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Asbestos in the lungs of persons exposed in the USA

A.M. Langer, R.P. Nolan

ABSTRACT: *Asbestos in the lungs of persons exposed in the USA. A.M. Langer, R.P. Nolan.*

Tissues obtained at autopsy or biopsy from 81 workers and 2 household persons, were chemically digested. The asbestos fibres recovered were characterized by analytical transmission electron microscopy. Among the 83 causes of death were 33 mesotheliomas, 35 lung cancers, 12 asbestosis and 3 from other cancers.

Of the three major commercial asbestos fibre types, amosite was found to be the most prevalent fibre, occurring in ~76% of the cases, followed by chrysotile in ~60% and crocidolite in ~24%. Amosite and chrysotile were observed as the single commercial fibre in ~22 and ~17% of the cases respectively, whereas crocidolite and tremolite were found as the single fibre type in only ~2.5% of the cases.

Among the fifteen cases where chrysotile and tremolite occurred together, the amount of chrysotile fibre always exceeded tremolite. However, tremolite was also found in ten additional cases where chrysotile was not detected. Amosite was present in four, amosite plus crocidolite in three, and crocidolite alone in one.

Amosite was present in all of the insulation workers' lungs studied and was found in the highest concentration in this exposure category. The highest chrysotile concentration was found among workers in general trades. Although most prevalent in shipyard workers lungs, crocidolite concentration is not statistically different among the exposure groups studied. Although crocidolite was found in twenty cases, amosite accompanied it in eighteen of these. Eleven of the 20 cases were from shipyard workers. Of the 8 mesothelioma cases, 7 also contained amosite. Crocidolite alone only occurred in 1 of the 33 mesothelioma cases analysed.

We concluded the following: crocidolite exposure occurred among USA insulators and a large percentage of other workers as well; insulation workers are primarily exposed to amosite; mixed fibre exposures are associated with more mesotheliomas than single fibre exposures; chrysotile only exposure is associated with ~12% of the mesothelioma cases studied; and if tremolite exposure is associated with chrysotile exposure, the chrysotile amount exceeds that for the associated tremolite.

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Studies to determine the types, concentration and morphology of asbestos fibre retained in human lung tissue by analytical transmission electron microscopy (TEM) are important in understanding the aetiology of asbestos-related disease. This is especially so in situations where asbestos-related disease occurs, but the nature of the past exposure is uncertain. Such information has been sought for decades [1].

Recently, the limitations of lung content analysis for asbestos have been viewed negatively not so much for the information gathered but rather for the lack of agreement between epidemiological claims and the results of lung content analysis that apparently refute them [2]. This is especially so for the asbestos fibre type associated with mesothelioma. For example, the 1976 study by POOLEY [3] of Canadian chrysotile miners and millers raised the issue that tremolite (an amphibole mineral sometimes associated with chrysotile asbestos ores) was an additional agent in the induction of asbestosis. Later, this was expanded to include mesothelioma [4]. Despite all of the criticisms, analysis of the fibres found in lung tissues are critical to understanding the aetiology of asbestos-related disease.

Current postulates concerning asbestos and disease

There exist in the USA important claims concerning asbestos exposure and asbestos-related disease which lung content analysis can help resolve. Consider the following six postulates:

The mortality experience of insulation workers cannot be related to crocidolite exposure. Outside of the asbestos cement industry, how extensive has crocidolite usage been in the USA? It has been claimed that crocidolite was not imported into the USA much prior to 1930, and it was not used in insulation products. Therefore, USA insulators were not exposed to it before 1930 [5] (see also Appendix). During the Second World War, US warships used amosite only and military shipyard workers at this time, unlike those in the UK, were either minimally or entirely unexposed to crocidolite. Using these claims an argument concludes that chrysotile may be the agent responsible for the majority of mesotheliomas observed in pre-1930 exposed American insulation and shipyard workers, especially those whose exposures began before the widespread introduction of amosite around

1930. Therefore, the pre- and post-1930 mesothelioma experience of the insulation workers, which is much the same, is chrysotile-related. These assertions have influenced the regulatory policy in the USA on fibre type and diseases [6]. Is this claim regarding crocidolite usage in the USA supported or refuted by lung content analysis and crocidolite consumption information?

All the asbestos fibre types induce mesothelioma equally well. The US Department of Labor's Occupational Safety and Health Administration in its most recent asbestos standard, still does not distinguish among the asbestos fibre types in terms of mesothelioma risk [7]. This position stands in opposition to that taken by 14 other industrial countries which permit different workplace exposure levels for the different asbestos fibre types [8]. Crocidolite's permissible exposure level is frequently one-tenth the value for chrysotile.

The relationship between asbestos fibre type and mesothelioma is frequently couched in subtle semantics, as reflected by several recent papers in the USA literature and exchanges they provoked [9, 10]. This exchange focused on the importance of fibre type in producing mesothelioma rather than relative fibre potency. A less potent fibre may produce more tumours in a population because it is more widely used. Chrysotile was therefore deemed more dangerous than crocidolite. Which fibres types are present in the lungs of workers dying with mesothelioma?

Chrysotile exposure alone does not cause human mesothelioma. Some investigators claim that chrysotile alone cannot cause pleural and peritoneal mesothelioma at any dose. Are there any cases of mesothelioma in which only chrysotile can be found in the lung?

Chrysotile exposure is invariably associated with tremolite exposure. In addition to crocidolite, tremolite has been the focus of several studies in the fibre carcinogenesis field. It has long been known that inhalation of tremolite asbestos is associated with human mesothelioma [11]. Tremolite was reported in the lungs of chrysotile-exposed miners and millers in Thetford, Quebec [3, 12]. Tremolite has been found in greater concentration than chrysotile in the lungs of forty Thetford cases [13]. Results of epidemiological studies suggest that the lung cancer and mesothelioma experience of chrysotile-exposed workers are so varied that perhaps tremolite played a role [14]. Tremolite form, asbestos fibre or cleavage fragment, is yet another issue as is the presence of other non-amphibole fibrous minerals, for example, diopside. This claim has been carried into end-product industries and industries which receive and process chrysotile fibre from sources outside of the Thetford area. If chrysotile exposure is associated with mesothelioma or lung cancer, and chrysotile alone is weakly or non-mesotheliomagenic, then the logical conclusion must be that the associated tremolite, which may accompany the chrysotile, is the aetiological agent in these diseases. Are these assertions supported by lung content studies?

Exposure to mixtures of fibres is more dangerous than exposure to a single type. The fibre synergy hypothesis was proposed almost 20 yrs ago in an attempt to explain and correlate mesothelioma mortality with lung content studies [15]. Many more mesotheliomas occurred in workers in the UK whose lungs contained more than one fibre type as opposed to lungs which contained only one. One American investigator insisted that his fibre consumption data reflected chrysotile exposure in the American insulation workers before 1930 and to chrysotile-amosite mixtures after 1930, resulting in a very similar mesothelioma proportional mortality experience. The hypothesis was abandoned largely because the experience of the American insulation workers was thought not to fit the pattern.

After all, chrysotile fibre is found in pleural tissues, and more mesotheliomas are found in cohorts exposed to both amphibole fibres and chrysotile [15, 16]. What do the fibre data show?

Product type and work environment controls the nature of exposure, dose and disease. The fibre types and amounts found in American workers' lungs in large measures reflect the products used and the nature of the work environment where the products were manipulated [17]. That is, the insulation trades tended to be exposed both to amphibole- and chrysotile-containing products, and their work was often confined to cramped and poorly ventilated areas so that high concentrations of mixed asbestos dust were generated and subsequently inhaled. Therefore can dose explain, at least in part, the high incidence of asbestos-related disease among insulation workers?

In summary, do lung content studies (fibre types, amounts and their character) support or refute these six postulates?

Material and methods

Almost exclusively, pulmonary tissues were referred to our laboratory through consultation. For each case asbestos exposure was established on the basis of occupational and/or personal history. The questions asked were often not if exposure to asbestos dust occurred, but rather to which fibre types and concentrations? Further, did these reflect the working environment and was there any correlation with a specific disease? The selection was clearly biased toward cases with occupational exposure and asbestos-related diseases. The underlying questions was always: "What is in this lung?"

The tissues were obtained at either autopsy or biopsy, and sent for verification of diagnosis and quantitation of asbestos lung content. The majority were formalin-fixed bulk tissues although some were mounted in paraffin blocks. The 83 tissues examined represent 81 persons occupationally exposed to asbestos in the work place, and 2 persons thought to have been exposed in a domiciliary setting (table 1).

A control group for these specimens was not collected during the period of analysis. The specimens were collected over many years. No case came with a control specimen. Limitations existed for the development of a control group retrospectively. Rather,

Table 1. — Information provided with the tissue specimens examines

	Exposure category			
	Category 1 Insulator/ pipe coverer	Category 2 Shipyards worker	Category 3 Other trades	Category 4 Family members
Total n=83	23	28	30	2
Males n=80	23	28	29	0
Females n=3	0	0	1	2
Age data n=64	13	27	24	0
Average age yrs	60.9±7.2	60.9±9.5	56.5±9.3*	65+
Range	54–74	45–78	31–68	-
Trades identified	Insulator (21) Pipecoverer (2)	Electrician (3) Welder (2) Machinist (2) Shipfitter (2) Pipefitter (2) Labourer (1) Sheetmetal (1) Sailmaker (1) Seafarer (1) Chipper and caulker (1) Shipyards (12)	Construction (5) Railroad (3) Plasterer (3) Brake repair (2) Pipefitter (2) Plumber (2) Electrician (1) Welder (1) Labourer (1) Sheetmetal (1) Maintenance (1) Rubber (1) Undercoater autos (1) Other traders (6)	Housewife (2)

The average age for all patients was 59.3±9.2 yrs, range 31–78 yrs. Data for "Trades identified" are presented as numbers in parentheses. *: the ages of "other trades" are younger than the persons making up the other exposure categories ($p < 0.05$ by t-test); +: age available for one housewife only.

results were compared with lung content analysis data collected among persons who died in the general population of New York City, during 1966–1968, the years of maximum asbestos consumption in the USA [18, 19]. These persons had no known occupational asbestos exposure and did not die of any asbestos-related disease. None of the 83 cases reported here had a lung content analysis comparable to anyone in the general population.

Information provided for each case

The information which accompanied each tissue specimen varied in detail. The most complete included the person's name, age, sex, occupational history, years in a specific trade(s), clinical history, primary cause of death (if deceased), secondary or contributing causes of death, *e.g.*, asbestosis, in lung cancer or mesothelioma, and notation of tobacco and alcohol consumption. Complete data were available

for only 63 of the 83 cases studied. Twelve of the 28 shipyard cases were noted as shipyard worker, rather than by specific trade, such as an electrician, in a shipyard. Incomplete data sets are noted (tables 1 and 2).

Exposure categories

After review of the data provided and preliminary analysis of 83 tissues received, it became apparent that three major exposure categories existed. Category 1: insulation workers and pipecoverers. Specimens obtained from twenty three individuals had occupational histories of either insulation work or pipe covering (table 1). Occasionally, the occupational history of the insulation worker noted work in other dusty trades. Insulation and pipecovering trades involved exposure to thermal system products. Only one insulation worker and one pipe coverer had exposure in a shipyard, insufficient to generate a separate exposure category. They were included as part

Table 2. — Distribution of asbestos-related diseases among the exposure categories studied

Diseases [#]	Category 1 Insulator/ pipe coverer n=23	Category 2 Shipyards worker n=28	Category 3 Other trades n=30	Category 4 Family members n=2	Total of groups n=83
Mesothelioma	9 (39.1)NS	12 (42.9)NS	12 (40.0)NS	0 (0.0)	33 (39.76)
Lung cancer	8 (34.8)NS	12 (42.9)NS	13 (43.3)NS	2 (100.0)	35 (42.17)
Asbestosis ⁺	6 (26.1)**	2 (7.1)**	4 (13.3)NS	0 (0.0)	12 (14.46)
Other cancers	0 (0.0)	2 (7.1)	1 (3.4)	0 (0.0)	3 (3.61)

Data are presented as number within the category and percentages with that category in parenthesis. #: ascertainment by clinical information, occupational histories, and review of pathology materials. +: asbestosis as a cause of death. Asbestosis was also noted as present in 5/33 mesothelioma cases, 9/35 lung cancers, 1/3 other cancers. Total of all asbestosis, 27/83 cases or 32.5%. Note 85.5% malignancies among the cases. NS: percentage of mesothelioma and lung cancer among exposure categories 1, 2, 3, not significantly different. **: $p < 0.01$, percentage of asbestosis deaths among categories 1 and 2 are statistically different.

of category 1 exposure. Category 2: shipyard workers. Specimens obtained from 28 individuals comprise this group (table 1). Any worker noted as having an exposure component which included a shipyard environment, who was not an insulation worker or pipe coverer, was included in this category. Duration of shipyard work was not a factor in exposure classification. For example, in table 1, three electricians are included as shipyard workers because their individual occupational histories indicated employment in this setting. Category 3: other trades and family members. Specimens obtained from 30 individuals comprise this group (table 1). If a worker had no experience as an insulator or pipe coverer and never worked in a shipyard environment, the individual was placed in this category. Only 2 of the 83 cases were nonoccupationally exposed and for exposure comparisons they are grouped with other trades (category 3).

Tissue preparation

Lung parenchyma specimens were obtained from individuals who developed mesothelioma, lung cancer, asbestosis and other cancers (table 2). Weighed aliquots of formalin fixed bulk tissues (~1–5 g) were completely digested with 5% potassium hydroxide [20]. A hot water bath, set at ~95°C, accelerated the reaction, which was invariably complete after ~6 h. Tissues impregnated in paraffin tended to be smaller in size, some as small as 20 mg. This has not been considered an obstacle in that successful analysis of small specimens obtained by transbronchial lung biopsies, has been reported [21]. These were subjected to xylene and ethanol baths to dissolve and remove the paraffin. The recovered specimen was washed in distilled water, weighed and subjected to alkali digestion following the above protocol.

It has been reported that some paraffin blocks may be contaminated with short chrysotile (<1 µm) fibres [22]. However, the origin of the fibre was unknown, and the issue raised was one which called for the use of control blocks. In this study only fibres >1 µm in length were counted and thereby avoided this confounder. The chemical digestates were centrifuged at 10,000×g and resuspended in distilled water 5–8 times. This technique is similar to that used for lung content analysis of exposed persons in the general population [18, 19].

A 10 µL aliquot taken from a 10 mL final dispersed KOH-cleared suspension, was micropipetted onto carbon-coated formvar support, nickel locator grid. Four to six such grid preparations were made and allowed to dry. After drying, the grids were examined by TEM to insure particle distribution homogeneity and integrity of the substrate. The dust residue was examined by analytical electron microscopy. The three diagnostics required for identification of fibres were morphology, structural characteristics determined by selected area electron diffraction, and chemical characterization by energy dispersive spectroscopy [23].

Lung content analysis

Mineral residues were examined over a range of magnifications, from 600–50,000× on the TEM view-

ing screen. Fibre counts were made at 10,000–20,000× magnification on the TEM screen by systematic x-y traverses. Fibres were noted on a morphological basis and a preliminary separation of chrysotile and amphibole was made. It must be noted that some fibres were too thick, thereby preventing transmission of diffracted electrons, even when the beam was accelerated at 100 kV. Representative thin fibres had their selected area electron diffraction patterns photographed and the plates were analysed to verify the presence of an amphibole or chrysotile structure. Common Laue zone patterns for the amphibole asbestos minerals were used for identification [24–26]. Specific amphibole species were determined by chemical characterization using energy dispersive X-ray spectrometry. Each spectrum obtained was compared with standards for identification.

Fibres were enumerated and counted on at least 10 grid openings, and based on the area of the preparation scanned, fibre number was calculated and expressed as millions of fibres·g⁻¹ of wet tissue. For data presentation, the values are expressed as fibres·g⁻¹ of dry lung tissue (10 g wet tissue is equivalent to 1 g dry). Fibre concentration values are expressed as those >1 µm in length present in 1 g of dry lung tissue. The fibre length limitation applied in counting was instituted to avoid incorporating background chrysotile into the final chrysotile count. This ubiquitous object, a single chrysotile fibril with an average length of about <1.0 µm, is commonly found in the lungs of persons who die in New York City [18, 19] with no known exposure to asbestos, especially in the occupational setting. The chrysotile values given here are therefore biased towards exposures which are point source in origin. This also holds, but to lesser degree, for the amphibole asbestos minerals. The limits of detection ranged from ~10,000–100,000 fibres·g⁻¹ dry lung tissue. The 1 µm length limit has been embraced by others for similar reasons [27].

Variance is necessarily associated with individual fibre counts. Under ideal conditions of assay, it is related to the actual concentration of fibres present in the specimen and their distribution on the prepared grids. However, it is also related to the amount of tissue digested, from where in the lung the specimen was obtained and preparation protocol.

Fibre count in the present study was carried out on at least 10 grid openings, the values obtained were averaged, and the scatter about the mean calculated. As the number of fibres increased, the spread around the mean decreased. An interesting discussion of the problems in interpreting the results of lung content analysis (both random and systematic errors) is in the literature [2]. Most of the error sources were well known in the analytical community [28, 29] and some of these have been recently discussed [30].

The concentration of fibres >1 µm in length (fibres·g⁻¹ of dry lung tissue), ranged considerably. All the data sets contained high or low value outliers which generated arithmetic averages with large standard deviations. Therefore, all statistical comparisons are made on the basis of geometric means (GM) and geometric mean standard deviations (GS) which greatly reduce the effects of outliers.

Results

Fibre types found in the 83 cases

Amosite, chrysotile and crocidolite fibres, the major commercially used asbestos fibres, either singularly or in combination, were recovered from all but 2 of the 83 parenchymal tissues studied (table 3). Amosite was the most prevalent fibre found, occurring in ~76% of the tissues examined, followed closely by chrysotile, found in ~60%. Crocidolite was quantified in 23% of the cases (table 3). In one tissue specimen a single crocidolite fibre was found and it was noted as present, raising its prevalence to 24%.

Greater amounts of chrysotile were found than either amosite or crocidolite ($p<0.01$) and greater amounts of amosite than crocidolite ($p<0.01$). This quantitative trend reflects the general fibre consumption figures over the past eight decades. However, rather than a chrysotile to amphibole tonnage consumption ratio of 19:1, the data indicate only a ~2.6:1 lung content ratio, favouring chrysotile. The role that chrysotile degradation and/or elimination played in this finding is unknown.

Both amosite and chrysotile asbestos were found as the single asbestos fibre type in 39% of the tissues, as compared to crocidolite which occurred alone in only two of the tissues studied (table 3 and 4).

Tremolite-actinolite (primarily tremolite with some ferrotremolite) and anthophyllite were also found in the tissues studied, with tremolite-actinolite occur-

ring more frequently (in ~30% of the tissues studied) and twice as the only fibre type detected (tables 3, 5 and 6). When both tremolite and chrysotile occurred in the same tissue (in 12 cases where tremolite was quantified) chrysotile concentration always exceeded tremolite (table 5).

Tremolite was found in 10 cases without chrysotile, but was associated with amosite and/or crocidolite in 8 of these (table 6). Anthophyllite was found in ~33% of the cases studied although it never occurred as the single fibre type detected and it was quantified in only half the cases.

Fibre types and concentration by exposure category

Among the insulation workers (category 1), all of the cases had amosite recovered from their lung tissues (table 7) and in some, crocidolite was also found. Similar findings have been reported by others [31, 32]. The latter report found crocidolite in 7 of the 13 cases examined, at concentrations slightly higher than those reported here. Amosite concentration ranged over almost three orders of magnitude. Amosite occurred with highest concentrations in category 1 as compared to those in the other two exposure categories ($p<0.001$). The next highest amosite concentration was found among the category 3 exposure workers. Chrysotile was found in 12 and crocidolite was found in 3 of 23 cases in category 1 (table 7).

Table 3. — Presence and concentrations of fibre types found in lung tissues of the 83 cases

Fibre type	Cases n	Cases %	Fibre concentration $10^6 \times \text{fibres} \cdot \text{g}^{-1}$ dry lung tissue* GM	Range	Cases with one fibre type n	Cases %	Lone fibre cases fibre observed %
Amosite	63	75.9 [‡]	7.5 ± 6.5	0.2–350	18	21.7	18/63 (28.6)
Crocidolite	20 ⁺	24.1 [‡]	2.7 ± 5.6	0.1–89	2	2.4	2/19 (10.5)
Chrysotile	50	60.2 [‡]	26.3 ± 29.5	0.1–7790	14	16.8	14/50 (28.0)
Tremolite-actinolite	25 [#]	30.1	6.0 ± 6.5	0.1–177	2	2.4	2/25 (8.0)
Anthophyllite	27 [§]	32.5	3.4 ± 4.4	0.1–50	0	0.0	0/27 (0.0)

Amphibole only, 22/83 (26.5%); chrysotile only, 14/83 (17.0%). GM: geometric mean. *: fibres $>1\mu\text{m}$; +: 19 of 20 cases report quantities, 1 case single fibre found (present) and quantities based on 19 cases; #: 21 of 25 cases report quantities, 4 cases single fibre found (present) (see table 6) and quantities based on 21 cases; §: 14 of 27 cases report quantities, 13 cases single fibre found (present) and quantities based on 14 cases; ‡: significant difference between percentage occurrence of crocidolite and amosite ($p<0.02$), crocidolite and chrysotile ($p<0.01$). Crocidolite is less prevalent.

Table 4. — Asbestos-related diseases and concentration where a single commercial asbestos fibre type is detected

Lone fibre found	Mesothelioma	Lung cancer	Asbestosis
Amosite GM+SD	5.8 ± 6.1	7.1 ± 5.3	40.6 ± 1.5
Range	0.2–34.8	0.6–110.0	30.0–55.0
Cases n	6	10	2
Chrysotile GM+SD	125.6 ± 7.2	87.5 ± 51.8	338.8 ± 34.9
Range	11.0–770.0	0.1–5440	140–820
Cases n	4	8	2
Crocidolite	3.0	7.0	-
Cases n	1	1	0
Total cases n (%)	11 (36.4)	19 (54.3)	4 (33.3)

GM: geometric mean. For amosite: asbestosis $>$ mesothelioma ($p=0.02-0.05$); asbestosis $>$ lung cancer ($p=0.05$); and mesothelioma – lung cancer (ns). For chrysotile: asbestosis $>$ mesothelioma ($p<0.001$); asbestosis $>$ lung cancer ($p<0.01$); and mesothelioma $>$ lung cancer ($p<0.01$).

Table 5. - Tremolite and chrysotile in pulmonary tissues in quantifiable concentrations

Chrysotile 10 ⁶ ×fibres·g ⁻¹ dry lung tissue	Tremolite	Job description	Cause of death	Other fibres
1344.0	14.0	House painter/ plasterer	Lung cancer	BLD
1340.0	14.0	Plasterer	Lung cancer	BLD
820.0	2.0	Plasterer	Asbestosis	BLD
610.0	20.0	Shipyard	Asbestosis	Amos, Croc
366.0	50.0	Shipyard	Lung cancer	Amos, Croc
301.0	177.0	Shipyard	Lung cancer + asbestosis	Amos, Croc
280.0	60.0	Insulator	Mesothelioma	Amos
220.0	4.0	Engineer	Lung cancer + asbestosis	BLD
15.0	1.4	Shipyard	Mesothelioma + asbestosis	Amos
7.0	2.0	Insulator	Lung cancer	Amos
7.0	0.6	Insulator	Mesothelioma	Amos, Croc
1.0	0.5	Shipyard	Lung cancer	Amos
0.7	Present	Shipyard	Mesothelioma	Amos
0.2	Present	Shipyard (machinist)	Mesothelioma	Amos
0.1	Present	Shipyard (electrician)	Mesothelioma	BLD
33.1±28.6	7.0±6.7			

BLD: below level of detection; Amos: amosite; Croc: crocidolite. Chrysotile: tremolite ratio range 410:1 to 2:1, quantitative values (n=12), arithmetic mean ratio ~12:1 and geometric mean ratio ~4.7:1.

Table 6. - Tremolite presence with chrysotile below limit of detection

Tremolite 10 ⁶ ×fibre·g ⁻¹ dry lung	Amosite	Crocidolite	Disease	Job description
94.0	-	-	Asbestosis	Construction worker
69.7	34.8	-	Mesothelioma/asbestosis	Insulator
12.0*	-	-	Mesothelioma	Housewife**
7.0	-	7.0	Lung cancer	Housewife
3.0	22.0	3.0	Mesothelioma	Railroad worker
1.9	5.8	-	Lung cancer	Pipecoverer
1.8	0.6	-	Lung cancer	Shipyard worker
1.0	15.8	1.3	Lung cancer/asbestosis	Maintenance worker
0.3	0.4	3.4	Mesothelioma	Electrician/powerplant
Present+	0.2	-	Mesothelioma	Welder
GM 4.9±6.7	GM 3.2±8.4	GM 3.1±2.0		

GM: geometric mean; *: presence of anthophyllite also (600,000 fibres·g⁻¹ dry lung tissue). **: Occupation of husband unavailable; +: noted as present. (one fibre detected).

Table 7. - Fibre type, concentration* by category of exposure (trade)

Trade		Amosite	Crocidolite	Chrysotile	Tremolite-actinolite	Anthophyllite
Category 1	GM	15.6±4.7	1.6±3.7	13.7±30.1	22.7	9.8
Insulator/ pipe coverer (n=23)	Range	0.8-320.0	0.6-7.0	0.8-5400.0	0.6-70.0	1.0-44.0
	%	100	13	52.2	26.1	21.7
Category 2	GM	3.4±6.9	2.5±8.2	16.8±21.9	28.0	13.0
Shipyard worker (n=28)	Range	0.2-91.0	0.1-89.0	0.1-7790.0	0.1-177.0	0.3-50.0
	%	75.0	39.3	67.9	32.1	21.4
Category 3	GM	6.6±7.1	4.2±2.5	76.0±24.0	23.3	4.3
Other trades household (n=32)	Range	0.2-350.0	1.3-14.0	0.4-5440.0	1.0-94.0	1.0-12.0
	%	59.4	15.6	62.5	31.3	12.5

GM: geometric mean. *: concentration of fibres are given in 10⁶×fibres·g⁻¹ of dry lung tissue; fibres >1 µm length.

A large proportion of shipyard workers (category 2) also had amosite (~75%) and chrysotile (~68%) recovered from their lung tissue, but crocidolite (~39%) occurred with greater frequency than in the other two exposure categories (table 7). However, the concentrations found among the exposure categories were statistically indistinguishable ($p>0.05$). The other trades (category 3) also had amosite and chrysotile recovered from lung tissues, and some crocidolite as well. The amount of chrysotile was greatest in cat-

egory 3 exposure, with about equal amounts found among cases in the other two categories (table 7).

The category 3 group contained tissues from three railroad workers. Amosite fibre was found in two (22×10⁶ and 55×10⁶ fibres·g⁻¹ dry lung tissue), and crocidolite in one of these (3×10⁶ fibres·g⁻¹ dry lung tissue). The mixed amphibole exposure occurred in a person with mesothelioma. The chrysotile-only exposure hypothesis for all railroad workers [33] is not supported by these findings.

Amosite concentration ranged over almost three orders of magnitude. The concentration of chrysotile, greatest in the category 3 exposed workers, ranged over almost five orders of magnitude (tables 3, 4 and 7). The tissues obtained from shipyard workers (category 2) tended to have lower concentrations of amosite and chrysotile as compared to those found in insulation workers and workers in other trades (category 3).

Fibre types, concentrations and asbestos-related diseases by exposure category

Among the insulation workers studied, asbestosis is cited more frequently as a cause of death as compared to the other exposure categories (table 2). Fibre concentrations in insulation workers' lungs indicate that only their amosite exposure was more intense than that experienced by workers engaged in other trades or workers in the shipyard environments (table 7).

Workers in all exposure categories had virtually the same mesothelioma mortality. However, these cases were selected from a nonrandom sample of persons known to have been occupationally exposed to asbestos (table 2).

Four of 33 mesotheliomas (~12%) occurred in individuals whose lungs contained chrysotile asbestos as the major commercial fibre type (table 4). It has been reported in Germany that 72 of 843 mesotheliomas (~8.5%) had occurred in workers whose lung content analysis found only chrysotile [27].

The concentration of amosite alone, and chrysotile alone, was greater in those with asbestosis, than in those with mesothelioma ($p < 0.01$). The chrysotile-only mesothelioma cases contain very high fibre concentrations (table 4). Twenty-two mesotheliomas are associated with mixed-fibre exposures and eleven with exposure to single fibre type exposures. High concentrations of uncoated fibres in the lungs of persons with asbestosis has been reported previously, and a general correlation was found between degree of scarring and fibre concentration [34, 35].

Discussion

Lung content analysis for mineral fibre is of the residual fibre population. The long, durable fibres are preferentially retained while both short and non-durable fibres are removed. However, many of the lungs examined in this study indicate the presence of very high concentrations of chrysotile, on a fibre number basis, as compared to the amphibole fibres present in the same tissue specimen. Chrysotile is, in some instances, biopersistent [19, 36]. This would mean, (if the elimination data are in principle correct and exposure variables are normalized), that extraordinarily greater amounts of chrysotile would have been inhaled during the lifetimes of these workers. Compare the concentrations of chrysotile and crocidolite as shown, for example, in table 3. The geometric mean chrysotile content of the lungs studied is $\sim 26 \times 10^6$ fibres·g⁻¹ of dry lung tissue as compared to $\sim 2.7 \times 10^6$ fibres·g⁻¹ for crocidolite, about a

10-fold difference (table 3). If 99% of the chrysotile and 80% of the crocidolite inhaled during life was eliminated, back-calculation yields an almost 200-fold differential in the original inhaled average dose of these two fibre types: $2,600 \times 10^6$ chrysotile to about 14×10^6 crocidolite, deposited in a volume of tissue corresponding to the 1 g of dry lung tissue. Time since cessation of exposure is an important unknown variable among the cases. However it seems unlikely that the high chrysotile fibre concentrations were determined only in recently retired or currently employed workers, as opposed to those determinations made for crocidolite. Values for different fibre types obtained on single lung specimens support this conclusion. Use of lung content analysis in the resolution of the original postulates raised take these processes into consideration. Quantitation of exposure based on retained fibre number is a relative index.

Examination of the six postulates

The mortality experience of American insulation workers cannot be related to crocidolite exposure.

Crocidolite has been found in the lungs of about 24% of the American workers studied and is more prevalent in the lungs of shipyard workers (tables 7, 8). Crocidolite was found in 39% of the tissue specimens obtained from individuals who had some history of shipyard work (table 7). Five tissue samples with crocidolite were obtained from a railroad worker, an undercoater of automobiles, an electrician, the wife of an insulator, and a maintenance worker (table 8). A trace of crocidolite was found in the tissue of a construction worker. Crocidolite is also present in the lungs of 13% of the insulation workers studied (table 7). It is important to note that amosite accompanied crocidolite in ~90% of the cases where crocidolite was found (table 8). This suggests that exposure to these fibre types covaried as the result of either specific products or work sites. Its distribution among the exposure categories suggests it was widely used.

LANGER and NOLAN [17] found that for American insulation workers, amosite was universally present while crocidolite occurred less commonly in their pulmonary tissues. In all studies, higher prevalence of the amphibole minerals was observed than would be anticipated by USA commercial consumption figures. For example, crocidolite was found in 39% of shipyard workers when only 1–2% of the total asbestos consumed in the USA was this fibre type.

SELIKOFF [36] commented during a discussion that crocidolite-containing cigarette filters [37] may have been the source of crocidolite fibre found in the lungs of insulation workers reported by KOHYAMA and SUZUKI [32]. The data now available suggest that this speculation was unwarranted. The historical consumption data of SELIKOFF [37] are not accurate (see Appendix) and ample opportunity existed for many American workers to be exposed to crocidolite. Further, crocidolite filters in Kent cigarettes were introduced in 1952 and accounted for a total of ~110 metric tonnes consumption between 1952–1956 [38]. This was only a small percentage of the total yearly crocidolite consumption (~20 metric tonnes·annum⁻¹ as

Table 8. - Crocidolite and other fibres, in pulmonary tissues of 20 workers

Crocidolite	Amosite	Chrysotile	Job description	Cause of death
10 ⁶ ×fibres·g ⁻¹ dry lung tissue				
88.5	90.5	301	Shipyard (welder)	Lung cancer + asbestosis
50.0	50.0	366	Shipyard	Lung cancer
20.0	65.0	610	Shipyard	Asbestosis
14.0	1.0	BLD	Undercoat autos	Lung cancer
7.0	21.0	BLD	Insulator	Asbestosis
3.4	0.4	BLD	Electrician	Mesothelioma
3.0	22.0	BLD	Railroad	Mesothelioma
3.0	BLD	BLD	Shipyard	Mesothelioma
3.0	1.0	BLD	Shipyard	Mesothelioma
2.0	5.0	2.0	Shipyard	GI cancer
1.3	15.8	TR	Maintenance	Lung cancer + asbestosis
1.0	30.0	0.3	Insulator	Asbestosis
1.0	1.0	BLD	Shipyard	Mesothelioma
0.7	14.0	BLD	Shipyard (machinist)	Mesothelioma
0.7	BLD	BLD	Wife (insulator)	Lung cancer
0.6	12.0	7.0	Insulator	Mesothelioma
0.6	16.8	1.5	Shipyard (electrician)	Mesothelioma
0.4	1.5	BLD	Shipyard	Lung cancer
0.1	0.2	BLD	Shipyard	Lung cancer
TR	4.5	BLD	Construction	Lung cancer

Geometric mean ($\pm$ SD) for crocidolite 2.4 ± 5.6 , amosite 6.7 ± 6.6 and chrysotile 17.1 ± 22.4 . BLD: below level of detection; GI: gastrointestinal; TR: trace or one fibre detected. Nineteen cases were those in which crocidolite was quantifiable, 18/20 cases associated with amosite (90%), and 8/20 cases, associated with chrysotile (40%).

compared to ~8,000 metric tonnes·annum⁻¹ of crocidolite consumed in other applications).

It is noteworthy that both insulation and shipyard workers were exposed to amphibole-containing and mixed-fibre products. In the former instance, insulator contact was with amosite fibre and, to a lesser degree, depending on time, crocidolite. For shipyard workers, many trades worked in this environment. Fibre exposure was, in part, bystander in character with attendant lower quantitative total exposure (table 5).

The first postulate, that crocidolite exposure categorically did not occur, especially among insulators, is rejected on the basis of lung content analysis. Whether or not some or even all of the early mesothelioma deaths reported among insulators were crocidolite induced, is unknown. For workers exposed after 1930, the answer is known: yes, some were exposed to crocidolite; and all were exposed to amosite.

All the asbestos fibre types induce mesothelioma equally well. The data generated in this study suggest that the mixed fibre types are associated with more mesotheliomas ($n=22$) than exposure to any of the three commercial fibers alone ($n=11$). Among the mesothelioma cases amosite and chrysotile occur more frequently than crocidolite.

Chrysotile exposure alone does not cause human mesothelioma. Compare the data for the different fibre types, in table 4, where concentrations for single asbestos fibre types, by asbestos disease, are given. The amosite and chrysotile exposed populations comprised of almost an equal number of cases (18 and 14 respectively). For mesothelioma, ~22 times more chrysotile fibres, on average, are present than amosite. The geometric mean value of $\sim 126\times 10^6$ fibres·g⁻¹ of dry lung tissue of chrysotile compared to the 6×10^6 fibres·g⁻¹ of dry lung tissue for amosite. This difference

is similar to that in studies of chrysotile-exposed workers who succumbed with mesothelioma [39]. If these numbers are qualitative indices of exposure and the fibre population represents retained dose, a worker must inhale many orders of magnitude more chrysotile fibre, as compared to amphibole fibre, to achieve the same risk for mesothelioma. The single asbestos fibre type in the mesothelioma cases provides further evidence that chrysotile occurs without tremolite, and at very high doses can produce pleural mesothelioma [36].

Chrysotile exposure is invariably associated with tremolite exposure. Unlike earlier reports of chrysotile miners and millers, in this series of cases when chrysotile and tremolite were found together in the same lung specimen, chrysotile content always exceeded tremolite. Only in 2 of 83 cases was tremolite the only asbestos fibre type detected. The lung content analysis obtained on 94 miners and millers from the Thetford area of Quebec indicated an opposite relationship. Exposure to these ores, some known to contain tremolite, may not reflect a general pattern for all persons who are chrysotile exposed. Based on our data, the tremolite claim does not hold for all chrysotile exposures [14, 35].

Rather, tremolite occurs with highest concentrations in the lungs of plasterers (table 5). Patching, taping and spackling compounds marketed in the USA are known to have contained tremolitic talc in addition to chrysotile. This may be a source for tremolite but these materials have been shown to contain cleavage fragments rather than asbestos [11]. In seven individuals who succumbed with mesothelioma, amosite and/or crocidolite was found in six. Five of the seven involved shipyard work and the others involved insulation work (table 6). In seven of nine cases where tremolite was found without chrysotile, amosite and/or crocidolite was also present. In four

cases where tremolite was found as trace, three contained amosite. Of the total 25 cases (11 with mesothelioma) where tremolite was found, nine contained amosite and/or crocidolite.

Chrysotile exposure may be associated with tremolite exposure. However, when tremolite is found without chrysotile present, it is generally associated with other types commercial amphibole asbestos. Calcic-amphibole contamination of amosite needs to be considered as well as other sources of tremolite unrelated to chrysotile.

Exposure to mixtures of asbestos fibres is more dangerous than exposure to a single type. These data allow re-examination of risk following exposure to mixed-fibres as compared with the risk following exposure to the commercial asbestos minerals alone. Mesothelioma occurred in four cases where chrysotile was the only asbestos fibre found, as compared to seven cases where only a single amphibole asbestos fibre type was found. Mixed-fibre populations were associated with 22 of the 33 mesotheliomas. These numbers only roughly approximate the multiplicative model postulated by ACHESON and GARDNER [15] ($22 \sim 7 \times 4$).

Product type and work environment control the nature of exposure, dose and disease. The majority of the mesotheliomas (22), occurred in persons whose work environment provided opportunities for intense as well as mixed-fibre exposure. An observation which mitigates against dose as a controlling factor (e.g., insulation workers are exposed to high concentrations of dust) is that the two commercial amphibole fibres are present in lowest concentrations in individuals with mesothelioma. The data also indicate that chrysotile alone may induce mesothelioma in humans, but the fibre exposure required is much higher than that associated with exposure to amosite and crocidolite. If chrysotile consumption was 19-fold greater than that of amphiboles asbestos during the past three-quarters of a century, why are chrysotile-only mesotheliomas not more common? The question is not so much whether or not chrysotile is mesotheliomagenic but rather how potent is it? The data indicate that it is not as potent an agent as, for instance, crocidolite on a fibre-for-fibre basis.

Conclusion

The pulmonary tissues of a group of asbestos-exposed persons in the USA, who died of asbestos-related diseases, were examined. Amosite was observed with the greatest frequency, followed by chrysotile, anthophyllite, tremolite-actinolite and crocidolite. In terms of concentrations, as indexed by fibre number, chrysotile was the most abundant fibre found, followed by amosite, tremolite-actinolite, anthophyllite and crocidolite.

The frequency and exposure category occurrence of the amphibole asbestos varieties amosite and crocidolite suggest that specific products, e.g., pipe insulation containing amphibole fibres, used by specific trades, and work environments, to a large degree explain the disease pattern. The frequency of occur-

ence and concentration data are so skewed from USA consumption figures, that the usefulness of the latter in gauging exposure is questionable. For example, crocidolite consumption in the USA tended to average only about 1–2% of the total fibre used in commerce over many decades. However, it was found to be present in the lung tissues of 24% of all workers and ~39% of shipyard workers. A similar distribution holds for amosite. For American insulators, the presence of amosite is ~30-fold greater than is indicated by consumption figures. Amphibole exposure among shipyard and insulation workers has been noted previously [13]; risk of peritoneal mesothelioma is thought to be especially increased following exposure to amosite [40].

The Rochdale studies which focus on mesothelioma are frequently said to reflect gross fibre consumption figures, i.e., 98% chrysotile, 2% crocidolite exposure [41]. However, a small portion of the Rochdale works was engaged in manipulating crocidolite only. The lung content found was consistent with the known exposure to chrysotile although crocidolite was also present at a concentration 300-fold higher than that of the general UK population [42]. Again, in such an example, usage of consumption figures are limited, perhaps even misleading, as exposure surrogates.

This argument, on ratios of fibre types, has been used periodically by the investigators to support the contention that the commercial asbestos fibre types have about equal mesotheliomagenic potential. A recent review in the USA accepted the consumption data at face value, which led to the same erroneous conclusion: chrysotile produces as much malignant disease as the amphiboles [43].

Some amosite pipe lagging was made with calcined diatomaceous earth and magnesia. Manipulation of such a product generates a complex aerosol. The role that crystalline silica and particulates $<2.5 \mu\text{m}$ in diameter in lung fibrosis in insulation workers remains unclear. Such components of the workplace aerosol may be associated with the small, rounded opacities which frequently accompany irregular scar patterns in asbestosis.

There may be many explanations for the high concentrations chrysotile observed in tissues: firstly, there is greater opportunity for chrysotile exposure because more of the fibre was used; secondly, as chrysotile fibre bundles disaggregate, the number of individual fibrils may actually increase with time of tissue residence, leading to a higher exposure index; thirdly, chrysotile possesses some biopersistence; and lastly, the mineral recovery process may produce an increase in fibre number as an artifact of preparation.

Fibres $>5 \mu\text{m}$ in length found in this study constituted from ~5–50% of the fibre populations measured. Unfortunately, such data are of limited value here. The great range of tissue masses examined, lack of information concerning location of specimen in terms of anatomical site, and the problems associated with number of fibres counted introduces uncertainty [28, 44–46]. There appears to be more long fibres in these tissues than have been reported in bulk samples when the latter are examined by transmission electron microscopy [36]. Based on the

data in the present study, the ability to unequivocally distinguish between the effects of dose and fibre length was not possible. Considering the short-fibre elimination bias, it may never be possible.

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Appendix on crocidolite consumption information

Crocidolite usage in the USA

In the 1960's, when data were yet to be gathered concerning mortality experience of working cohorts exposed to only one fibre type, the position of many investigators, especially those in the USA, was that all varieties of asbestos possessed virtually the same ability to produce disease.

In a presentation at the International Pneumoconiosis Conference held in Johannesburg in 1969, the mesothelioma mortality experienced among North American insulation workers was reported. Although these workers experienced high mortality from mesothelioma, their exposure history was unknown. SELIKOFF [1] speculated that for a century earlier, scant information was available on the composition of USA insulation products. However, he went on to state: "Until 1930 chrysotile was almost the entire fibre used, amosite making its appearance later and crocidolite practically not at all." "This is not to say that it can be proven that crocidolite was never used before 1930 for insulation in the USA. Rather, if any were so utilized, it could only have been in very small amounts. Therefore, crocidolite exposure of American insulation workers before 1930 and probably before 1940 is unlikely to have occurred to any significant extent, and is still a very minor affair."

Crocidolite was widely used outside the USA for insulation and lagging [2], and the emerging South African experience dramatically underscored the importance of crocidolite as a mesotheliomagenic fibre [3, 4]. The qualifiers of SELIKOFF [1] were noted and data were presented concerning mesothelioma mortality among the American insulation workers: 22 mesotheliomas occurred among 373 deaths (~5.9%), 2 prior to 1954 and 20 between 1954 and 1968. Clinical latencies calculated from onset of exposure suggested important exposures occurred before 1930, earlier than the time period the authors had reason to believe that crocidolite or amosite, was introduced into commerce. Sixteen of 22 mesotheliomas were peritoneal and therefore amphibole fibre was suspected by many to be the aetiological agent.

The issue regarding inclusion of crocidolite into insulation was again discussed in a paper published three years later [5]. Presumably based on the same

evidence as presented in his 1970 paper, SELIKOFF [5] now stated the following: "Crocidolite was not used for insulation work in the USA during the period covered by our study. Thus, exposure to this fibre cannot explain the cancer risk observed."

These arguments were repeated so often that they gradually became accepted by members of the American community. At an international meeting on asbestos diseases held in Johannesburg in 1977, McDONALD [6] stated "... (it) is fairly clear that insulators in North America had not been exposed to crocidolite."

Occasionally studies of fibre exposure in trades other than those involving insulation application and removal are used for discussion. A good example of this involved machinists in steam locomotive repair yards [7, 8]. MANCUSO [8] stated in his 1988 paper (as underscored by the title of that paper, "Relative risk of mesothelioma among railroad machinists exposed to chrysotile") that during the time period of hire and principal exposure of his mesothelioma cases (1920-1929), the lagging used for steam locomotive: "... was almost exclusively, if not solely chrysotile". "Exposure occurred to amosite or crocidolite as packing or other material ... would have been comparatively limited in nature and scope."

The more circumspect statements concerning exposures are not reflected in this article title nor in its text. The author further buttressed his fibre type argument with the same Department of Commerce importation data and went to state that: "... this limited amount of fibre (crocidolite) was never used for insulation."

This latter statement was given further authority with a declaration attributed to HUEPER [9]. In the paper by MANCUSO [8] earlier data was repeated and did not reference nor cite his earlier paper in which analysis of six insulation specimens obtained from locomotives showed that four contained amosite only (analyses by F.D. Pooley, University of Wales).

The papers by T.F. Mancuso stood in diametric opposition to advertisements which appeared in trade journals, *The Engine*, of almost 100 yrs ago (1897) which proclaimed the availability of blue asbestos removable boiler and steam pipe covering, for locomotives. These materials were still advertised 25 yrs later (*Asbestos*, August, 1921) [10].

Crocidolite importation into the USA

The data used to bolster their exposure theory were later challenged [10]. Data for importation of raw crocidolite fibre into the USA, for the years 1916 through 1930, was from the Department of Commerce [1], and those available from the United States Bureau of Mines (as provided in their yearly reports titled "Mineral resources") [10]. These data differ considerably. Prior to the first import figures shown [10] in the time period 1916-1929, rather than "no data" for both crocidolite and amosite (generally interpreted as "none"), 35,040 metric tonnes of crocidolite found its way to USA asbestos manufacturers. It is important to note that these importation figures are for unprocessed fibre, not for finished products. That 35,040 metric tonnes of fibre were used entirely for valve packings and woven braids is doubtful.

The asbestos cement industry was growing, and consumed much of the fibre. However, crocidolite was used in insulation products.

Crocidolite in USA insulation products

Importation figures provided by the United States Bureau of Mines showed that crocidolite greatly increased in the USA as the result of lagging required for shipbuilding during World War I, and experienced another period of tonnage importation just prior to World War II. It was further concluded that based on marketing data found in the trade journal *Asbestos* that amosite had replaced crocidolite as a component of high temperature insulation rather than the other way around.

The American company Asbestos Limited, which held an association with Cape Asbestos, Ltd. of London, was headquartered in New York City*. Its fibre processing plant was located in Boundbrook, New Jersey. It was here that blue fibre was opened and carded, according to customer specifications. Raw crocidolite was derived from deposits in Griqualand (the operation located in the Asbestos Hills of South Africa, north of Koegas and just south of Kuruman, the locality studied by WAGNER *et al.* [3]). Asbestos Limited manufactured magnesia block insulation, advertised as "Best 85% magnesia is made with blue asbestos" (*Asbestos*, March, 1921). Its application included the product line New Era Insulation, for moderate- and high-temperature systems (*Asbestos*, July, 1941). Steam locomotives were particularly emphasized.

That thermal insulation products contained asbestos well past the 1930s was verified in a later study in New York City [12]. Of 798 asbestos-containing thermal insulation specimens examined in New York City, 11 (~1.38%) contained crocidolite.

The exposures of American insulation workers were not adequately described in previous reports. Crocidolite was available and did find its way into USA insulation products. It is only its market share which is unknown.

Crocidolite found its way into USA military shipyards

Shipyards in the USA, employed the services of thousands of insulators and pipe coverers. Spray insulation containing crocidolite (*via* the Limpet pro-

cess) was used in some nonmilitary shipyards (*Asbestos*, September, 1936)†.

Naval shipyards during World War II engaged in both construction and repair operations. However, the Navy specified the kind of lagging which was to be used aboard American warships, and such requirements were codified by the Navy Department. Insulation products allowed on ships were to be composed of asbestos fibre with a specific chemistry. When considering the bulk chemistry of available commercial fibres it was obvious that only amosite could be used and if specifically calls for the use of amosite for machinery and piping insulation [13].

However requirements for ships in the UK differed. All three major fibre types were permitted to be used on ships and crocidolite was extensively applied aboard warships [14]. Early mesothelioma studies in the UK focused on work in military shipyards [15]. Some international investigators outside the USA interpreted this to mean that crocidolite was also used aboard American ships, and if mesothelioma occurred among American insulation workers who worked in military shipyards, this was indirect evidence of crocidolite exposure. However, US Naval specifications rebutted this presumption, and the use argument was no more compelling than the importation data referred to earlier.

Still other investigators suggested that British ships were re-outfitted in USA ports during the war and they had been the source for crocidolite exposure to American shipyard workers. This most certainly occurred, and citations in the literature support this‡.

In retrospect, insulation workers, at least those who lived in cities with shipbuilding industries, were probably exposed to at least some crocidolite in this manner. However, those engaged in environments where foreign-ship repairs were undertaken during World War II may have experienced significant exposures; brief periods of work may have resulted in significant lifetime risks [15, 17, 18].

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*Three further points are noteworthy: the corporate headquarters of J. Manville was at 22 East 40th Street, just across Fifth Avenue from Asbestos Limited. The plant in Boundbrook, New Jersey, was located approximately 3 km from the John-Manville (JM) facility in Manville, New Jersey, and the first reports of mesothelioma in the area, attributed to work at JM only, came from Somerset Hospital in Somerville, NJ, about 4 km from Manville and Boundbrook [11]. In retrospect, the mesothelioma experience reported was attributed to exposure at the JM facility, but likely contained cases exposed at the Asbestos Limited facility as well. The proportion of cases from each facility when contributed to the total experience is unknown.

†Crocidolite was sprayed, e.g., in the Sun Shipbuilding and Drydock, Co., in Chester Pennsylvania. Tankers from the Gulf Refining Company (e.g., Gulf Belle, Gulf Dawn) were sprayed under decks and on bulkheads; passenger ferries were sprayed as well, e.g. Princess Anne of the Virginia Ferry Company. *Asbestos* (1936).

‡Through President F. Roosevelt's office, and the approval of the Congress, A. Harriman negotiated with and received cooperation from East Coast Shipyards to repair British warships in 1940. As an illustrative example, the battleship HMS Rodney was called into action off Greenland to join in the pursuit of the Bismark [16]. The Rodney was crossing the Atlantic on escort duty after which it was to make for Boston to repair one of its engines which had broken down. It steamed on a single propeller. After the sinking of the Bismark, the Rodney resumed its heading for North America. We assume that British warships carried their crocidolite lagging into USA ports.

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