Chrysotile Biopersistence in the Lungs of Persons in the General Population and Exposed Workers

Arthur M. Langer and Robert P. Nolan

Environmental Sciences Laboratory, Applied Sciences Institute of Brooklyn College, Brooklyn, New York

Lung burden analysis was performed on 126 autopsy cases of persons who died in New York City from 1966 through 1968. Of the 126 cases, 107 were probably non-occupationally exposed, judging by occupational history and asbestos body content of lung. Fifty-three of the 107 cases contained short chrysotile fibers/fibrils, <5 µm in length, present in 3-fold greater amounts than were found in laboratory background controls. The fiber concentrations ranged from 1.8 to 15.7 × 10^6 f/gm/dry lung tissue, and the proportion of fibers ≥5 µm in length was only 0.34% of the total chrysotile population found. Other inorganic particles present included fragments of amphiboles. In contrast to these data, the lung parenchyma of persons occupationally exposed to asbestos commonly showed the presence of other fiber types, especially amosite and crocidolite, at very much higher concentrations and greater fiber length. Any chrysotile present would usually be in fiber bundle form, with both fibers and fibrils >5 µm in length. Comparison of the lung fiber content of occupationally exposed persons with that of the general population showed marked qualitative and quantitative differences. Fibers are durable, and are retained in a range of concentrations. Their length and dose, among other factors, which control their biological potential are different in the two populations; the risk factors for chrysotile-induced disease are not the same. — Environ Health Perspect 102(Suppl 5):235–239 (1994)

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Durability, Retention, and Biopersistence

Biopersistence of inorganic dust in the lung is held to be a requirement for the production of chronic disease. Durability, particle size, and depositional pattern affect the ability of scavenging cells to intercept, phagocytize, and sweep breakdown products out of the lung parenchyma.

If a fiber is not broken down within a phagolysosome, translocation may only decrease lung retention at the expense of accumulation at another tissue site. Persistence in the host is preserved. For mineral fiber, especially the amphibole asbestos varieties, the mucociliary escalator may save the lung but at the expense of increased risk of malignancy in other organs. Pleural drift and mesothelioma indicate that this is biologically important.

Biopersistent, durable, inorganic particles may have very low biological activities, causing for example, benign pneumoconioses. Chest radiographs obtained on workers occupationally exposed to barite (*1*), tin oxide in the absence of free silica (*2*), zircon dust (zirconium silicate) in the refractory industry (*3*), and dust in iron foundries (*4*) show a profusion of opacities with little or no clinical disease.

Chrysotile asbestos is considered to possess low carcinogenic potential because of its inherent instability in a biological host, since it lacks both durability and biopersistence (*5*). Studies using electron microscopy showed some magnesium loss from the chrysotile structure, detectable only for relatively thin fibers (*6,7*). By using radiolabeling, chrysotile has been shown to degrade *in vivo* (*8*). Electron microscopy studies have also shown what appears to be fibril disaggregation from the fiber bundle, as well as some thinning of the fibril wall, within the phagolysosome

Table 1. Asbestos body content of standard aliquots of pulmonary tissues obtained from 3000 persons who died in New York City, 1966–1968[a]; present study population and case distribution for TEM assay.

Sex	Total cases scanned	(%) cases by sex	Asbestos bodies found in scan				Positive cases by sex	
			0	1–4	5–14	>15	n	%
Male	1971	(65.7)	958	802	152	59	1013	51.4
%			(48.6)	(40.7)	(7.7)	(3.0)		
Female	1029	(34.3)	593	392	40	4	436	42.4
%			(57.6)	(38.1)	(3.9)	(0.4)		
	3000	(100.0)	1551	1194	192	63	1449	(48.6)
(% of population)			(51.7)	(39.8)	(6.4)	(2.1)		
Number of cases selected from each category for present study			32	57	18	19	126	
(%)			(25.4)	(45.2)	(14.3)	(15.1)	(100.0)	

[a] From Langer et al. (*16*).

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Address correspondence to Dr. Arthur M. Langer, Environmental Sciences Laboratory, Applied Sciences Institute of Brooklyn College, Brooklyn, NY 11210. Telephone (718) 951-4242, (718) 951-4793. Fax (718) 951-4438.

Table 2. Occupations of 25 persons whose tissue aliquot contained no asbestos bodies.

Age at death[a]	Sex	Principal occupation(s)
45	M	Handyman
53	M	Bartender
75	M	Porter
46	M	Factory worker (appliances)
50	F	Stock broker
80	F	Office secretary
79	F	Housewife
76	F	Housewife
76	M	Dress manufacturer
68	M	Presser; tailor
47	M	Paint factory
58	M	Shipping clerk; messenger
83	M	Salesman
84	M	Asphalt laborer
63	M	Pastry chef
56	M	Office clerk; salesman
62	M	Porter; elevator operator
50	M	Foundry worker
68	M	Waiter
75	M	Salesman; clerical
54	M	Restauranteur
80	M	Restaurant worker; porter
69	M	Restaurant worker; roofer
71	M	Bus driver
50	M	Butcher

[a]Average age at time of death 64.6 years (±13.4).

Table 3. Occupations of all 19 persons whose tissue aliquot contained 15 or more asbestos bodies.

Number of asbestos bodies	Age at death[a]	Sex	Principal occupation(s)[b]
>99[c]	63	M	Pipecoverer
>99	55	M	Welder-shipyard
>99	65	M	Elevator operator[d]
>99	72	M	Plasterer
>99	51	M	Electrician, shipyard
>99	59	M	Pipecoverer, insulator
92	73	M	Carpenter, shipyard
52	67	M	Laborer, shipyard
42	72	M	Electrician, shipyard
37	64	M	Truck mechanic
35	40	M	Painter, shipyard
32	48	M	Plumber
29	62	M	Plasterer
29	73	M	Pipefitter
28	58	M	Laborer; carpenter
20	72	M	Longshoreman; porter
19	56	M	Laborer, construction
17	57	M	Laborer, construction; longshoreman
17	64	M	Painter

[a]Average age at time of death 61.6 years (±9.4). [b]New York State death certificates record last employment only if decedent was still actively working. Certificates frequently state "retired." Most data from interview with next-of-kin. [c]Count stopped at 99 to comply with program format. [d]Last employment as shown on death certificate. No interview was available with next-of-kin. All cases are male.

(*9,10*). Animal studies have shown that chrysotile is effectively eliminated from the lung after exposure by inhalation (*11*). These data, and more, have led some investigators to conclude that "chrysotile disappears from the lung," i.e., it lacks biopersistence. The implications of such a statement regarding carcinogenicity are obvious. If chrysotile is neither durable nor retained, the likelihood of its exerting a lasting or chronic biological effect is significantly diminished.

However, the study of human tissues shows that sometimes, even many years after cessation of exposure, chrysotile fiber is encountered in lung tissues, and occasionally at exceedingly high concentrations. Trace amounts of chrysotile have been reported in lungs of persons in the general population (*12*), and high concentrations in lungs of some occupationally exposed workers (*13*). This study explores the phenomenon of chrysotile persistence in human lungs.

Materials and Methods

During the years 1966 to 1968, 7 lung specimens, obtained from selected anatomical sites, were removed from each of 3000 persons who died at one of three hospitals in New York City: Mount Sinai Hospital, Manhattan; Veterans Administration Hospital, the Bronx; and Elmhurst General Hospital, Queens (*14*). The specimens were collected for a study involving the quantitative determination of asbestos bodies and uncoated fibers, visible by light microscopy, in the lungs of these people, and its possible bearing on morbidity and mortality. In addition to autopsy protocol, clinical records, occupational histories, and a complete personal profile was known for each case. Similar studies had been done in urban areas elsewhere (*15,16*).

These studies (*17–20*) showed a strong correlation between the presence of both asbestos bodies and uncoated light-visible fibers with sex (males greater than females),

Table 4. Chrysotile detected among 126 cases studied by TEM.

Number of chrysotile fibrils/fibers counted	Exposure categories by number of asbestos bodies found: 0		1–4		5–14		≥15		Total chrysotile	
	N	xf[a]	N	xf	N	xf	N	xf	$N^o \times 10^6$	f/g/dry
≤9	5	3.4	10	4.3	1	1.0	3	4.7	19	<0.58[c]
10–27	10	19.3	20	20.0	8	15.0	5	20.0	43	0.64–1.73
≥28	17	175.2	27	113.4	9	94.1	11	134.5	64	>1.79[d]
Total	32	3188	57	3504	18	970	19	1594	126	
	N	(%)	N	(%)	N	(%)	N	(%)	N Total	
Chrysotile[b]										
≥5 µm	7	(0.22)	6	(0.17)	11	(1.13)	28	0(1.76)	52	
1–5 µm	100	(3.14)	151	(4.31)	136	(14.02)	463	(29.05)	850	
<1 µm	3081	(96.64)	3347	(95.52)	823	(84.85)	1103	(69.19)	8354	
									9256	

[a]xf = average number of chrysotile fibers/fibrils found among cases (N). [b]These values were converted from length of the object on the viewing screen, at a particular scan magnification, to µm. [c]Limit of detection is 0.064×10^6 f/g/dry lung (64,000 fibers). [d]Range of positive cases, $1.79–15.74 \times 10^6$ f/g/dry lung.

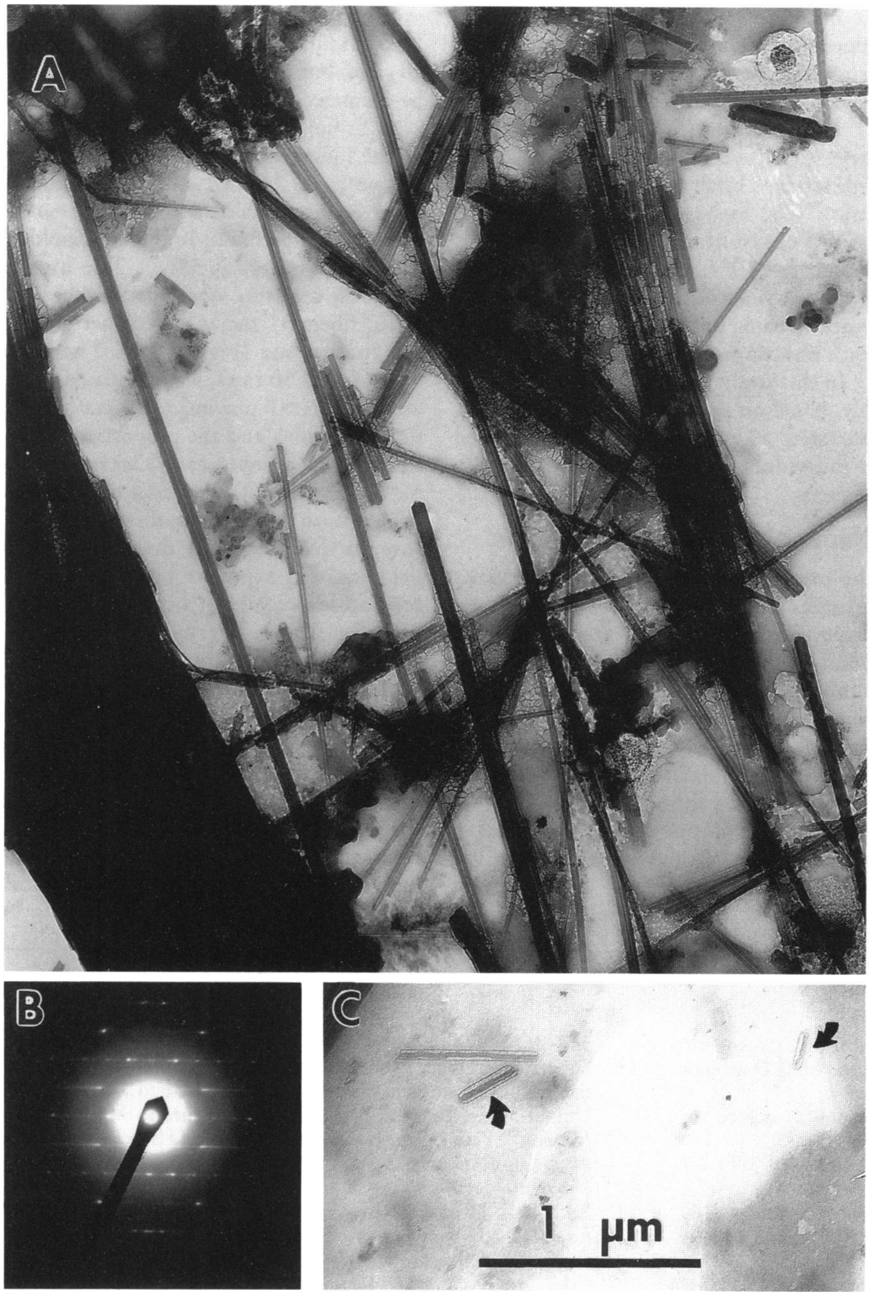

Figure 1. Chrysotile recovered from an occupationally exposed worker's lung (A), with fiber displaying characteristic structure (B), and from the lung of a person in the general population (C). Scale in (C) is approximate for (A) as well. The 18 μm^2 area represented in (A) is about 1/625th the area of an entire grid opening. Compare this chrysotile concentration with that in (C), with the fibrils shown counted in an opening of 11 236 μm^2. The numerical difference of chrysotile concentration is about × 20,000 and a mass difference in excess of × 1 million. These illustrate the opposite outliers of chrysotile exposure.

age (prevalence and amounts increased with age), and occupation. The overall asbestos body distribution is given in Table 1.

These studies clearly indicated that asbestos bodies, and the accompanying fibers with diameter ≤1 μm, were not uniformly distributed among the general population, but rather along an exposure continuum, in which most of the group had experienced little or no direct exposure to asbestos. They would provide a reliable tissue burden benchmark for ambient air exposure, against which the chrysotile levels found in persons subjected to workplace exposure to asbestos could be compared. Chrysotile biopersistence, across a range of exposures, may be explored utilizing this material.

It was decided to make a more detailed examination of a number of cases, using transmission electron microscopy (TEM). Bulk tissues from 126 cases were subjected to complete alkaline digestion, from which the particles were recovered by centrifugation. Aliquots of the dust suspension were transferred to grid substrates and examined by TEM. Twenty-eight specimens were analyzed with an RCA 3G microscope with a magnification ×31,000, and the remainder with a Hitachi HU11E-125 microscope with a magnification ×42,000. The asbestos fiber that was counted was identified as chrysotile on the basis of morphology and structure. Amphibole fibers were presumably also present but could not be identified.

The study population, selected on the basis of asbestos body content, occupation, and personal history, is shown in Tables 1–4.

Results

The completed study showed that the general population dying in New York City between 1966–1968 experienced a wide range of exposures (Tables 1–3). The greatest concentrations and highest prevalence of asbestos bodies occurred in males, especially workers in occupations involving asbestos-product use or installation. These included pipe-coverers, shipyard workers, and general construction workers (Table 3). Two plasterers are listed among the occupations (when) plasterers in New York City sprayed asbestos-containing fireproofing on steel structures during building construction. Most of the cases were not occupationally exposed. These included women and white-collar workers, who made up an important proportion of the category without asbestos bodies.

At least some chrysotile fiber was found in the lungs of 124 of 126 persons in the study, but it was decided to recognize that there was a background level. This was set at the highest level found on "control" grids, nine fibrils in nine fields (one per field opening of 11,236 μm^2 area). In 19 of the lungs studied, the fibril count was ≤9. Setting the statistical population at approximately three times this value, at 27 fibrils, there were 64 (50.8%) statistically positive cases out of 126 (Table 4).

There are three important caveats: First, the background level observed varied in these two tissue populations so that the highest value, that reported in the 1971 study (*12*), was used for all cases. Second, some of "the ≤9 cases" included short fibers, not fibrils, suggesting a "real" exposure had occurred. Third, four of six cases with >99 asbestos bodies had almost no chrysotile in their tissues, and the two others had only modest amounts, slightly more than three times the background level.

Virtually all the chrysotile in nonoccupationally exposed persons was composed of short fibrils, most ≤1 μm in length, with the modal class between 0.2 and 0.5 μm (Figure 1C). The asbestos bodies in the occupational group were characteristically amphibole fibers. However, it should be noted that many occupationally exposed workers had lung burdens the chrysotile contents of which indicated intense, prolonged exposure (*12,20*), being several orders of magnitude higher than the general population. The chrysotile fibers were much longer also (Table 4).

Most of the chrysotile fibers/fibrils observed in this study were ≤5 μm in length. Only 52 of 9256 (0.56%) chrysotiles observed were longer (Table 4). There was a trend, however, which suggested that the lungs of individuals with, apparently, occupational exposure to asbestos contained more chrysotile, fibers/fibrils > 1 to 5 μm, and > 5 μm in length (Table 4).

The quantitation of the chrysotile levels in the 64 positive cases, counting all fibers and fibrils, including those <1 μm in length, gave values between 1.8 and 15.7 × 10^6 fibers per gram of dry lung tissue. The values for remaining 62 cases ranged from below the detection limit, 0.064 × 10^6 fibers per gram of dry lung tissue to 1.73 × 10^6 fibers per gram (Table 4). The highest chrysotile levels found did not correlate with asbestos body content nor with occupation. The highest "general population" level of chrysotile >5 μm in length, was about 1.7 × 10^6 fibers/g of dry lung tissue, in an 80-year-old male. His exposure source remains unknown, and his cause of death was coronary heart disease.

In this study, amphibole fiber (presumably, based on morphology and diffraction character) >5 μm in length was restricted to individuals who were occupationally exposed.

Discussion and Conclusions

The presence of chrysotile in lung tissues indicates durability, retention, and host, biopersistence; and the trace amounts found in the general population are predominantly short fibrils. Rare outliers were found. Only in lungs of some heavily exposed workers were high chrysotile concentrations found; in these instances they appeared to be long unaltered fiber. The present study supports the tissue assay guidelines used in our laboratory, which exclude fibrils less than 1 μm in length from analysis, since they appear to represent nonoccupational exposure. Chrysotile fiber elimination most certainly occurred in all cases, but in proportions that could only be estimated.

Chrysotile asbestos had been detected in the lungs of 50 of 83 persons (60.2%) known to be exposed to asbestos either in their occupation or as bystanders of an exposed occupation or in the households of asbestos workers (*13,21*). The highest chrysotile exposure was calculated at 7790 × 10^6 fibers >1 μm in length per gram of dry lung tissue (Figure *1A*). The mean value, for all 50 cases, was calculated as 715 × 10^6 fibers >1 μm in length per gram of dry lung tissue, and the proportion of long fibers in the asbestos varied between 5 and 50%. Analysis of selected fibers showed preservation of both chemistry and structure. It would appear, therefore, that in occupational exposure to chrysotile not only are doses higher, but the proportion of long fibers is greater than in the chrysotile to which the general population is exposed.

The biological activity of chrysotile may depend on its durability and persistence, but the influence of the other factors—fiber length and dose—clearly affect the asbestos-disease risk (*22,23*). For this reason, the general population is not at the same risk as those that are occupationally exposed.

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