionite	30	2
Shortened Erionite	0	32

J.C. Wagner. Biological Effects of Short Fibers. Proceedings of the VIIth International Pneumoconiosis Conference Part II, DHHS #90-108, 1990.

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Crocidolite and Erionite Inhalation Studies In Rats

Dust/Fiber	Pathology				Tumors
	Fibrosis Gradings 4 rats/sacrifice				
	3 mths.	6 mths.	12 mths.	24 mths.	Meso.
UICC Crocidolite	2.9	3.0	4.1	3.9	1
Shortened Crocidolite	2.0	2.0	3.3	2.8	0
Erionite	2.4	3.0	4.0	4.0*	24
Shortened Erionite	2.9	3.0	3.0	3.1	0

* 1 animal only remained for sacrifice

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J.C. Wagner. Biological Effects of Short Fibers. Proceedings of the VIIth International Pneumoconiosis Conference Part II, DHHS #90-108, 1990.

Percentage and Number of Fiber per Gram of Dried Lung Tissue (x 10^6)

	Fiber Size (µm) L.	D.	24 Months
SHORT	3 – 5	< 0.5	1.0% 63.0*
CROCIOLITE	> 1	< 0.5	15.1% 948.6
LONG	> 6	< 0.5	5.8% 2529.3
CROCIDOLITE	3 – 6	< 0.5	8.4% 3663.1

* No. of fibers

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J.C. Wagner. Biological Effects of Short Fibers. Proceedings of the VIIth International Pneumoconiosis Conference Part II, DHHS #90-108, 1990.

Translocation of Fibers Less Than 5 μm In Length

- Nose only inhalation of kaolin-based refractory ceramic fiber
- GML 4.5 μm (GSD 2.1), GMD 0.6 μm (GSD 1.2)
- Pleural tissue:
  GML 1.5 μm (GSD~2.0 μm)
  GMD 0.09 μm (GSD ~1.5 μm)
- Parenchymal tissue:
  GML 5.0 μm (GSD ~2.3)
  GMD 0.3 μm (GSD ~1.9)
- Fibers rapidly translocate to the pleural tissue

T.R. Gelzleichter, et al. Fundam Appl Toxicol 30:31-46, 1996.

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RCF Exposure and Pleural Plaques

Exposure Metric	Pleural Changes (% Subjects)	Subjects	Odds Ratio (95% Confidence Interval)
RCF Production Duration (years):		**All Plants (n=1008)**	
0 - 10	10 (1.6%)	645	---------
>10 - 20	12 (4.0%)	301	2.5 (1.0-6.1)
>20	5 (8.1%)	62	3.2 (0.9-9.7)
RCF Production Latency (years):		**All Plants (n=1008)**	
0 - 10	3 (0.8%)	388	---------
>10 - 20	8 (1.9%)	419	2.2 (0.6-10.5)
>20	16 (8.0%)	201	7.4 (2.3-32.6)
Cumulative Exposure (fiber-months/cc):		**Two Plants (n=637)†**	
> 15 - 45	4 (2.5%)	163	2.2 (0.5-11.8)
> 45 -135	8 (5.4%)	148	5.6 (1.5-28.1)
> 135	6 (9.8%)	61	6.0 (1.4-31.0)

* Asbestos duration and age ($\leq$ 50 yrs, > 50 yrs) were significant in all exposure models.
† Excludes 371 workers from three plant locations with no historical fiber exposure data.

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J.E.Lockey, et al. Chest, 121:2044-2051, 2002.

Mineral Fibers in Lungs and Parietal Pleura of Sheep from Central Turkey

Lung	0.8 x 10^6 tremolite fibers/g dry LT
	0.4 x 10^6 chrysotile fibers/g dry LT
Parietal pleura	0.7 x 10^6 tremolite/g dry pleura
	5.0 x 10^6 chrysotile/g dry pleura

Erionite vs. tremolite fibers in lung
GML (GSD): 5.4 (2.48) vs. 3.6 (2.05)

Fibers were shorter and thinner in parietal pleural than lungs but fibers longer than 5 μm were also detected and both erionite and asbestos fibers migrate towards the parietal pleura.

K. Mitchev, et al. AJRCCM 167:A685, 2003.

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Impressions

- Evidence that environmental exposure to mineral fiber is associated with significant non-malignant as well as malignant pleural disease in humans.
  - tremolite – actinolite
  - tremolite-actinolite-richterite-winchite transition fiber
  - anthophyllite
  - erionite
- The threshold at which various pleural changes occur is not well defined.

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Impressions

- There appears to be a substantial difference in the pulmonary parenchymal response between asbestiform versus cleavage fragment configurations. This is not as clear in regard to the pleural tissue.
- The impact of the tremolite-actinolite like amphiboles in regard to the pleural tissue that are <5 μm in length but have a high aspect ratio has not been defined.

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Impressions

Translocation of Fibers to Pleural Surface

- Both animal and human studies suggest this is a function of size and in large part limited to short thin fibers.
- Pathways to the pleura are not well understood.
- The pleural inflammatory response may differ from the parenchyma response in regard to type, magnitude, and timing.
- Approach the pleural tissue as a distinct pulmonary compartment separate from the lung parenchyma. *(Gelzleichter)*

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