PLAINTIFF'S EXHIBIT IHF78

AN EPIDEMIOLOGICAL STUDY OF LUNG CANCER IN ASBESTOS MINERS*

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Ever since the pronounced increase in the incidence of lung cancer among males became apparent, there have been attempts to associate it with one or another of the various elements in the environment of man. The approach used by some workers has been to suspect one or several substances and then set about in an intensive search for lung cancer among persons who have had any exposure to those materials. In this connection, Smith (52) writes: "The tendency of authors reporting the coincidental occurrence of primary lung cancer with silicosis or with any other theoretical etiologic conditions, has been to emphasize the percentage relationship in extremely small series of cases, with control cases which are not in any way comparable."

It would seem inevitable that asbestos should come under scrutiny in this manner, because prolonged exposure to this material is known to cause a specific type of pneumoconiosis, and because persons who show this form

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of pneumoconiosis often come to autopsy and provide a ready source of material for study. It was in this way that reports of the simultaneous occurrence of lung cancer and asbestosis began to accumulate after the report of a case by Lynch and Smith[66] in 1935. Within the next ten years, about 15 additional cases were reported, and in 1954 Merewether[76] reviewed all deaths from asbestosis recorded in England since March, 1924. Lung cancer occurred in 16% of these cases. Gloyne,[41] whose work is also frequently referred to as establishing a connection between asbestosis and cancer of the lung, reported in 1951 that cancer of the lung was present in 14.1% of asbestosis cases examined by him. In 1941, Nordmann and Sorge[76] claimed to have produced lung cancer in mice which they exposed to asbestos dust.

Since 1951, additional cases of cancer of the lung coexisting with asbestosis have been reported, and, according to Hueper[58] about 100 such cases had been reported up to 1955. As a result, an association between the two diseases appears to have been accepted by many authors, and several writers were using the term "asbestosis cancer" of the lung. Werber[89] in 1952, stated categorically that in 7% to 17% of cases of asbestosis, after a latent period of about 1 1/2 to 20 years, carcinoma becomes established in the lung.

On the other hand, not all authors accepted this alleged association without reservation. Saupe[80] in 1939 reported that he had discovered no cases of lung cancer among 620 cases of asbestosis which he had examined; and in 1942, Holleb and Angrist[48] expressed the opinion that the number

of cases of asbestosis with lung cancer was too small for statistical evaluation. In 1947, Wegelius[66] reported 126 radiologically diagnosed cases of asbestosis among 476 workers in Finland, and found no cases of lung cancer in this group. Goldblatt and Goldblatt in their section of Merewether's latest book,[44] state: "But at no stage in all these impressive researches was any clue obtained which might have offered any support to the possibility that asbestos could act as a carcinogen. There is no reliable criterion by which one can anticipate carcinogenicity and, as is well known, relatively minute changes in the structure of a chemical carcinogen are sufficient to diminish or eliminate carcinogenic action.

If asbestos is indeed to be regarded as a carcinogen, the need is felt to demonstrate some property which can be regarded as something more than inertness."

These authors advance the theory that, until some more experimental evidence of direct carcinogenesis by asbestos or a decomposition product of it can be obtained, asbestos might be considered as a "co-carcinogen" which only induces a further development of a preneoplastic condition brought about by something independent of the asbestos, such as an endogenous factor.

Thus the literature, while tending to support the thesis that asbestosis is in some way related to the development of lung cancer, is by no means unanimous. Altogether, it is perhaps more confusing than enlightening. A careful review shows that the majority of the reports are clinical and not epidemiological. They lack many elements necessary for the application of

epidemiological techniques to their content and most of the authors do not make claim to having done so. What has happened is that succeeding authors have drawn conclusions and generalised beyond the scope of the works which they quote. Nowhere, for example, have we found reforences to a population of asbestos workers, although several authors who have quoted the observed incidence of lung cancer in autopsies of persons who also had asbestosis imply that this incidence applies to asbestos workers, generally. We have likewise been unable to find any study which actually calculated the incidence of lung cancer among a population of persons who had asbestosis, and not just those who came to autopsy. With the exception of a paper by Doll [28], none of those reviewed gave any data on exposure and dust concentrations, and even Doll's paper merely mentions "scheduled" areas, by which is meant, "those areas where processes are carried on which were scheduled under the Asbestos Industry Regulations of 1931 as being dusty."

There is, furthermore, a complete lack of definition of terms as used in the published literature. For example, the term "asbestosis", as used, may refer to changes observable only by microscopic examination of the lung tissue, or it may mean a radiologically detectable condition.

Most of the published reports obviously included women among their cases, but some of them do not give the number or proportion of women involved in the study.

There is also a lack of uniformity as to what type of exposure most studies have dealt with. Of 99 cases enumerated by Hueper[58] in 1955, only

ten appear to have originated in the United States, and seven in Canada. Some of the earlier reports apparently included asbestos miners, but it can be assumed, since 82 of the 99 cases had originated in England, and since no asbestos mining operations are carried on in that country, that most of the reported cases have involved workers in the textile or fabricating industries.

Such factors as smoking habits, family history of cancer, length of time in the industry, and age of the individual case are also notably absent in the majority of these reports.

With this understanding of the limitations of the existing literature with respect to epidemiological generalization, it may be of value to consider in somewhat more detail some representative earlier publications, a few of which were referred to briefly above.

One of the most detailed studies and one which deserves the most serious consideration is that reported by Doll[20] in 1955. This study reviews causes of death among asbestos workers based on Coroners' records. It also attempts to estimate the risk by studying records of men who worked for at least 20 years in exposed situations. Doll concluded that lung cancer was a specific industrial hazard of certain asbestos workers and that, after 20 years of exposure, the risk is ten times as great as for the general population.

This article is important for several reasons, in addition to the definite conclusions at which it arrives. For example, it begins by stating that "in view of the infrequency of asbestosis, this large number of cases

(61 cases of lung cancer) suggests—but does not prove—that lung cancer is an occupational hazard of asbestos workers." Neither this article or any previous one which we have examined presents any figures to prove that asbestosis is an infrequent occurrence. Estimates of the number of persons potentially exposed to asbestos dust in the United States alone vary from 10,000 to 35,000 and the incidence of asbestosis of any degree might be higher than Doll imagines.

This study, like so many others, involves autopsy records. The number of persons involved in the statistical analysis is only 113 representing only 1,042.25 man years of life. It is also true that in selecting men who had been employed for at least 20 years, the study automatically excluded those who died from other causes after shorter employment.

Another reason why this publication is of importance is a statement which it contains to the effect that "the strongest evidence that it (lung cancer) may be a hazard (in asbestos workers) has been produced by Merewether and by Gloyne."

In 1951 Gloyne [41] presented a review of 1205 autopsies on persons who had worked in various dusty occupations. This number included 132 asbestos workers, of whom 121 showed "pneumoconiosis"—presumably asbestosis. Primary cancer of the lung occurred 17 times in this group, an incidence rate of 14.1% for lung cancer among autopsied asbestosis cases. There were in his series 796 cases with silicosis, and 6.9% of these also showed primary cancer of the lung. The incidence of lung cancer in other

forms of pneumoconiosis was 6.7%, and in 169 cases which proved not to have any type of pneumoconiosis it was 8.3%. Gloyne considered "the mortality of the asbestos workers" to be "disturbing". First of all, it is obvious that the paper does not deal with the "mortality of asbestos workers", and secondly, it must be borne in mind that all of Dr. Gloyne's cases were submitted to him for study because the findings were unusual for uncomplicated pneumoconiosis. It can reasonably be assumed that cases, including those of asbestosis, in which the findings were not considered unusual were not sent to Dr. Gloyne for examination. As a matter of fact, in the same paragraph in which he expresses concern over the incidence rate in asbestosis, Dr. Gloyne himself points out that the rate for lung cancer based on necropsies at the London Chest Hospital was 21.3% while the figures of the Registrar-General showed only 2.4%. He thus recognized that autopsies on a certain selected group of cases were not representative of the general population. It would seem, then, that notwithstanding the value of Dr. Gloyne's work, its importance as an index of the prevalence of lung cancer in asbestotics has been misinterpreted by some who have quoted him. All that it really shows is the fact that in a group of 121 cases, selected for special study primarily because they seemed abnormal by preliminary examination, 17, or 14.1% had lung cancer.

Merewether [75] in 1947, in the report of the Chief Inspector of Factories, reviewed all cases reported between 1924 and 1946 in which asbestosis was the cause of death or a coexisting condition. This work was later extended to include all such cases reported up to December, 1954, by

which time there were 344 deaths including 205 males and 139 females. Among them were 55 cases (16%) of cancer of the lung, 41 in males and 14 in females. It is quite possible that a large number of asbestotics who did not die of their asbestosis, or in whose death certificate it was not mentioned, may have been missed. The import of this 16% is enhanced by the simultaneous statement that the incidence of lung cancer in autopsies of the general population is only 1%. The danger of attempting to compare a rate found in 344 cases with the rate for the general population without respect to age, occupation, and many other variables, such as smoking habits, is obvious.

Lynch [70] who with Smith [63] had reported the first case in 1935, reported four cases of carcinoma of the lung in a series of 49 autopsies on workers in an asbestos manufacturing plant who were shown to have "demonstrable deposits of asbestos in the lungs." This, of course, is not necessarily identical with the disease asbestosis. Lynch, himself, points out that, although this is an incidence of 8.2%, "both figures are too small for very serious statistical types of calculation." Nevertheless, later writers have used this paper to strengthen the case for an association of carcinoma of the lung with asbestosis. It is also of interest that Klotz [63] found only the same number of cases of lung cancer in a series nearly 10 times as large, i.e., four in 478 cases of asbestosis.

Behrens, as quoted in Merewether [76], estimated that, of 309 cases of asbestosis in the literature, 44 showed associated cancer of the lung—giving an incidence of 14.2%. This is an illustration of generalizing an incidence

obtained in a group of cases which were undoubtedly reported only because some of them showed lung cancer, to possibly hundreds of asbestotics whose cases were never reported. The same applies to the conclusion of Teleky[65] who appears to have reviewed reports of 39 autopsies on persons with asbestosis among which six cases of lung cancer occurred. Information from sources such as these does not justify generalizations with regard to mortality rates.

Perhaps no one has written so extensively on the subject as has Hueper[52-59]. In 1955 he reviewed the cases[58] reported prior to that date and enumerated a total of 99. Eleven of these were those discussed by Doll[28] and may have been cases covered by other authors. Eight were discovered by Kennaway and Kennaway[62] in an analysis of death certificates and, unless Merewether's study was incomplete, these cases should have been included in his report. Of the remaining 80, it is quite possible that the 31 contributed by Merewether and the 17 by Cloyne contain some duplication with each other or with those of other English authors.

Principles of the Epidemiological Method

Doll[30] has pointed out that much of what is now thought to be pertinent concerning the comparative frequency of lung cancer in different population groups has been developed from the analysis of clinical material, particularly surgical and autopsy records, supplemented to some extent by the reported impressions of various clinicians based upon their personal observations. More recently, however, attention has turned to the systematic

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investigation of this problem by the same methods that have proved so successful previously in the study of communicable diseases, that is to say, by epidemiological methods.

In order to apply this method of investigation to the problem under discussion, we were of the opinion that a study should be planned so as to provide:

1. A well-defined population group.
2. Available data for all members of this population, including the healthy as well as the ill.
3. A sample which is truly representative of the population.
4. Reliable and valid observations relating to the problem of the study.

A serious defect, common to most of the studies which have been reported, is that little or no information concerning the healthy people in the group seems to have been available to the author. In order to draw a generalization regarding all asbestos workers, it is necessary for a study to include living persons as well as the dead. Limiting the investigation to autopsied cases, as has been frequently done in earlier studies, still further restricts its use in generalization. The problem with which we are concerned is whether asbestos miners experience more lung cancer than does the general population. The answer necessitates the collection of reliable information on asbestos miners as a group, as well as on the general population.

It seems advisable to discuss the differences between the epidemiological approach and that used in the studies which have been reported to date. A very important consideration is the fact that lung cancer, in spite of its increasing numbers, is still a disease of low incidence; that is, in a given population not many persons will contract this particular disease. This fact requires that large samples or groups must be studied to provide meaningful results.

Recognizing the difficulty of obtaining such large samples, most earlier writers deviated from the epidemiological method and sought to circumvent the requirement of observing well persons by:

1. Comparing the relative frequency of cancer in various sites.
2. Comparing the relative frequency of cancer in a group of hospitalized patients.
3. Comparing the relative frequency of cancer in a group of cases coming to autopsy.

Attempting to compare two population groups, looking only at the relative frequency of cancer in various body sites, may result in finding a higher percentage (relative frequency) in one of the groups, when, in fact, the mortality rate of cancer of a particular organ is exactly the same in both groups. This is very clearly demonstrated in the excellent article by Dorn[33]. The mortality rate from a particular cause is the true measure of comparison.

It is apparent that selected groups such as hospitalized patients or autopsy cases may not be in any way representative of a larger group, and that in dealing with such samples, the observer may easily find more cases of a given disease than would be found in another group of the same size, but representative of the general population. It is true that investigation of cases from such a sample can furnish information valuable for research, but the use of this information in drawing generalisations is necessarily restricted. It is the obligation of both the investigator and of those who read his report to make proper comparisons and to draw only those conclusions which are valid and justified. A good statistical study of cases of cancer of the lung occurring in a group of autopsies can lead to a proper inference concerning the frequency of lung cancer among cases coming to autopsy, but only to such cases. For information from such a study to be projected to some larger group, it is necessary that the autopsies represent a good sample of that larger group. To assume that such is the case in any particular series is dangerous and likely to be false.

There is some danger that the figures reported by some authors may be misconstrued as applying to asbestos workers or even asbestos miners, when, in fact, the authors in question do not make this generalization, nor can the generalization be made for the reasons stated. Close study of the reports reveals that the percentages quoted relate only to the group of autopsies covered by the particular investigation.

The present study, in contrast to the earlier works, has been planned to utilize the epidemiological method. A well-defined group of asbestos miners has been established in such a way that it constitutes a good sample of the whole population of asbestos miners in Quebec. Data for all members of this group have been collected and analyzed. Those concerning lung cancer have received most careful consideration. Details of the methods employed will be set forth later, but the type of approach is considered to permit of fair comparisons and valid generalizations.

Collection and Analysis of Data

A preliminary survey of potential sources of information in February of 1956 involved discussions with the physicians in charge of the asbestos companies' programs and with clinicians, pathologists, representatives of City and Provincial health departments and of the Canadian Cancer Society, and other interested persons. It was found that morbidity data, although somewhat limited, were available from such sources as the hospitals in Montreal and Quebec City, and the 13 Cancer Detection Centers in the Province. However, because of the high mortality in lung cancer, it seemed advisable to depend upon data relating to deaths. These we found to be obtainable at the vital statistics department of the Ministry of Health in Quebec City. From the preliminary survey, it was apparent that extensive and detailed information could be gathered with respect to both the persons employed in the asbestos mining industry and mortality figures for the general population.

Following this exploratory survey, the initial effort was directed to the collection of data relating to all workers who had been processed through the clinic at Thetford Mines since its inception in 1947, and similar information regarding all workers at Asbestos, P.Q. Data from the clinical records included the age, family and personal medical histories, smoking habits, number of years of exposure, an estimate of weighted exposure, and the course of the individual's health status or the cause of his death.

From this information it was possible to formulate a "cohort" which could be well defined, should be representative of the whole group, and could be followed for a definite period of time. All of the available experience indicates that the development of asbestosis in less than five years of exposure must be somewhat rare. Accordingly, the cohort was defined as including every MINER who had a total exposure of five or more years, and who was on the employment rolls in 1950. (OFFICE AND OTHER NON-EXPOSED PERSONNEL, REGARDLESS OF LENGTH OF EMPLOYMENT, WERE NOT INCLUDED.) This cohort was then followed by means of the annual physical examination records through a six-year interval, 1950 through 1955. All data regarding this group were then tabulated in order to determine the characteristics of the cohort. For those who survived the entire period, reference was made to the physical examination results and x-ray findings at the end of the period. Those who had died were tabulated separately and the cause of death corroborated by examination of the death certificates. A further search was made concerning those in the original cohort who remained unaccounted for when the living and the known dead had been tabulated. They represent men who had left employment through retirement or resignation. Eventually, all but a small number of these were accounted for as either

living or dead, and in the latter event, the cause of death was substantiated in a similar manner, and the results added to the original list of deaths.

Death certificates for the Province of Quebec for the years 1952 to 1955, inclusive, were reviewed in the department of vital statistics of the Provincial Health Ministry, together with statistical summaries of the causes of deaths in the Province by counties. All cases in which death was certified as having been due to primary cancer of the lung were examined for such information as place of residence, occupation, date of death, hospital in which death occurred, and whether or not an autopsy was performed. Cases in which lung cancer was given as a cause of death, but in which it was not specified as to whether the cancer originated in the lung, were also reviewed in an effort to include all instances of primary carcinoma of the lung in the study.

The statistics for the Province of Quebec relate to population, total deaths from all [illegible] and deaths from lung cancer. These were collected and tabulated by counties and by sex for the years 1950 to 1955, inclusive. From them, death rates for the general population of Quebec and of individual counties were calculated for specific years and analyzed by cause.

Practically all employees of one company are covered by a group policy of life insurance which, fortunately, nearly all of them continue to carry when they retire. A very few are not covered by this policy, and those who leave the industry for one reason or another except retirement usually are no longer covered, but this is likewise a small number. As an additional

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Practically all employees of one company are covered by a group policy of life insurance which, fortunately, nearly all of them continue to carry when they retire. A very few are not covered by this policy, and those who leave the industry for one reason or another except retirement usually are no longer covered, but this is likewise a small number. As an additional

check upon the information obtained from the clinical records of this group, the records of the life insurance company were examined for all death claims paid under the policy, and particular notice was taken of the claims in which the proof of death was based on cancer of the lung.

Deaths from lung cancer among asbestos miners were thus determined from the clinical records in the medical service of the industry and checked by means of the death certificates and insurance company records. The deaths were then verified individually by reviewing them with the physicians in charge of the medical services. In this manner, there was established a list of cases in which primary cancer of the lung is considered to have been proved as the cause of death. A few cases in which lung cancer is strongly suspected but not proved as the cause of death were considered separately. Mortality rates have been calculated using both the "proved" and the total of "proved" and "suspected" cases during the years under observation. Comparisons were then made between the death rates from the same cause among specific segments of unexposed persons. All lung cancer deaths, both suspected and proved, were carefully analyzed to determine possible relationship or correlations between the development of lung cancer and any factor known from the clinical records such as family history of cancer, personal history of heavy smoking, coexistence of asbestosis, or exposure to asbestos.

In addition to this analysis of deaths occurring in the cohort and during the years under observation, every known death from cancer of the lung, as well as every case diagnosed but still living, has been tabulated and

analyzed. They will be discussed separately from those included in the population and time-interval under study.

A comparison of lung cancer mortality in the asbestos-producing counties has been made with that in counties which are far removed from the asbestos mines and in which, presumably, no asbestos miners live.

Finally, in order to broaden the comparison of death rates in different population groups, the rates have been collected for Canada generally, and for the United States, according to the most recent published and unpublished material.

Results and Interpretation

The cohort which was constructed according to the criteria described in the preceding section has been considered individually and compared with the general population. Description of the cohort will be presented here as a preface to the results of the study.

Original Cohort	6091
Lost Persons Deducted	133
Final Cohort	5958
Living in 1955 (working and retired)	5771
Dead by 1955	187
Cancer of lung	9
Questionable cancer of lung	3
Other causes	169
Unknown causes	6
Smokers	4673
Nonsmokers	1265
Unknown	20

Tables 1, 2, 3, and 4 present age, number of years of employment, weighted average exposure, and smoking habits of the cohort.

A comparison of the exposure to asbestos dust is presented in Table 3. All members of the cohort were placed in one of three categories, representing increasing degrees of exposure based on a weighted average of the years spent at various levels of dustiness. The degree of dustiness for each job category was determined after consultation with persons familiar with the environment and conditions in the various work areas. For the purposes of calculation, the assumption has been made that the relationship between these categories is linear, and that category II is twice as dusty, and catetory III three times as dusty as category I.

The fourth variable, smoking habits, was similarly tabulated and is shown in Table 4. This was included because the information was available and because smoking was regarded as one of the variables which, besides the environment, could conceivably influence the development of lung cancer. As used in this presentation, the term smoker refers to a cigarette smoker, habitually smoking more than five cigarettes per day. Persons who smoke pipes or cigars exclusively were not considered to be smokers for the purpose of this study.

TABLE 1

Number and Percentage Distribution by Age

Age	Number	Per Cent
20-44	3901	66
45-54	1124	19
55-64	615	10
65 +	315	5
Unknown	3	*
Totals	5958	100%
Average Age	41	

* Less than .5%

TABLE 2

Number and Percentage Distribution by Length of Employment

Length of Employment	Number	Per Cent
5-9	1795	30
10-19	2398	40
20-29	922	16
30-39	603	10
40-49	185	3
50 +	55	1
Totals	5958	100%
Average Years of Employment	18	

* Less than .5%

TABLE 3

Number and Percentage Distribution by Exposure Category

Exposure Category	Number	Per Cent
I	2031	34
II	2150	36
III	1772	30
Unknown	5	*
Totals	5958	100%
Average Exposure	2.0	

* Less than .5%

TABLE 4

Number and Percentage Distribution by Smoking Habits

Smoking Habits	Number	Per Cent
Smokers	4673	79
Nonsmokers	1265	21
Unknown	20	*
Totals	5958	100%

* Less than .5%

— Table 5 presents the year-by-year experience of the cohort and indicates the number of deaths each year from specified causes. In general, a case was considered to be "proved" as one of primary cancer of the lung when the records showed that the diagnosis had been supported by an autopsy or surgical resection of the lung with microscopic examination of the removed tissue. In one case so considered, however, diagnosis was confirmed by bronchoscopy with visualization and biopsy. In another, although there was no autopsy, the diagnosis of primary cancer of the lung seems to have been beyond question.

TABLE 5

Year-by-Year Experience of Cohort and Death Rates per 100,000 Man-Years of Risk

Year	No. Alive At Beginning of Year	Cause of Death: Proved Primary Ca. of Lung	Suspected Primary Ca. of Lung	Other Causes	Unknown	Man-Years of Risk
1950	5958	1	2	12	1	5950
1951	5942	2	0	17	1	5932
1952	5922	0	0	37	0	5903.5
1953	5885	2	1	34	0	5866.5
1954	5848	1	0	33	4	5829
1955	5810	3	0	36	0	5790.5
Totals		9	3	169	6	35271.5

"Proved" rate per 100,000 man-years of risk = $\frac{9}{35271.5}$ = 25.5

"Total" rate per 100,000 man-years of risk = $\frac{12}{35271.5}$ = 34.0

The term "suspected" primary cancer of the lung was applied to those cases in which the diagnosis remains in doubt but some of the evidence points to cancer of the lung. There were three such cases.

The term "man-years of risk" has been used to mean the number of men at risk for the year under observation. An individual who lived throughout the year was counted as a full man-year of risk, but one who died during the year was counted as one-half a man-year.

Deaths occurring in the cohort, and in which lung cancer is considered to have been proved as a cause, are shown in ~~table below~~ Table 6. In Table 7 are also shown are three deaths which have been considered as "suspected" lung cancer cases.

TABLE 6

"Proved" Cases of Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Autopsy	Asbestosis
1. A. J.	66	Yes	26 yrs. in Cat. II	10-12-51	Yes	Yes
2. N. P.	65	Yes	34 yrs. in Cat. I	5- 3-55	Yes	No
3. R. M.	65	Yes	37 yrs. in Cat. I	7-20-55	No	No
4. C. B.	59	Yes	32 yrs. in Cat. I	8-20-50	Yes	No
5. A. S.	48	Yes	22 yrs. in Cat. II.	-51	Yes	Yes
6. W. F.	61	Yes	33 yrs. in Cat. III	4-30-53	Yes	Yes
7. L. D.	56	Yes	30 yrs. in Cat. II	11-22-53	Yes	Yes
8. E. L.	37	Yes	16 yrs. in Cat. I	8- 5-54	Yes	No
9. A. R.	68	Yes	28 yrs. in Cat. III	5- -55	Bronch.	No

TABLE 7

"Suspected" Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Autopsy	Asbestosis
1. J. T.	49	Yes	32 yrs. in Cat. III	10-25-50	No	No
2. R. D.	46	Yes	33 yrs. in Cat. III	7- -53	Yes	Yes
3. P. P.	65	Yes	42 yrs. in Cat. II	9-30-55	No	No

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An indication of the importance of these "suspected" cases in interpreting the results of the calculations is desirable before further discussion of the mortality rates which are derived in later tables. For example, it happens that the rate found for the proved cases is close to the "expected" rate based on the general population figures for the Province as will be shown later, and on which basis, we should find eight deaths from lung cancer among the cohort. Actually, nine cases were observed. If, however, the three additional "suspected" cases are included, increasing this figure to 12, the total would be very close to the 95% level of significance. However, having found just 12 cases, we are not above this level, and THEREFORE ~~[illegible]~~g the hypothesis that asbestos miners do not have a higher mortality from lung cancer than does cannot be rejected.
the general population. Nevertheless, the occurrence of 12 cases in this sample would increase the rate to a point which approaches the significant level. Because of the tremendous importance of the questionable cases in this respect, some detail regarding them will be given here.

In one of these cases, the suspicion of cancer of the lung is based upon the x-ray interpretation and, although no autopsy was performed, the death certificate indicates that death was due to lung cancer. It is well known that the x-ray appearance of fibrosis, especially if a localized density or a superimposed tuberculous lesion is present, can simulate that of a tumor, and by itself, does not justify the inclusion of this case as one of "proved" cancer of the lung. A second case was certified as having died by reason of hydrothorax, possibly due to lung cancer, but again there was no surgery and no post-mortem examination. In the third case, although it was subjected to autopsy, two pathologists disagreed as to whether lung cancer was present. The death was certified as having been due to chronic myocarditis with nephritic and pulmonary congestion, and possibly cancer of the lung. On the basis of these facts, it seems unwarranted to include these three cases among "proved" instances of lung cancer. On the other hand, they cannot, in fairness, be disregarded completely. It is for this reason that mortality rates have been calculated both ways.

Table 8 gives the rates by age groups.

TABLE 6

Number of Persons and Number of
Lung Cancer Deaths by Age Groups

Age Group	Persons	Lung Cancer Deaths	
		Proved	Total
20-44	3901	1	1
45-54	1124	1	3
55-64	615	3	3
65+	315	4	5
Unknown	3	0	0
Total*	5953	9	12

Annual Lung Cancer Death Rates per 100,000
Man-Years of Exposure by Age Groups

Age Group	Proved	Total
20-44	4	4
45-54	15	44
55-64	81	81
65+	212	265
Unknown	0	0
Total*	25	34

The rates by length of employment are shown in Table 9. During the first 40 years of employment, the rate rises, an observation which seems plausible since the men were growing older. However, after 40 years of exposure there are no "proved" cases reported for a total of 240 men during the six years, or about 1440 man-years of exposure. When the "suspected"

cases are added, one case does show up in this period. This would produce a rate of 69 per 100,000, again demonstrating the importance of these questionable, but unproved, cases to the final conclusion, because, if there were no cases in this number of men with long exposure, and if asbestos is a carcinogenic agent, it must be concluded that these 240 men have demonstrated considerable resistance. This is a biological phenomenon which has been observed previously and is consistent with the theory of an intrinsic or endogeneous factor in cancer. The only other explanation would be that the susceptible members of this age group had died earlier of lung cancer. Table 18 which appears later in this section indicates that the members of the cohort did not die from lung cancer at a younger age than the general population.

TABLE 9

Number of Persons and Number of Lung Cancer Deaths by Length of Employment

Length of Employment	Persons	Lung Cancer Deaths	
		Proved	Total
1-9	1795	0	0
10-19	2398	1	1
20-29	922	3	3
30-39	603	5	7
40-49	185	0	1
50+	55	0	0
Totals	5958	9	12

Annual Lung Cancer Death Rates per 100,000 Man-Years of Exposure by Length of Employment

Length of Employment	Proved	Total
5-9	0	0
10-19	7	7
20-29	54	54
30-39	138	193
40-49	0	90
50+	0	0
Over-all	25	34

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The rates by weighted exposure are shown in Table 10, and it will be noted that they present strong evidence against asbestos being a carcinogenic agent, for, if exposure to asbestos is in any way connected to lung cancer, we would expect that the longer and heavier the exposure, the higher the rate that would be found. The only possible error in this interpretation could occur if the weighted exposures were inversely related to years of employment, in which case the heaviest weighted exposure (category III) would show the shortest length of employment. Table 11, which lists the number of persons in various exposure categories by length of employment indicates that this error has not occurred. In fact, the average number of years of employment for each exposure category is almost identical.

TABLE 10

Number of Persons and Number of Lung Cancer Deaths by Exposure Category

Exposure Category	Persons	Lung Cancer Deaths	
		Proved	Total
I	2031	4	4
II	2150	3	4
III	1772	2	4
Unknown	5	0	0
Totals	5953	9	12

(Table 10 continued on next page.)

TABLE 5 (continued)

Annual Lung Cancer Death Rates per 100,000
Man-Years of Exposure by Exposure Category

Exposure Category	Proved	Total
I	33	33
II	23	31
III	19	37
Unknown	0	0
Over-all	25	34

TABLE V II

Number of Persons in Various Weighted
Exposure Categories by Length of Employment

Length of Employment	Weighted Exposure Categories I	II	III	Unknown	Total
5-9	707	598	490	0	1795
10-19	663	883	851	1	2398
20-29	314	363	243	2	922
30-39	247	218	137	1	603
40-49	76	67	41	1	185
50+	24	21	10	0	55
Totals	2031	2150	1772	5	5958
Average years of exposure	17.8	17.8	16.6	29.0	17.5

Table 12, which develops the rates for smokers and non-smokers, is most striking. It shows that not a single case of lung cancer developed among the 1265 nonsmokers and that all cases of lung cancer, both "proved" and "suspected", occurred in smokers.

Table 12 was so striking that it was felt that further verification was necessary. It was possible that some abnormal distribution may have occurred, e. g., the nonsmokers may have included a larger percentage of young men. Consequently, additional Tables, 13, 14, and 15 were constructed to show the distribution of smokers and nonsmokers by age, length of employment, and degree of exposure. Although there are slight differences, they do not account for the fact that all observed cases of lung cancer were in smokers. In respect to age (Table 13) the combined average age of the smokers was 4.9 years less than that of the nonsmokers. Table 14 shows that as far as length of employment is concerned, the smokers had worked about 2.3 years less on the average than the nonsmokers. With longer exposure and greater age, one would expect the nonsmoking group to show a higher rate if lung cancer were due to asbestos. Table 15 shows that the average exposure category was almost the same for the two groups. Therefore, this variable seems to be of no importance in accounting for this difference.

The result of this additional analysis is that none of these factors appears to lessen the effect of Table 12.

TABLE 12

Number of Persons and Number of Lung Cancer Deaths
by Smoking Habits

	Persons	Lung Cancer Deaths	
		Proved	Total
Smokers	4673	9	12
Nonsmokers	1265	0	0
Unknown	20	0	0
Totals	5958	9	12

Annual Lung Cancer Death Rates per 100,000 Man-Years of Exposure
by Smoking Habits

	Proved	Total
Smokers	32	43
Nonsmokers	0	0
Unknown	0	0
Over-all	25	34

TABLE 13

Number of Smokers and Nonsmokers by Age Groups

Age Group	Smoker	Nonsmoker	Unknown
20-44	3200	689	12
45-54	896	224	4
55-64	411	202	2
65 +	164	150	1
Unknown	2	0	1
Totals	4673	1265	20
Average Age	39.3	44.2	40.7

Percentage Distribution of Smokers and Nonsmokers by Age Groups

Age Group	Smoker	Nonsmoker	Unknown
20-44	68.5	54.5	60.0
45-54	19.2	17.7	20.0
55-64	8.8	16.0	10.0
65 +	3.5	11.8	5.0
Unknown	*	.0	5.0
Totals	100%	100%	100%

* Less than .05%

TABLE 14

Number of Smokers and Nonsmokers
by Length of Employment

Length of Employment	Smoker	Nonsmoker	Unknown
5-9	1408	377	10
10-19	1967	426	4
20-29	722	199	2
30-39	433	166	4
40-49	110	75	0
50 +	33	22	0
Totals	4673	1265	20
Average Length of Employment	17.0	19.3	16.0

Percentage Distribution of Smokers and Nonsmokers
by Length of Employment

Length of Employment	Smoker	Nonsmoker	Unknown
5-9	30.1	29.8	50.0
10-19	42.1	33.7	20.0
20-29	15.4	15.7	10.0
30-39	9.3	13.1	20.0
40-49	2.4	5.9	.0
50 +	.7	1.8	.0
Totals	100%	100%	100%

TABLE 15

Number of Smokers and Nonsmokers
by Exposure Category

Exposure Category	Smoker	Nonsmoker	Unknown
I	1553	474	4
II	1691	452	7
III	1425	338	9
Unknown	4	1	0
Totals	4673	1265	20
Average Exposure Category	2.0	1.9	2.3

Percentage Distribution of Smokers and Nonsmokers
by Exposure Category

Exposure Category	Smoker	Nonsmoker	Unknown
I	33.2	37.5	20.0
II	36.2	35.7	35.0
III	30.5	26.7	45.0
Unknown	0.1	0.1	.0
Totals	100%	100%	100%

Comparison of the Cohort Experience with that of the Province of Quebec, Dominion of Canada, and the United States

In order to make a comparison of the experience among asbestos miners with that of the general population of the Province of Quebec, statistics were gathered, as stated earlier, in the office of the Division of Demography in the Provincial Ministry of Health. The data on total deaths, deaths from all forms of cancer, and deaths from cancer of the lung were obtained by sex and by county for the years 1950 through 1955. In addition, all death certificates which specified primary cancer of the lung, and all those which indicated lung cancer but did not specify the origin, were examined for the years 1952 through 1955.

Table 16 gives a tabulation of the number of deaths from lung cancer in the Province and in the cohort for the years 1950 through 1955, and shows the annual rate per 100,000 in these segments. It will be noted from the table that the mortality rate for the "proved" cases in the cohort is only slightly higher than the rate for the Province. When the "suspected" cases are included in the calculation, the rate for the cohort rises to 33.8 per 100,000 which is about 50% higher than the rate for the Province. This, it will be recalled from the previous discussion of the effect of the "suspected" cases on the results, approaches but does not exceed the significant level.

TABLE 16

Comparison of Cohort with Province of Quebec

	Number of Persons	Lung Cancer Deaths							Annual Rate per 100,000
		1950	1951	1952	1953	1954	1955	Total	
Province	1,198,000*	196	220	245	303	303	357	1624	22.6
Cohort	5,923+								
Total		3	2	0	3	1	3	12	33.8
Proved		1	2	0	2	1	3	9	25.3
Province (excluding asbestos workers)	1,192,000	193	218	245	300	302	354	1612	22.5

In the Province figures, it has been assumed all male lung cancer deaths are for men of 20 + years.

* Approximate mid-point of the enumerated population for 1951, and the estimated population for 1954. (Rapport, Div. de la Demographie)

+ Number alive in cohort at beginning of 1952.

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