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Relative Risk of Mesothelioma Among Railroad Machinists Exposed to Chrysotile

Thomas F. Mancuso, MD

This study challenges the assertion of low relative risk of chrysotile in the causation of mesothelioma. Data are provided on the time period use of various types of asbestos in the United States and in insulation materials. The focus of the study is on mesothelioma among railroad machinists employed in the steam locomotive era who were exposed to chrysotile. Within a cohort of machinists alive January 1, 1945, a sub-cohort method was applied to all successive machinists hired in each of the respective years (1920–1929) followed through 1986. The total cohort was 181 and the number of deaths 156, with 14 mesotheliomas identified among 41 cancer deaths. The findings demonstrated an extremely high relative risk for machinists exposed to chrysotile for the induction of mesothelioma in the individual year of hire cohorts. A similar observation was noted for other crafts hired in the same time period. One mesothelioma occurred for every 13 machinists hired in the succeeding years (1920–1929) and constituted 34% of all cancer deaths. It is concluded that chrysotile is far more hazardous in the induction of mesotheliomas and that the asbestos cancer risk in the steam locomotive eras was much higher than had been previously estimated.

Key words: railroad, mesothelioma, chrysotile, machinists, epidemiology, crafts

INTRODUCTION

The direction of this brief paper is to focus on a specific time period of asbestos exposure in the United States as a basic means to identify the type of asbestos used in the railroad industry in the steam locomotive era, which is the subject matter of this study.

Chrysotile represents approximately 95% of the total world production of all forms of asbestos, with Canada its largest producer [Rosato, 1959]. It is contact with this type of asbestos, according to Hueper [1965], that furnishes the chief cause of asbestos pneumonioconiosis and cancer, especially in the United States, because contact with amosite and crocidolite have been comparatively minor, and these varieties represent but a small fraction of the total amount of asbestos produced and used. Estimated U.S. asbestos consumption of 1920–1930, which includes the time

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TABLE 1. Estimated U.S. Asbestos Fiber Consumption (Tons)

Year	Crocidolite	Amosite	Canadian chrysotile	Other	Total
1920	No data	No data	152,000	4,000	156,000
1925	No data	No data	200,700	4,100	204,800
1930	1,907		198,200	8,500	208,607

Total amosite and crocidolite (Combined Tons)*	
1931	823
1932	212
1933	233
1934	152
1935	501
1936	1,432
1937	2,928
1938	3,282
1939	6,129

*Source: U.S. Department of Commerce.

period of this paper (1920–1929), is shown in Table 1 as well as consumption estimates for amosite and crocidolite combined by year from 1930–39.

The question of relative risk in the induction of mesotheliomas among railroad machinists relates to the form of chrysotile asbestos that has been provided from the Canadian chrysotile mines for many decades for commercial use in the United States. (It is this form of chrysotile asbestos, to which exposure has occurred and mesotheliomas developed, that is addressed in this investigation.)

The foundation and exploration of the employee-specific year of hire approach in the evaluation of the use of different types of asbestos in insulation materials in the United States was provided by Selikoff, who has conducted the most extensive work in this area [Selikoff et al., 1970]. The basic information on asbestos type relative to the time periods derived from various reports and communications are as follows:

- The largest asbestos manufacturer in the United States first used crocidolite in 1929 (for sheet packing, *not* insulation) and never used crocidolite for the manufacture of insulation at any time (1928–1968), employing it in only two products (asbestos cement pipe and packings) [Pundsack, quoted by Selikoff et al., 1970].
- The very small amount of imported crocidolite in the United States was used for valve packings and woven braid [Pundsack, quoted by Selikoff et al., 1970].
- Until approximately the early 1940s, chrysotile was primarily utilized in the manufacture of asbestos insulation products. [Selikoff et al., 1973].
- The limited amount of imported amosite distributed throughout the United States had its most extensive use in the maritime industry, in shipbuilding and repair, (in particular in naval vessels), with the first application of pipe covering in 1937 [Fleisher et al., 1946].
- During the 1950s, amosite was the predominant type of asbestos in insulation materials [Cooper and Miedema, 1973].
- Smither [1963], referring to one of the world's largest producers of amosite, stated that as far as he was able to ascertain, "The only asbestos not implicated in association with mesothelioma is amosite."

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In terms of the historical perspective of exposure to asbestos in the railroad industry, the principal and most extensive exposure in volume and dimensions occurred in the application and removal of asbestos lagging on the boilers of steam locomotives. A description of these work practices has been provided by Mancuso [1983]. Chrysotile was the type of asbestos used since the first application of asbestos in the steam locomotive era for the lagging of the locomotive boilers, and this continued through the succeeding decades.

In addition to chrysotile, if some other potential exposure to amosite or crocidolite as packing or other material occurred at some point in time, the actual exposure would have been comparatively limited in nature and scope.

From the evaluation of data relative to the type of asbestos, year and amount, and the time-period use of various types of asbestos, it is reasonable to conclude that the type of asbestos used for lagging insulation for steam locomotives for railroad company A was almost exclusively, if not solely chrysotile during the 1920–1929 period. This would also apply to 1930–1939 and into the 1940s and later. The last steam engine repair for railroad company A occurred in 1957.

The nature and extent of the relative risk from exposure to chrysotile asbestos, in terms of the subsequent development of mesotheliomas, constitutes the main emphasis of the present study of railroad machinists hired during the years 1920–1929. The methodology used is the concept of individual year-of-hire cohorts of the same craft in succeeding years exposed to the same asbestos conditions and each observed since date of hire.

The concept of reproducible effects has been well established in animal experiments. Exposure to the same carcinogenic agent, for a specific number of the same animal species, under the same conditions, observed for the same length of time, provides the basis for estimation of relative risk. The results of the present epidemiological study represent the equivalent of a successive series of human experiments on the occupational exposure to chrysotile asbestos among machinists hired 1920–1929 in the steam locomotive era of the railroad industry. It is not the purpose of this investigation to evaluate the various theories involved in the development of the actual cancer process, but rather to focus on the disease itself, the occurrence of mesothelioma following exposure to chrysotile asbestos.

MATERIALS AND METHODS

In a previous study, data were presented on a cohort of white male railroad machinists alive on January 1, 1954 who had been employed before 1935 [Mancuso, 1983]. This paper is based on a similar but earlier seniority list prepared by railroad company A, as a regular employment procedure of railroad machinists and other crafts, alive January 1, 1945, who were employed before 1935. Within this cohort, successive sub-cohorts were established representing those machinists hired in each of the specific years 1920–1929, inclusive, followed through 1986. The study is unique in using an internal control comparison rather than the general population.

In this respect, the method differs from other epidemiological studies by focusing on the individual year of hire and relating the cancer risk *solely to those hired* during that specific year. In essence, the successive cohort method provides the means for internal comparisons and for the investigation of reproducible effects in terms of relative risk.

TABLE II. Seniority Cohort of Railroad Machinists in Railroad Company A Alive in 1945 and Subcohort Hired 1920–1929

	Total number
Cohort of white males hired before 1935, alive in 1945	285
Deaths with causes of death information	252
Subcohort white males hired 1920–1929; employed in 1945	181
Deaths with causes of death information	156
Not known to be deceased in 1986.	25

It is recognized that the 1945 seniority list represents a survivor group and that other machinists could have left or retired before 1945. The identification of the deceased was derived from the death claim records of the International Union of Machinists and Aerospace Workers. Death certificates were coded by an experienced nosologist according to the 8th Revision of the International Classification of Diseases, Injuries and Causes of Death.

RESULTS

The analyses are confined to those machinists hired 1920–1929 for railroad company A. Table II relates to the description of the successive cohorts. There were 181 white males alive and employed in 1945 who were hired from 1920–1929, inclusive. Among this group, 156 were identified as dead in 1986.

Table III is a presentation of the successive cohorts representing machinists hired for each of the successive years 1920–1929. In railroad company A, the table shows for each year of hire, the number in the cohort and the number of deaths. Also shown is the distribution of mesotheliomas, lung cancers, and other types of cancer in the respective year of hire by age at hire.

Among the 156 deaths, 36 primary sites in the 41 cancer deaths were identified: 14 (35%) of all cancers were mesotheliomas. The same employer railroad company A was identified on 13 of the 14 mesothelioma deaths. As a point of reference on the rarity of mesotheliomas in the general population, Selikoff et al. [1965] cite the observation of 3 mesotheliomas of the pleura and no mesothelioma of the peritoneum among 31,652 deaths in a study of 1,048,183 men and women reported by the American Cancer Society.

Table III illustrates the extremely small size of the successive cohorts of machinists in which deaths due to mesothelioma occurred. The basic observation from this simple analysis shows that for each hire year from 1920 through 1929 (with the exception of 1921 and 1928, with only 9 and 1 hired in those years, respectively), mesothelioma incidence was replicated, for each of the successive cohorts of machinists hired in the same year, at comparable age at hire, employed at the same workplace, exposed as a specific craft to the same asbestos working conditions in the steam locomotive era.

In terms of relative risk in the development of mesothelioma from exposure to chrysotile asbestos, what is most striking is the occurrence of mesothelioma in such a small number of deaths and cohorts in each respective individual year of hire. On

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TABLE III. Successive Cohorts by Year of Hire and Age From 1920 to 1929 Among Railroad Machinists by Cancer Cause of Death

	Year of Hire										
	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929	Total
Number in cohort	12	9	19	27	25	44	15	17	1	12	181
Number of deaths	10	8	15	26	23	39	12	14	0	9	156
Cancers	Age at hire										
Mesotheliomas	(23)	—	(20) (21)[e]	(20) (21) (24)[a]	(29)	(25) (29) (29)[a]	(25)[b]	(24) (25)	—	(29)	14
Lung	(19)	—	(21) (21)[e]	(22) (28)[d]	(44) (33)	(25) (32)	(22)	(35)	—	(31)	11
Mouth								(29)			1
Stomach				(41)							1
Colon		(32)				(29)					2
Cecum						(33)					1
Rectum			(26)			(36)[c]					1
Bladder	(22)		(40)[d]								1
Prostate				(43)	(41)[d]	(30)					2
Adrenal			(21)								1
Reticulum cell sarcoma	(26)										1
Site unknown					(27)						
Primary cancers	4	1	6	6	3	8	2	4	—	2	36
Total cancers	4	1	7	7	5	9	2	4		2	41

[a]Asbestosis
[b]Endothelioma of pleura
[c]Hospital record
[d]Part II of death certificate for each cancer or "other significant conditions" not included in total
[e]Same case

the average, one mesothelioma death occurred for each 11 deaths, or if one referred to all 181 of the cohort, the relative risk would be one mesothelioma in every 13 machinists hired.

The precision of the reproducibility is further demonstrated for those hired in specific years. In 1922, of the 19 machinists hired, 2 mesotheliomas occurred in men hired 6 months apart.

In 1923, of the 27 machinists hired, 3 mesotheliomas occurred: 2 were hired in the same month, 10 days apart, at ages 20 and 21. The third case, hired 6 months earlier, at age 24 also had asbestosis. A machinist hired within 2 months of the third mesothelioma case, at age 24, also had asbestosis listed on the death certificate. In 1925, among the 3 mesotheliomas, 2 were hired 2 months apart at ages 25 and 29, and in 1927, the 2 mesotheliomas were hired 5 months apart at ages 24 and 25.

It is recognized that other cases of mesothelioma may have occurred among the machinists who retired or left before 1945, the year of the seniority list. This is illustrated with the following case (S), a machinist who retired in 1943 and died in 1946 (age 69) with a pleural endothelioma, with prior employment in 1916 with railroad company A at the same facility.

The medical report of this case is included because it represents the earliest death (1946) and the earliest exposure that would be related to the use of chrysotile asbestos by workers employed by railroad company A.

> The post mortem examination showed that ____ was suffering from a malignant tumor which had its origin in the walls lining the lung surface and the inside of the chest wall. This had started in the left chest and had progressed to involve the cells and lining of the abdominal organs (peritoneum) and to a lesser extent the sac surrounding the heart and the lining of the right lung. It became clear that the tumor had extended through the chest wall in the front into the tissue which we had cut into on Tuesday morning which was indeed part of the tumor.
>
> This is a very unusual type of cancer since it had spread so widely it of course was unapproachable by any type of treatment. We regret that we were unable to establish the diagnosis during life." Signed by Medical Director–Internist of railroad company A hospital. (This information was obtained by chance from the victim's family.)

Hochberg [1951] considered endothelioma as mesothelioma in his review of histological origins of tumors.

The probability that other cases of mesothelioma had occurred was confirmed from communications with former physicians of the same railroad hospital serving employees of company A. In reconstructing a series of observations during the follow-up investigation, it was determined that a presentation of mesotheliomas had been made to the local medical society. In terms of historical perspective, it appears that Otto [1986] was the first clinician in the United States to report, in 1967, the occurrence of mesotheliomas among railroad workers to a medical society. There was no publication. The presentation was directed at a series of 10 mesotheliomas (1957–1966) in which 9 were male employees of railroad company A. The occupations at the time of clinical evaluation were: executive (engineer), track foreman, 3 machinists, 2 boilermakers, shop foreman, engine carpenter. The duration of life from diagnosis for 8 cases was 9 months. Otto [1986] believed that other cases of mesotheliomas may have occurred but were not recorded on the death certificates.

Within this context (in the group of mesotheliomas in our study) was a machinist hired in 1922, who had a mesothelioma of the pleura diagnosed in 1965 and died in 1966. Despite the established diagnosis, the death certificate was signed at time of death by a physician other than the treating medical attendant, who recorded lung cancer as the primary cause of death. Obviously, the physician signing the death certificate was unaware of the prior diagnosis of mesothelioma. This case represents either the extension of the original mesothelioma into the lung, or constitutes two primary tumors, and has been identified in both categories in Table III.

Further, it was learned [Otto, 1986] that the thoracic surgeon for the same railroad hospital serving employees of company A "had operated on more than 20 mesotheliomas in 15 years." No details are available on these cases. Another physician [Baur, 1985] confirmed that approximately 20 cases of mesothelioma had been diagnosed among employees of company A from 1957–1971 who had been exposed to asbestos insulation in production and repair of steam engines at the same facility.

These additional cases of mesothelioma are very important because, based on

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the mesothelioma deaths in the present study for that period, they would have had an interval between hire and year of death of 35–46 years and therefore would have been hired during the 1920–1929 period of this present study. Mancuso [1983] had access to only 7 mesotheliomas for the specific time period of 1957–1971 for company A.

In reference to lung cancer. Table III also shows that there were 11 deaths due to cancer of the lung among the 36 primary cancer deaths, compared to 14 cases of mesothelioma. Lung cancer deaths occurred in each of the repective year of hire of machinist cohorts from 1920–1929 (with the same exception of 1921 and 1928, with 9 and 1 hired). In 1923, a lung cancer was noted in Part II of a death certificate.

The most striking observation was the closeness of the dates of hire between some of the cases of cancer of the lung and those of mesothelioma which relate to the variation in human response. For the 1929 cohort of machinists with 2 cancer deaths (one cancer of the lung, and the one case of mesothelioma), each was hired on exactly the same day, at comparable ages (31 and 29). The lung cancer patient died 9 years later (1980) than the mesothelioma patient (1971). For the 1925 cohort, the hire dates of a patient who died of cancer of the lung and another of mesothelioma were 5 days apart, at ages 32 and 25. The lung cancer patient died 4 years before (1967) the mesothelioma case (1971). The other pair of lung cancer and mesothelioma patients were hired one month apart in 1925, at ages 25 and 29. The lung cancer patient died in 1972 and the mesothelioma patient died in 1985, 13 years later. In 1923, the hire dates were one month apart for the deaths due to lung cancer (with pleural plaques cited on the death certificate) and mesothelioma: the employees were hired at ages 22 and 20. The lung cancer patient died in 1952 and the one with mesothelioma 26 years later, in 1978. In another closely matched pair, cases with lung cancer (Part II) and mesothelioma were hired one month apart at ages 28 and 21: the lung cancer patient died in 1972 and the one with a mesothelioma in 1977, 5 years later.

In Table III, for year of hire 1920, a rare type of cancer, reticulum cell sarcoma, occurred among 10 deaths and is mentioned because, in animal experiments by Gibel et al. [1976], reticulum cell sarcomas were induced by chrysotile asbestos (oral administration). Wagner [1962] produced such neoplasms by intrapleural inoculation.

For year of hire 1922, there was one death categorized as due to cancer of the adrenal, in a cohort of 19. This is cited because another death due to cancer of the adrenal occurred in the 1945 cohort, a machinist hired in 1918. (There were 11 machinists hired in 1918.) Schepers [1965] cited his own observation of many years before—of a case of primary carcinoma of the adrenal in which asbestos bodies were demonstrable in the adrenals. This type of cancer warrants further investigation.

Table IV shows the distribution of the mesotheliomas by year of hire, year of death, age at death, and years from first employment to death. For the 1920–1929 cohort of machinists, the pattern of prolonged latency continued to be seen in the succeeding decades.

The evidence that marked variation in human response can and does occur in the latency period for the development of mesotheliomas following the same type of work exposure to dust containing asbestos is provided not only in the successive individual year of hire cohorts as shown in Table IV, but also within the respective year of hire as previously cited. A striking illustration is the 1925 year-of-hire cohort. The two mesothelioma cases that were hired 2 months apart (October and December) had a date of death difference of 14 years (46 and 60 years). For the two cases that had the same age at hire, 29 years, the interval difference was 23 years (37 and 60).

TABLE IV. Mesotheliomas in Successive Cohorts of Railroad Machinists Hired 1920–1929 by Year of Hire, Age at Death, Interval in Years, Year of Death and Type

Hire date	Age at hire	Interval in years[a]	Age at death	Year of death	Type
1920	23	64	87	1984	Pleura
1922	20	45	65	1967	Pleura
1922	21	44	65	1966	Pleura[b]
1923	21	54	74	1977	Pleura
1923	20	55	75	1978	Pleura
1923	24	61	84	1984	Pleura[d]
1924	29	33	62	1957	Pleura
1925	29	37	66	1962	Pleura
1925	29	60	88	1985	Pleura
1925	25	46	71	1971	Pleura
1926	25	36	61	1962	Pleura[c]
1927	24	41	65	1968	Pleura
1927	25	48	72	1975	Unspecified
1929	29	42	71	1971	Pleura
		1930–1939			
1939	33	39	72	1978	Pleura(?)

[a]Years from first employment to death ("latent or lapsed period")
[b]Also had lung cancer specified on death certificate
[c]Endothelioma of pleura
[d]With asbestosis

Similarly, in a comparative study on insulation workers, among the 22 deaths due to mesothelioma [Selikoff et al., 1970], for the 15 employed in 1920–1929 exposed to chrysotile, the interval between year of hire and death varied from 25 to 43 years. An illustration of a relatively short latency period following exposure to chrysotile was cited by Scansetti et al. [1984], who reported on the development of pleural mesothelioma in a worker involved in opening chrysotile asbestos fibers (on an intermittent basis) to increase the surface area for filter purposes in the wine industry. Symptoms developed 7.5 years after first exposure to the chrysotile asbestos.

Table V shows the lung cancer deaths by successive cohorts (1920–1929) by year of hire, age at death, year of death, and elapsed years between first employment and death. (The table also includes the observations on the 1930–1939 successive cohorts.) For the 1920–1929 cohort, the interval in years from first employment and death was 27–51 years. There was marked variation in the latency period even for those hired in the same year; for example, 1923.

If one compares the mesotheliomas and the lung cancers hired in the same year, the age at hire for the mesotheliomas, with just a few exceptions, is less than that of the lung cancers. If one compares the interval in years from first employment to death between the mesothelioma and lung cancers for those hired in the same year, in general, the latency period of the mesotheliomas was longer than that of the lung cancers.

The fact that there were 6 mesotheliomas, an extremely rare cancer identified from 1972, and only 3 lung cancer deaths for a cohort (1920–1929) of machinists with the same medical and hospital facilities and care during the same period of time, strongly suggests that other cases of lung cancer may have occurred and were not

TABLE V. Lung Cancers in Successive Cohorts of Railroad Machinists Hired 1920–1929 by Year of Hire, Age at Death, Interval in Years, Year of Death

Hire year	Age at hire	Interval in years[a]	Age at death	Year of death
1920	19	47	65	1967
1922	21	27	47	1949
1922	21	44	65	1966[b]
1923	22	29	50	1952[c]
1923	28	49	76	1972[d]
1924	44	28	72	1952
1924	33	47	80	1971
1925	25	47	71	1972
1925	32	42	74	1967
1926	22	30	52	1956
1927	35	35	70	1962
1929	31	51	82	1980
		1930–1939		
1934	39	30	68	1964
1939	33	40	72	1979
1939	33	38	71	1977
1939	23	32	54	1971
1939	29	46	74	1985

[a]Years from first employment to death ("latent or lapsed period")
[b]Also had mesothelioma
[c]With large pleural plaque
[d]On Part II of death certificate

recorded on the death certificates. Higher death rates from lung cancer following exposure to chrysotile have been previously reported. The possibility exists that the criteria used by some railroad doctors in the diagnosis of lung cancer, asbestosis, and silicosis may have lessened the recording of such diseases on death certificates. For company A, the criterion for one of the physicians was that a diagnosis of silicosis or asbestosis could not be made without biopsy and examination of the tissues by a pathologist.

Table VI provides data on the following 10-year period by a successive year-of-hire cohort (1930–1939). This is shown as supplementary information to provide a visual display of how economic conditions (the Depression that occurred after 1929) influenced the number of workers exposed. For five years no railroad machinists were hired and only a few were hired in the other years. Excluding 1939, this meant that only 18 machinists had been hired through 1938.

For the 7 hired in 1934, there was one death due to lung cancer at age 68, after an interval of 30 years since first employment. In 1939, there were 4 lung cancers and one mesothelioma among 26 deaths in a cohort of 34. The 1939 sub-cohort was of particular interest in terms of reproducibility and range of latency period because 24 of the 34 machinists were hired on the same day. Within this group, hired on the same day at the same age, there was one mesothelioma and two lung cancers. One machinist hired the day before (age 29) also developed lung cancer, as did a machinist hired at age 23 one month later. The latency period for the lung cancers of the 1939 subcohort (Table V) ranged from 23 to 46 years. For the 1930–1939 cohort there were

TABLE VI. Successive Cohorts by Year of Hire and Age From 1930 to 1939 Among Railroad Machinists by Cancer Cause of Death

	Year of hire								
	1930	1931–1933	1934	1935	1936	1937	1938	1939	Total
Number in cohort	4	0	7	0	5	2	0	34	52
Number of deaths	2	—	7	—	4	1	—	26	40
Cause of death	Age at hire								
Mesotheliomas								33	1
Cancer of lung			39					33 33 23 29	5
Cancer of pancreas								34	1
Cancer of bladder								35,34	2
Cancer of prostate			48[a]						
Myelogenous leukemia					53				1
Carcinomatosis[b] (primary unknown)			36			51		42[b]	3
Total cancers			2		1	1		9	13

[a]Part II on Death Certificate
[b]Includes Melanoblastoma with enlarged liver

TABLE VII. Cases of Mesothelioma Among Railroad Craft Workers, Employed 1920–1929 for Company A 1945 Cohort

Case	Craft	Year of hire	Number hired	Age at hire	Interval years	Age at death	Year of death
1	Boilermaker helper[a]	1921	1	35	40	75	1981
2	Machinist helper[a]	1922	6	38	36	76	1958
3	Boilermaker helper	1925	14	21	53	74	1978
4	Boilermaker helper	1925[b]	14	23	59	81	1984
Employees company A not in cohort							
5	Machinist	1926		24	44	67	1970
6	Executive (engineer)[a]	1926		19	39	57	1965
7	Boilermaker[a]					69	1958
8	Engine carpenter[a]					66	1959

[a]Identified by Otto
[b]Asbestosis

also two cancers of the bladder and a melanoblastoma. The three cases of carcinomatosis, primary unknown, out of 13 cancers represent a critical loss of information.

Table VII provides information about mesotheliomas among different worker crafts of company A that relate to our study by year of hire (no special study was conducted). The occurrence of cancer in a boilermaker helper hired in 1921 (only 1 was hired for the year) complements the successive cohorts among machinists, providing a continuity for 8 successive years, 1920–1927. Data on workers in the other crafts hired in 1922 and 1925 who developed mesothelioma supplement the machinists' observation for those years.

:9 Among Railroad

7	1938	1939	Total
	0	34	52
	—	26	40
		33	1
		33	
		33	5
		23	
		29	
		34	1
		35,34	2
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1	Age at death	Year of death
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The most striking observation was the indication of relative risk to size of number hired for that year among the boilermaker helpers (case 3, 4). The 2 deaths due to mesothelioma were derived from only 14 hired in that category in 1925 in company A at that facility. One of the death certificates, in addition to mesothelioma, specified "asbestosis many years" in Part I of the underlying causes of death.

Case 5, an employee machinist of company A in the work facility of the adjoining state, had been hired in 1926. The diagnosis was made at the same company A hospital. He died in 1970 at age 68.

Case 6 was employed at the same location and facility of company A in 1926, first as a laborer and subsequently as a machinist helper. In 1928–1932 he was lagging boilers of the steam locomotives. From 1933 on, he was assigned to nonshop work at various geographical locations of company A, with a continual rise into management positions. After war service (1943–1946) he returned to his original place of employment as an executive engineer until 1963. Case 6 is of particular interest because it illustrates two basic principles. First, in epidemiological studies, the last job (in this instance, executive) can be misleading because it does not reflect the early years of exposure to hazardous and carcinogenic material (asbestos) that occurred in the work environment. Second, that the carcinogenic risk continues after the exposure to the carcinogen has ceased.

Two clinicians for company A hospital attended and signed 11 of the mesothelioma death certificates, 8 for machinists and 3 for other crafts. The exposure and risk of all crafts and workers to asbestos insulation material, including boilermakers in the steam locomotive era, have been previously described [Mancuso, 1983]. Lieben [1967] cited the occurrence of a mesothelioma in a railroad boilermaker who had applied asbestos insulation on steam engines for 25 years.

The identification of the mesotheliomas among the various crafts demonstrated again a basic public health principle known for decades: that the disease follows the trail of the exposure, whether to infectious, toxic, or carcinogenic agents, regardless of the location of the exposure, the job title, or type of industry. Selikoff [1964] referred to this concept: "floating fibers do not respect job classifications—insulators share their exposure with other trades, e.g., electricians, plumbers, sheet metal workers, steamfitters, carpenters, boilermakers, foremen and even the architect." Similarly, beyond the workplace, children and family members of asbestos workers have developed mesotheliomas and asbestos related diseases following limited and intermittent exposure.

DISCUSSION

In the examination of relative risks from various forms of asbestos, there is a need to put into proper perspective the references which have been made to ore contaminants, which have been identified as derived from the chrysotile mines. The epidemiological investigations of health effects that pertain to chrysotile are solely directed at the form of chrysotile that has been provided in prior decades from the Canadian chrysotile mines for commercial distribution and use in the United States and elsewhere. The chrysotile, as supplied and distributed throughout the United States, was not processed in any way to remove any ore contaminant before use and human exposure occurred. In essence, the mesotheliomas which have occurred and are the subject of epidemiological studies relate to the form or type of chrysotile that was provided for commercial use.

On one occasion Wagner, who reported the major study on mesotheliomas, stated "all mesotheliomas caused by commercial asbestos have been due to crocidolite." [1979] although he did not always espouse this view [Gilson and Wagner, 1967].

Experimental Observations

Wagner et al. [1980] conducted extensive experimental studies on animals with all types of asbestos, by intrapleural innoculation and by inhalation. Wagner observed in summary: "These experiments produced some surprising results, in particular, although the crocidolite sample had produced more mesotheliomas than did the chrysotile after intrapleural injection, after inhalation, the sample of chrysotile from Canada produced as many mesotheliomas as did crocidolite; this was in spite of the fact that the retention of chrysotile dust in the lungs was very much less than that of crocidolite. This experiment has cast some doubt on the epidemiological evidence that crocidolite is much more hazardous than chrysotile as far as mesotheliomas are concerned."

Subsequently, Wagner [1986] referred to a series of cases (12) of mesothelioma in a preliminary investigation of the chrysotile mine and the production of commercial chrysotile in Cyprus which had occurred among individuals exposed to the chrysotile mine dust with ore contaminants (containing tremolite) similar to those observed from the chrysotile mines of Canada.

A series of experiments have consistently demonstrated that chrysotile, more than any other form of asbestos, gets to the pleura and is retained in the pleura as the basis of subsequent disease.

Le Bouffant [1980], in a study of human tissues, noted a preferential migration of chrysotile fibers to the pleura, with a significant increase and accumulation in the pleura, in comparison with the lung parenchyma. "The median percentage of chrysotile fibers was 3% in the lung and 33% in the pleura." In one series of cases, the median concentration in the pleura was 3000 fibers (chrysotile) per gram of dry tissue.

Sébastien et al. [1979, 1980], in similar studies on human tissues, also demonstrated that the retention of asbestos fibers in the parietal pleura was type- and size-related, that inside the parietal pleura most of the fibers were short chrysotile fibers, and that lung retention was not a good indicator of pleural retention.

Viallat et al. [1986], with intratracheal injection of small amounts of UICC chrysotile, demonstrated that the shortest fibrils reach the pleura very rapidly and can be retrieved from the pleural fluid of rats within one month.

Harington [1981], in his review on animal studies, cited that large numbers of short lower aspect fibers may induce mesotheliomas and that superfine chrysotile was the most carcinogenic of all the materials used.

Mowé et al. [1984] found that there was no correlation between latency and the total lung fiber concentration in malignant mesothelioma.

Identification of Mesotheliomas

Of particular significance are the observations by Churg et al. [1984] who identified, in one hospital, 6 cases of pleural mesotheliomas in 90 consecutive

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autopsies in the period of late 1980 to 1983, of long-term workers in the Thetford mines of the Quebec chrysotile industry. (In contrast, Hochberg [1951] had estimated that there had been between 1 per 1000 and 1 per 10,000 autopsied in the general population.) The mineral content in the lungs of 5 of the 6 deaths with mesotheliomas identified by Churg had only chrysotile and ore components. These observations concerning chrysotile in the lungs were found even after 22 (allowing for correction in case No. 2) years since last work exposure to chrysotile, and after an interval of 31–48 years between initial employment and death. Earlier, Gibbs [1978] had specifically cited the need for such a study of "autopsy material from persons who died at various periods after exposure to chrysotile to see how long the fibre remained in the lung." It is evident that chrysotile remains and that the cancer risk does not cease after exposure stops. The Churg cases and the mesothelioma cases that occurred after the age of 65 in this series, as well as in those workers who ceased asbestos exposure at earlier ages, also demonstrate this point.

The Churg et al. observation of 6 mesotheliomas in 90 autopsies during less than 4 years among the Thetford asbestos workers is also significant because McDonald et al. [1980] had reported only 13 mesotheliomas among Thetford chrysotile miners in Quebec during 19 years (1960–1978). These findings emphasize the necessity of ascertaining other cases of mesotheliomas which may have occurred before, during, and after the McDonald et al. and Churg et al. time periods of observation. A few instances will be cited.

Identification of mesotheliomas is basically difficult, but this may have been more difficult for some of the mining and surrounding rural areas in Canada because of limited professional resources. This was referred to by Selikoff et al. [1964] in discussing the various areas of the chrysotile mines in Canada:

> In Asbestos, a town with one of the largest chrysotile mines in the world, there is no pathologist, no hospital laboratory, postmortems are almost never done. Montreal and Quebec City are at least 75 miles from the areas in question and are not commonly utilized by the local population. Serious cases are sent to Sherbrooke 40 miles away. The only hospital in the Asbestos area is a small one used for maternity purposes (at least 2 years ago).

Cartier, physician for the asbestos companies' clinical facility in the Quebec area, in reporting on deaths before 1950, identified 2 cases of pleural mesothelioma associated with Thetford chrysotile mining operations [1952]. One asbestos worker had been employed for 26 years. The second, identified by autopsy in 1949 (referred to consultant pathologist Vorwald in the United States), was that of a company official, the treasurer of the Asbestos Company Thetford Mines, whose exposure was recorded as office work from 1920–1949, with a latency period of 29 years [Castleman, 1986]. (Wagner et al. [1960] referred to the 2 cases of mesotheliomas by Cartier from the Canadian Chrysotile mines.) It is apparent that unless residents of the area near chrysotile mines were accorded similar exceptional medical assistance of autopsies and special microscopic examination of the tissues by a consulting pathologist, it is very likely that mesotheliomas would not have been detected and recorded.

Braun and Truan [1958], in a study of asbestos miners (Thetford and Asbestos) in Canada, cited a death due to mesothelioma between 1956–1957. The identification as to whether it was from the Thetford or Asbestos mines was not given.

Death certificates are not an accurate reflection of the full number of mesotheliomas which have occurred, for several well-known reasons. Mesotheliomas may have been identified at some point in time by biopsy in hospital records but not recorded later on the death certificate at another location with a different doctor, as previously mentioned. Similarly, information derived from autopsies may not be recorded on the death certificates. (International Classification of Disease, Injuries, and Causes of Death did not include malignant mesothelioma until the eighth revision.) All of this is related to the basic problem of the infrequency of autopsies in various rural and urban areas, and the need for the particular services of pathologists. Further, cancers which have been reported on the death certificate as primary site unknown, or attributed to some other site, have been found on subsequent review of the microscopic slides by consultant pathologists to be mesotheliomas. Selikoff et al. [1979], in a series of reports utilizing all medical resources, demonstrated that the number of mesotheliomas was far greater compared to what was recorded on the death certificates among workers exposed to asbestos, and similar experiences have been reported by Newhouse and Wagner [1972]. Nevertheless, death certificates in research are very important. A complicating factor in Canada was the policy of the Quebec Ministry of Social Affairs, which has insisted on permission of the next of kin before providing a death certificate, with cause of death, even for research purposes [Nicholson et al., 1979]. Consequently, death certificates which could be critical in a research study could not be obtained from the appropriate relative if they had moved, died, or could not be found. Death registration in Quebec first became compulsory in 1926 [McDonald et al., 1970].

The most important fundamental difficulty in prior decades has been the proper diagnosis and identification of mesotheliomas, and the underreporting that occurred for this type of rare cancer. This was one of the major considerations of the IUCC Working Party on Asbestos and Cancer [1965], which was directed at the international coordination of research on asbestos. A series of recommendations was made which proposed that reference panels of qualified pathologists (who would review the cases of other pathologists) be set up on a regional, national, and international basis to assist in the diagnosis of mesothelioma and other tumors associated with exposure to asbestos.

In view of the uniqueness of the pathological services required, as well as the other factors, it is reasonable to conclude that the magnitude of underidentification of mesotheliomas in some periods of time may have been far greater than realized in the rural chrysotile mining areas of Canada and would tend to underestimate the relative risk of chrysotile in the induction of mesotheliomas.

Dust Estimations

In the consideration of dust estimates and dust exposures in the early years relative to chrysotile as well as other forms of asbestos, a considerable number of questions have been raised as to the appropriateness of such guesses and extrapolations about exposure levels in prior decades (as they may relate to subsequent development of lung cancer and mesothelioma). Selikoff [1978] was doubtful about the validity of the dose-dust estimate in the Quebec Study in view of the infrequent and fragmentary dust measurements made in earlier years. Wright [1978] was also

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A panel of scientists of the U.S. Government (NIOSH–OSHA) Asbestos Work Group [1980] concluded "that there was no evidence for a threshold or for a 'safe' level of asbestos exposure," after citing that "human occupational exposure to all forms of commercial asbestos fiber types, both individually and in various combinations have been associated with high rates of asbestosis, lung cancer, and mesothelioma."

Problems in Epidemiological Studies

In terms of mortality experience, the basic concept of mortality surveillance of workers employed in specific industries has been known and applied for decades by insurance companies. Hoffman [1918] cited increased risk of asbestos workers, leading American and Canadian life insurance companies to deny insurance coverage for such persons. Continued evidence of this risk was a 1930 survey of asbestos miners in Asbestos and Thetford mines in Canada, in which 42 cases of asbestosis were found among 195 asbestos miners, and an investigative report [1949] which cited extensive effects of asbestosis, the deaths, and air pollution from chrysotile mining operations [Castleman, 1986; Trudeau, 1974].

Of particular interest is the Braun-Truan study [1958] of lung cancer among miners of the Asbestos and Thetford mines in Canada, which provides illustrations of some of the problems of design, analysis, and reporting of results, which can understate the cancer risk. These are cited in broad terms, as necessary background in any evaluation and estimation of cancer risk from chrysotile. The study consisted of a combined cohort of 5,958 (6,091, less 133 lost to study), all of whom had at least 5 years or more employment, were alive in 1950, and were followed for 6 years through 1955. This automatically excluded the mesotheliomas of the Thetford operations that died before 1950 (2), as cited by Cartier [1952]. Other basic problems affected the evaluation. Enterline [1964] pointed out that an inappropriate statistical derivation of the expected rate for lung cancer was used, which submerged the positive lung cancer findings; that the same comparable diagnostic criteria (of confirmation) essential to the analysis was not used both for the study group and the control group. Mancuso [1965] cited the very short period of observation, which substantially limited the extent of the identification of the lung cancers; that the designated exposure categories were basically not tenable and therefore inappropriate for correlation. Selikoff [1964] also cited the dilution factor in the cohort, relative to age, duration, and lung cancers; the limitations of the availability of medical services; and problems with both the diagnostic and exposure criteria.

Sabourin [1957], in referring to the prepublication Braun-Truan report for the

Quebec Asbestos Mining Association, noted that cancer statistical data "was very poor in the Province, as the report of cancer as cause of death is not compellable by law, e.g., tuberculosis must be reported." In fact, occupational cancers when they do occur may not be reported in the literature. Hueper [1961], citing the published article (1958), pointed out that the Braun-Truan data "had missed 34 cases of asbestosis cancer of the lung studied at Saranac Lake Laboratories." Despite all these constraints, the prepublication Braun-Truan data identified a positive statistical association between lung cancer and asbestosis, but this unfortunately did not appear in the published paper. Another problem was that the marked differences between two groups in a study can be submerged when combined and used as a single cohort, which affect the analyses and interpretations that can be made. This related to the differences in the exposure categories for the Asbestos and Thetford miners as recorded independently in the prepublication report. These were then combined and the differences in the lung cancer rates were averaged in the published report, lessening the statistical sensitivity in control comparisons.

Epidemiological studies have the complicating problem of competing causes of death, in which individuals, workers, or residents may die of other causes, whether of asbestosis, or other disease or injuries, before the latency period has been met for the development of lung cancer and mesothelioma. Similarly, it is also recognized that mortality per se, although important, is only a very gross indicator of health effects; significant diseases may be sustained in prior years by those exposed, but not identified or reflected on the eventual death certificates. A further fundamental problem has been the use of the general population, with higher actuarial death rates than employed workers, as a control to derive the expected rate. This can be misleading and mask positive cancer findings among the workers studied.

Chrysotile Exposure

Mesotheliomas have also been reported following exposure to chrysotile in the manufacture, removal, and installation of brake linings; these commonly have been made with chrysotile asbestos. The pervasiveness of the automotive industry, with associated repairs and the very large population of workers who may have been exposed in prior years, represent a major area of concern. The seriousness of the problem is reflected in a review by Castleman et al. [1970, 1986] on asbestos disease among brake repair workers that documents a series of reports in the United States, Canada, and Europe. The following citations represent illustrations of particular aspects.

Langer and McCaughey [1982] reported a pleural mesothelioma in an auto repair man who had worked for many years, often replacing brake linings. The latency period since first exposure and death was 27 years. Chrysotile was identified and confirmed by electron diffraction analysis and no amphiboles fibers were found. It was estimated that 1 μg of chrysotile was present per 5 g of wet lung parenchyma.

Teta et. al. [1983], in a report on mesothelioma in the Connecticut tumor registry, cited 2 cases of mesothelioma (pleural and peritoneal) in women (clerical workers) who were employed at a friction products plant that manufactured brake linings using only chrysotile asbestos. Of particular epidemiological significance was the fact that the mesotheliomas were not cited on the death certificates and therefore were not included in the death certificate analysis of 122 women who died in a cohort study of that plant [McDonald, 1986].

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Vianna and Polan [1978], in a study of spouses with indirect, minimal, intermittent exposure to asbestos, cited 3 mesotheliomas that had occurred in women at ages 40, 77, 78, whose husbands were brake lining workers.

McDonald et al. [1970] identified two cases of primary malignant mesothelioma tumors in Canada, in persons who had been brake lining installers, and one who had worked in brake lining manufacture.

Godwin and Jagatic [1968] reported a case of peritoneal mesothelioma in a worker who wove brake linings made from chrysotile for three years and who died at age 43.

Mancuso [1983] reported a pleural mesothelioma in an auto mechanic who died in 1969 at age 58.

Clinical Epidemiology and Medical Economics

The findings of this study demonstrate a very high relative risk for those exposed to chrysotile asbestos in the development of mesothelioma with one mesothelioma eventually occurring for every 13 machinists hired in the years 1920–1929 by railroad company A.

The human experience, the manifestation of the disease, and the consistent repeated development of a specific rare cancer such as mesothelioma in successive cohorts following prior exposure to commercial chrysotile asbestos illustrate the basic principle that the nature of the asbestos exposure was sufficient for the induction of the mesotheliomas, regardless of the theoretical discussions and posturings surrounding the development of the cancer process.

This investigation also demonstrated again the importance in medicine of "clinical epidemiology" in the identification of occupational cancers by clinicians. Historically, virtually every occupational cancer was first identified by a clinician or surgeon. In this instance, physicians associated with the same railroad hospital of company A consistently diagnosed mesotheliomas, a rare type of cancer among workers employed by the same company in a small city. The clinicians and the thoracic surgeon unfortunately did not publish their findings of mesotheliomas that had occurred among the railroad workers. This illustrates the basic fact that occupational cancers and diseases can and do occur in specific industries and may not be reported in the medical literature; the absence of such reports does not mean that the specific occupational disease or cancer has not occurred. It is hoped that this paper will encourage physicians in industrial medicine in the application of "clinical epidemiology" and in the publication of their findings in the medical literature.

A final basic medical observation and concern is the occurrence of occupational cancer among the elderly. Of the 14 mesotheliomas in the cohort study, 12 died at ages 65 and over, as well as 7 of 8 in the craft designations. The occurrence of cancer in the older age group, because of the latency period, has been observed in virtually all occupational epidemiological studies of a wide range of industrial carcinogens. The substantial implications for medical economics, the interrelationship of governmental medical care and costs, and the importance of environmental controls of prevention in the early work years of life warrant a major national investigation.

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