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March 19, 1958.

ARTHUR J. VORWALD, M.D.
DEPT. INDUS. MED. & HYGIENE
RECEIVED
MAR 21 1958
FBI - DETROIT

Dr. Arthur J. Vorwald,
Department of Industrial Medicine & Hygiene,
Wayne University,
1401 Rivard St.,
DETROIT 7, Michigan.

Dear Dr. Vorwald,

Knowing your deep and special interest on
this problem of asbestosis and cancer, I am taking the liberty
to lend you this confidential copy of this "Epidemiological
Study of Lung Cancer in Asbestos Mines".

When you have time to read it, I would
appreciate to have your comments and remarks written in the margins
of this report.

Yours very truly,

PG/JS

(Signature)
Paul Cartier, M.D.

GOVERNMENT
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"CONFIDENTIAL"

AN EPIDEMIOLOGICAL STUDY OF
LUNG CANCER IN ASBESTOS MINERS*

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and

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Ever since the pronounced increase in the incidence of lung cancer among males in some regions, there have been attempts to associate it with one or another of the various elements in the environment of man. The hypothesis used by some workers has been to suspect dust or asbestos dusts and then set about in an intensive search for lung cancer among persons who have had any exposure to these materials. In this connection, Smith (1951) writes: "The tendency of authors reporting the accidental 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

* This study was made possible through a grant from the United Asbestos Mining Association.

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⁽⁵²⁾ in 1935. Within the next ten years, about 15 additional cases were reported, and in 1944 Marbut⁽⁷⁵⁾ 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 Neuper⁽⁵⁴⁾ 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 "asbestos cancer" of the lung. Werber⁽⁶⁹⁾ 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. Neuper⁽⁵⁰⁾ in 1939 reported that he had discovered no cases of lung cancer among 620 cases of asbestosis which he had examined; and in 1942, Hollish and Angrier⁽⁴⁶⁾ expressed the opinion that the number

of cases of asbestosis with lung cancer was too small for statistical evaluation. In 1947, Wegelius⁽³³⁾ 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 Marmorek's latest book,⁽³⁴⁾ 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 transformation 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 in 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 generalized beyond the scope of the works which they quote. Moreover, for example, have we found references 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 44 cases enumerated by Harper ⁽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 52 of the 59 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 cases 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⁽²⁸⁾ in 1955. This study reviews causes of death among asbestos workers based on Corcoran's 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 111 representing only 1,362.25 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 is (lung cancer) may be a hazard (in asbestos workers) has been produced by Macgregor and by Gloyne."

In 1951 Gloyne⁽⁴¹⁾ presented a review of 1203 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 asbestotic cases. There were in his series 176 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 asbestosis 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.

Marwether (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 53 cases (15%) 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 report of this 15% is enhanced by the simultaneous report 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⁽⁵⁰⁾ who with Smith⁽⁴³⁾ had reported the first case in 1935, reported four cases of carcinoma of the lung in a series of 19 autopsies on victims of asbestosis, asbestiforming 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 21%, 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 Kiets⁽⁵¹⁾ found only the same number of cases of lung cancer in a series nearly 10 times as large, i.e., four in 40 cases of asbestosis.

Behrens, as cited in Meszoweth⁽⁵²⁾, estimated that, of 300 cases of asbestosis in the literature, 44 showed associated cancer of the lung—giving an incidence of 14.7%. 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, is possibly numerous of asbestosis whose cases were never reported. The same applies to the conclusion of Telsky⁽⁸³⁾ who appears to have reviewed reports of 14 asbestosis or persons with asbestosis among which six cases of lung cancer occurred. Information from sources such as this does not justify generalizations with regard to mortality rates.

Perhaps no one has written so extensively on the subject as has Hooper⁽⁵²⁻⁵⁴⁾. In 1962 he reviewed the cases⁽⁵⁵⁾ reported prior to that date and estimated a total of 50. Eleven of these were those diagnosed by Doll⁽²³⁾ and 11, 12 other cases reported by other authors. Eight were discovered by Greenaway and colleagues⁽⁴²⁾ in an analysis of 8,000 coefficients and, unless Macerwencher's study was incomplete, these cases should have been included in his report. Of the remaining 30, it is quite possible that the 11 contributed by Macerwencher and the 17 by Glover contain some duplication with each other or with those of other English authors.

Principles of the Epidemiological Method

Loren⁽¹⁰⁾ 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

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 cancers 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 Page (30). 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 generalizations 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 work, 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 Thorford 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 worker who had a total exposure of five or more years, and who was on the employment rolls in 1950. 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 certificate. 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 1950 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 causes, 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 the 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

analysed. 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 countries has been made with that in countries 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	111
Final Cohort	5980
Living in 1955 (working and retired)	5571
Dead by 1955	157
Cancer of lung	9
Questionable cancer of lung	3
Other causes	164
Unknown causes	1
Smokers	4075
Non-smokers	1905
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 5. All workers 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 category III three times as dusty as category I.

The fourth variable, smoking habits, was similarly tabulated and is shown in Table 6. This was tabulated because the information was available and because smoking was regarded as one of the variables which, besides the environment, could significantly 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 purposes of this study.

TABLE 1
Number and Percentage Distribution by Age

<u>Age</u>	<u>Number</u>	<u>Per Cent</u>
20-44	3901	66
45-54	1124	19
55-64	615	10
65 +	317	5
Unknown	3	*
Totals	5958	100%
Average Age	41	
* Less than .5%		

TABLE 2
Number and Percentage Distribution by Length of Employment

<u>Length of Employment</u>	<u>Number</u>	<u>Per Cent</u>
5-9	1795	30
10-19	2398	40
20-29	922	16
30-39	603	10
40-49	185	3
50 +	55	1
Totals	5758	100%
Average Years of Employment	18	

TABLE 3
Number and Percentage Distribution by Exposure Category

<u>Exposure Category</u>	<u>Number</u>	<u>Per Cent</u>
I	2437	34
II	2150	34
III	1772	30
Unknown	5	*
Totals	5958	100%
Average Exposure	2.0	
* Less than .5%		

TABLE 4
Number and Percentage Distribution by Smoking Habits

<u>Smoking Habits</u>	<u>Number</u>	<u>Per Cent</u>
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				Man- Years of Risk
		Proved Primary Ca. of Lung	Suspected Primary Ca. of Lung	Other Causes	Unknown	
1950	3476	1	2	12	1	5750
1951	3462	2	1	15	1	5732
1952	3422	3	0	31	2	5693.5
1953	3385	2	1	34	3	5666.5
1954	3348	1	0	33	4	5627
1955	3310	2	0	36	2	5590.5
Totals		9	3	157	6	35271.5

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

Total rate per 100,000 man-years of risk = $\frac{18}{35271.5} \times 100,000 = 50.9$

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 tabulated form below. Also shown are three deaths which have been considered as "suspected" lung cancer cases.

"Proved" Cases of Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Autopsy	Asbestos
1. A. J.	66	Yes	26 yrs. in Cat. II	10-12-51	Yes	Yes
2. M. P.	65	Yes	34 yrs. in Cat. I	5-3-55	Yes	No
3. R. M.	65	Yes	37 yrs. in Cat. I	7-29-55	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	6-8-54	Yes	No
9. A. R.	68	Yes	28 yrs. in Cat. III	6-55	Emphysema	No

"Suspected" Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Autopsy	Asbestos
1. J. T.	49	Yes	32 yrs. in Cat. III	10-23-50	No	No
2. E. D.	44	Yes	33 yrs. in Cat. III	7-55	Yes	Yes
3. P. P.	65	Yes	42 yrs. in Cat. II	9-30-55	No	No

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 5% level of significance. However, having found just 12 cases, we are not above this level, and are not justified in rejecting the hypothesis that asbestos miners do not have a higher mortality from lung cancer than does 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 nephritis 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 6 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	1329	1	3
55-64	513	3	3
65+	315	4	3
Unknown	3	0	0
Totals	5763	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	12	44
55-64	21	31
65+	212	255
Unknown	0	0
Totals	25	34

The rates by length of employment are shown in Table 7. 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 149 men during the six years, 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 lung exposure, and if asbestos is a carcinogenic agent, it must be concluded that these 240 men have demonstrated considerable resistance. This a biological phenomenon which has been observed previously and is consistent with the theory of an intrinsic or endogenous factor in cancer. The only other explanation would be that the susceptible members of this age group had died earlier of lung cancer. Table 16 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 7
Number of Persons and Number of Lung
Cancer Deaths by Length of Employment

Length of Employment	Persons	Lung Cancer Deaths	
		Proved	Total
0-9	1795	0	0
10-19	2578	1	1
20-29	922	3	3
30-39	673	2	2
40-49	155	0	1
50+	55	0	0
Total	5978	3	12

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

Length of Employment	Proved	Total
0-9	0	0
10-19	7	7
20-29	34	34
30-39	156	173
40-49	0	70
50+	0	0
Over-all	25	34

The rates by weighted exposure are shown in Table 2, 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 3, 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 3
Number of Persons and Number of Lung
Cancer Deaths by Exposure Category

Exposure Category	Persons	Lung Cancer Deaths	
		Proved	Total
I	4031	4	4
II	2153	1	4
III	1772	1	4
Unknown	5	0	0
Totals	4959	6	12

(Table 3 continued on next page.)

TABLE 8 (continued)

Annual Lung Cancer Death Rates per 100,000
Men-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 9

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

Length of Employment	Weighted Exposure Categories			Unknown	Total
	I	II	III		
5-9	707	590	490	0	1795
10-19	663	583	851	1	2398
20-29	314	363	243	2	922
30-39	267	210	137	1	603
40-49	76	67	41	1	165
50+	26	21	10	0	57
Totals	2053	2150	1772	5	5935
Average years of exposure	17.6	17.6	10.6	29.0	17.5

Table 10, 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 10 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, 11, 12, and 13 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 11) the combined average age of the smokers was 4.4 years less than that of the nonsmokers. Table 12 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 13 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 10.

TABLE 10

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

	<u>Persons</u>	<u>Lung Cancer Deaths</u>	
		<u>Persons</u>	<u>Total</u>
Smokers	4573	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

	<u>Persons</u>	<u>Total</u>
Smokers	32	43
Nonsmokers	0	0
Unknown	0	0
Over-all	25	14

TABLE 11

Number of Smokers and Nonsmokers by Age Groups

Age Group	Smoker	Nonsmoker	Unknown
20-44	3200	699	12
45-54	896	234	4
55-64	411	282	2
65 +	164	158	1
Unknown	2	0	1
Total	4673	1273	20
Average Age	39.3	44.2	60.7

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	0	5.0
Total	100%	100%	100%

* Less than .04%

TABLE 12

Number of Smokers and Nonsmokers
by Length of Employment

<u>Length of Employment</u>	<u>Smoker</u>	<u>Nonsmoker</u>	<u>Unknown</u>
5-9	1483	377	10
10-19	1967	424	4
20-29	722	199	2
30-39	433	164	4
40-49	110	73	0
50 +	33	22	0
Total	4673	1265	20
Average Length of Employment	17.8	19.3	16.0

Percentage Distribution of Smokers and Nonsmokers
by Length of Employment

<u>Length of Employment</u>	<u>Smoker</u>	<u>Nonsmoker</u>	<u>Unknown</u>
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 13

Number of Smokers and Nonsmokers
by Exposure Category

<u>Exposure Category</u>	<u>Smoker</u>	<u>Nonsmoker</u>	<u>Unknown</u>
I	1553	474	4
II	1691	452	7
III	1425	318	9
Unknown	4	1	9
Totals	4673	1245	29
Average Exposure Category	2.0	1.9	2.3

Percentage Distribution of Smokers and Nonsmokers
by Exposure Category

<u>Exposure Category</u>	<u>Smoker</u>	<u>Nonsmoker</u>	<u>Unknown</u>
I	33.2	37.5	20.0
II	36.2	35.7	35.0
III	30.5	24.7	45.0
Unknown	0.1	0.1	0.0
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 1942 through 1955.

Table 14 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 14
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	1,112,000	196	203	248	303	303	337	1626	22.6
Cohort	9,123 +								
Total		3	4	0	3	1	3	12	33.6
Proved		1	2	0	2	1	3	9	25.3
Province (excluding asbestos workers)	1,192,000	193	218	245	300	302	316	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.
(Report, Div. de la Démographie)

* Number alive in cohort at beginning of 1952.

One further interesting observation from Table 14 is the rather marked increase in the total number of cases for the Province between 1950 and 1955. It is assumed that at least part of this increase is due to improved recognition and reporting of lung cancer during the interval. For this reason, the years 1954 and 1955 were thought to be more nearly representative of actual conditions. Even so, it is quite likely that the general population is not studied for lung cancer with the same diligence with which this disease is looked for in the miners, and it seems probable that the mortality rates for the Province may be low. This would appear to be substantiated by the fact that the reporting of cases in the cohort showed no such increase over the same period.

Table 15 was compiled to show the annual age-specific lung cancer rate of cases in which the death certificate merely read "cancer of the lung", as distinguished from those in which the diagnosis was confirmed by autopsy, surgery, or biopsy. The term "specified primary" refers to those cases in these two categories in which the tumor was specified as having originated in the lung. It will be noted that, of the total cases reported in 1955, a much higher percentage than in 1954 were specified as primary. The table also shows that a higher percentage of the total cases certified in 1955 were proved, again indicating increasing interest in this disease.

A comparison has been made between the age-specific rates shown in Table 13, and those for the cohort, shown in Table 4. An average of the 1954 and 1955 rates for the Province has been used, since the 1955 figure was higher and may have been exceptional.

This comparison, summarized in Table 14, shows that the observed number of deaths in our sample is not significantly greater than the expected number of deaths, based on the average of the 1954 and 1955 figures for the Province. It is true that, in the case of the age group of 65 and over, the Ray-Charles provides a figure which is almost significant at the 95% level. However, it should be noted that this number includes one of the unexpected but improved cases previously referred to. Furthermore, it is rather likely that the rate for the general population is understated in this age group, for the obvious reason that the exact cause of death in the very old is not a matter of the same intensity of interest as it is in younger persons.

TABLE 14

Comparison of the Actual and Expected Number of Lung Cancer Deaths by Age Among Asbestos Miners

Age Group	Province		No. of Miners	Expected* No. of Deaths	Observed No. of Deaths	
	Total Specified Primary	Rate per 100,000			Proven	Total
20-44	1.3		3901	8 ¹	1	1
45-54	64.5		1124	2	1	1
55-64	67.6		615	2	1	1
65+	80.5		415	1	4	3
Unknown	--		3	-	0	0

* Actually .4

* The expected number is based on the average of the 1954 and 1955 age-specific rates for the Province of Quebec.

Table 16 also answers a question previously raised. It shows that the members of the cohort have not died from lung cancer at an age earlier than the general population, and that such an explanation cannot be offered for the absence of lung cancer in 240 men with more than 49 years of employment referred to on page 24.

Before leaving this comparison of the Forvies with the miners, it should be shown that their age distributions are reasonably the same. That this is the case can be observed from the following tabulations:

Age Distribution of Adult Males for the Province of Quebec, 1951
(Rapport, 1954)

Age Group	Province		Percentage in Cohort
	Number	Percentage	
25-44	727,135	53	46
45-54	198,962	16	19
55-64	128,964	11	10
65 +	113,467	10	5
Total	1,156,498	100	100

It should be remembered that the miners retire and consequently, it can be expected that the oldest age group will be larger in the general population. The data presented in Table 17 indicates that the lung cancer rate generally decreases after age 70. Therefore, we could expect the rate for all people over 65 to be smaller than the rate for the group between 65 and 75, which would apply to the oldest group of miners. It is felt that by using the whole adult male population, we have developed rates for the general popu-

rates which are somewhat lower than if we had been able to include the people in the general population over 75.

A comparison between the asbestos miners and the population of the Dominion as a whole was made, using the statistical material from several sources and one source, Phillips (18) gave age - sex - specific rates for Canada for three periods between 1921 and 1928. Rates for males are given in Table III.

TABLE IV

<u>Age Group</u>	<u>Range of Years</u>		
	<u>1921-1922</u>	<u>1923-1924</u>	<u>1925-1926</u>
Under 25	0.2	0.2	1.0
25-34	0.3	0.3	0.3
35-44	0.3	2.2	2.0
45-54	0.3	0.4	0.3
55-64	1.5	11.3	12.7
65-74	0.3	11.3	17.1
75-84	1.7	17.0	22.7
85-94	11.1	22.7	71.3
95-100	11.1	22.3	101.0
75-100	12.7	22.3	61.3
75-100	11.3	22.3	61.3
65-100	2.3	17.0	22.7
55-100	1.4	11.3	17.1
All ages	2.0	7.1	11.3

17 Mortality from lung cancer in Canada "1921 to 1928"

These figures show strikingly the increase in rates between 1951 and 1952, and this increase is particularly marked after age 50, confirming an observation previously made, to the effect that until recently lung cancer has probably been under-diagnosed in the older age groups in the general population.

To use these figures for purposes of comparison, it is necessary to combine the rates for certain age groups in order to conform to the age distributions used in this study. Since the exact populations in each age group for the years indicated is not known, this must be an approximation. However, the rates would be something as follows:

<u>Age Group</u>	<u>Rate</u>
20-44	5
45-54	27½
55-64	69
65 +	90-95

These rates are, in general, lower than those developed for the total (proved and suspected) cases of lung cancer among the asbestos miners. The only large difference, however, is in the age group of 65 years and over, and it is quite possible that the rate for this group may have increased for Canada between 1952 and 1954 as it did for the Province of Quebec. (See Table 15.)

A further comparison has been made with an over-all rate obtained from the American Cancer Society for respiratory cancer deaths in Canada in 1953. This rate, for males, is 20.3 per 100,000, five more per 100,000 than Phillips' 1950-1952 rate, and compares with 25.3 per 100,000 for grouped cases and 22.8 per 100,000 for total cases among the asbestos miners in this study. It is therefore obvious that there are no important differences between the rates for asbestos miners and those for the general population of Québec and the Dominion of Canada.

Since it is probable that figures for the United States are more complete and, therefore, possibly more comparable to the data for the miners, age-specific rates were computed from "Vital Statistics of the United States", Volumes I and II, for 1952. These rates have been tabulated in Table 13.

TABLE 13

Number of Deaths and Death Rates per 100,000
by Age Groups for the Adult Male Population of
the United States—Data From
"Vital Statistics of the United States", Volumes I and II, 1952

Age Group	Population	Cases	Rate per 100,000
25-40	24,544,000	533	3.6
45-54	8,042,000	2979	34.9
55-64	6,349,000	5254	98.6
65 +	5,670,000	6487	114.3
Total	44,615,000	16,599	37.2

It is apparent that these rates compare favorably with those for the asbestos miners as shown in Table 6. Still other rates for the United States were obtained from the American Cancer Society, and for males, these were 25.3 per 100,000 in 1959, and 25.0 per 100,000 in 1955. They are not identical with the rate calculated from the figures of the office of Vital Statistics, but this is possibly because the American Cancer Society rates are for males of all ages. Nevertheless, they, too, compare favorably with the rates of 25 (or 36 for total cancer) obtaining among the asbestos miners.

Turning for a moment to a comparison between the asbestos miners and persons who are exposed to asbestos in one form or another (as distinguished from the general population groups just discussed, who have no exposure) an interesting observation can be developed by deduction. Shaper (52) has stated that there are about 35,000 persons exposed in the United States, and we have found that the Canadian mines employ about 8,000. Elsewhere, it has been estimated that the workers in England who have exposure total between 3,000 and 5,000. With workers in Africa, Denmark, Norway, and other countries, at least 50,000 persons must be exposed throughout the world, and it can be assumed that this number has been fairly constant in the 20 years since 1935 when the first case of asbestosis with lung cancer was reported. At least a million man-years of exposure has thus been accumulated, and this figure can be divided by the approximately 150 cases of lung cancer with asbestosis reported during the 20-year period. This gives a rate of 15 per 100,000 which is at least indicative that any lung cancer rate which can be

calculated for workers exposed to asbestos dust is not much greater than
that for the unexposed population.

Comparison Between Eight Counties
Adjacent to the Asbestos-Producing Areas
and Eight Selected Counties

To compare lung cancer mortality rates in the counties surround-
ing the asbestos-producing areas with another group of counties in which
no asbestos mines are likely to reside, the rates were computed on the
basis of figures for the years 1950 through 1955. The eight counties selected
for comparison were Argenteuil, Chateauguy, Montmagny, Perth,
Richillon, Riviere-du-Loup, St. Hyacinthe, and Terrebonne, mainly because
they represent a wide geographic distribution throughout the Province. The
counties selected because of their proximity to the asbestos mines include
Arthabaska, Beauce, Drummond, Frontenac, Megantic, Richmond, Sherbrooke,
and Wolfe. Table 19 shows the number of lung cancer deaths for the years
1950 through 1955 for each of these counties, and a mortality rate, based on
the adult male population in 1952. To emphasize the comparison, Megantic
County has been shown separately, as has the Province of Quebec and also the
Province with the eight 'asbestos-producing' counties subtracted. Because
of its unique lung cancer death rate, Montreal et Ile de Jesus has also been
listed in order to provide further comparison.

Consolidated	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2423	2424	2425	2426	2427	2428	2429	2430	2431	2432	2433	2434	2435	2436	2437	2438	2439	2440	2441	2442	2443	2444	2445	2446	2447	2448	2449	2450	2451	2452	2453	2454	2455	2456	2457	2458	2459	2460	2461	2462	2463	2464	2465	2466	2467	2468	2469	2470	2471	2472	2473	2474	2475	2476	2477	2478	2479	2480	2481	2482	2483	2484	2485	2486	2487	2488	2489	2490	2491	2492	2493	2494	2495	2496	2497	2498	2499	2500	2501	2502	2503	2504	2505	2506	2507	2508	2509	2510	2511	2512	2513	2514	2515	2516	2517	2518	2519	2520	2521	2522	2523	2524	2525	2526	2527	2528	2529	2530	2531	2532	2533	2534	2535	2536	2537	2538	2539	2540	2541	2542	2543	2544	2545	2546	2547	2548	2549	2550	2551	2552	2553	2554	2555	2556	2557	2558	2559	2560	2561	2562	2563	2564	2565	2566	2567	2568	2569	2570	2571	2572	2573	2574	2575	2576	2577	2578	2579	2580	2581	2582	2583	2584	2585	2586	2587	2588	2589	2590	2591	2592	2593	2594	2595	2596	2597	2598	2599	2600	2601	2602	2603	2604	2605	2606	2607	2608	2609	2610	2611	2612	2613	2614	2615	2616	2617	2618	2619	2620	2621	2622	2623	2624	2625	2626	2627	2628	2629	2630	2631	2632	2633	2634	2635	2636	2637	2638	2639	2640	2641	2642	2643	2644	2645	2646	2647	2648	2649	2650	2651	2652	2653	2654	2655	2656	2657	2658	2659	2660	2661	2662	2663	2664	2665	2666	2667	2668	2669	2670	2671	2672	2673	2674	2675	2676	2677	2678	2679	2680	2681	2682	2683	2684	2685	2686	2687	2688	2689	2690	2691	2692	2693	2694	2695	2696	2697	2698	2699	2700	2701	2702	2703	2704	2705	2706	2707	2708	2709	2710	2711	2712	2713	2714	2715	2716	2717	2718	2719	2720	2721	2722	2723	2724	2725	2726	2727	2728	2729	2730	2731	2732	2733	2734	2735	2736	2737	2738	2739	2740	2741	2742	2743	2744	2745	2746	2747	2748	2749	2750	2751	2752	2753	2754	2755	2756	2757	2758	2759	2760	2761	2762	2763	2764	2765	2766	2767	2768	2769	2770	2771	2772	2773	2774	2775	2776	2777	2778	2779	2780	2781	2782	2783	2784	2785	2786	2787	2788	2789	2790	2791	2792	2793	2794	2795	2796	2797	2798	2799	2800	2801	2802	2803	2804	2805	2806	2807	2808	2809	2810	2811	2812	2813	2814	2815	2816	2817	2818	2819	2820	2821	2822	2823	2824	2825	2826	2827	2828	2829	2830	2831	2832	2833	2834	2835	2836	2837	2838	2839	2840	2841	2842	2843	2844	2845	2846	2847	2848	2849	2850	2851	2852	2853	2854	2855	2856	2857	2858	2859	2860	2861	2862	2863	2864	2865	2866	2867	2868	2869	2870	2871	2872	2873	2874	2875	2876	2877	2878	2879	2880	2881	2882	2883	2884	2885	2886	2887	2888	2889	2890	2891	2892	2893	2894	2895	2896	2897	2898	2899	2900	2901	2902	2903	2904	2905	2906	2907	2908	2909	2910	2911	2912	2913	2914	2915	2916	2917	2918	2919	2920	2921	2922	2923	2924	2925	2926	2927	2928	2929	2930	2931	2932	2933	2934	2935	2936	2937	2938	2939	2940	2941	2942	2943	2944	2945	2946	29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It is apparent from the table that the lung cancer death rate for the eight counties immediately surrounding the asbestos-producing areas is practically identical with that of eight counties selected for comparison. While Magentic County has a rate exactly twice that of the combined eight selected counties, it is lower than the rate for the Province, and considerably lower than the rate for Minnesota. The figure for Minnesota would certainly be higher except for the very low numbers of deaths reported for 1930 and 1931, and it would appear that in these years some error in reporting has undoubtedly been made. On the basis of the other years, 1930 and 1931 deaths would be expected to be about 500 greater. This would result in a rate of 29 per 100,000.

The only possible conclusion from this comparison is that there is no evidence that the persons who live and work in the counties surrounding and adjacent to the asbestos-producing areas have any greater incidence of lung cancer than those who live elsewhere in the Province.

Discussion of All Recorded Lung Cancer Cases, Living and Dead, Surrounding the Asbestos Mines

Although a simple enumeration of all the known or suspected cases of cancer of the lung in these areas has no particular value from a scientific point of view, it is of interest to summarize such cases for the record. There were nine deaths prior to the beginning of the time period covered by the study, including one in which the diagnosis was mediastinal lymphosarcoma.

During the period covered by this investigation, there were nine proved cases and three suspected cases in the cohort. Through 1956 and to date in 1957, there were eight deaths, six of which were merely suggestive of cancer of the lung and included such diagnoses as mediastinal lymphosarcoma, mesothelioma, cancer of the leg with metastases to lung, abscess of lung, and cancer of the pancreas. One other was diagnosed on the basis of x-ray only. In addition, there are now living four cases in which the diagnostic evidence is strongly suggestive of lung cancer. This is a total of 13 cases of all types, including ten "suspected" but unproved cases, and four that are still living. The remaining 19 constitute the total of proved cases of cancer of the lung among the asbestos miners since 1940.

The proved cases averaged 59 years of age at death, and varied between 37 years and 66 years. Their working span covered periods varying from a minimum of 14 years to a maximum of 37 years. Only three men had less than 15 years of employment in the industry. Seven among those on whom such information is available had a weighted exposure placing them in category III, and six worked in an exposure represented by category I.

There were only 17 among these proved lung cancer cases in which we have information regarding the presence of asbestosis. Asbestosis was present in nine, although it was minimal in two. Two pathologists disagreed regarding its presence in another. At least seven of the 19 proved lung cancers, therefore, were not accompanied by asbestosis.

Summary and Conclusions

Interest in the question of whether there may be an association between lung cancer and exposure to asbestos has been evident since the report in 1935 by Lynch and Smith of a case in which lung cancer and asbestosis were both present. An additional case in which the two diseases co-existed were reported, a causal association appears to have been generally accepted by many authors, although some workers considered the correlation to be inconclusive. The present study was undertaken in an effort to determine whether a causal relationship did, in fact, exist between exposure to asbestos and cancer of the lung.

Since most earlier studies had been limited to examining the lung tumors found to occur in selected samples, such as cases coming to autopsy or death certificates in which asbestosis was mentioned, it was apparent that they could not fulfill the requirements of an epidemiological and statistical approach to the problem. The present study was, therefore, designed to meet the requirements of this method.

After a preliminary survey to explore the availability of reliable information, data were gathered on workers in the asbestos mines in Quebec, based on their medical records. A cohort was defined according to certain criteria and all workers who met these criteria were included in the study. Data relative to their characteristics were collected and their status at the end of a six-year-period of observation was determined. In the case of those who had died, an exhaustive search of death certificates and insurance records

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was carried out in order to determine as nearly as possible the exact cause of death. Mortality rates from lung cancer for the general population of the Province of Quebec and the various counties and for the Dominion of Canada, as well as the United States were calculated from statistics collected in the appropriate places. Comparisons of the rates obtained for asbestos workers and for the other population groups were made according to accepted statistical methods which have been explained in some detail.

Records were obtained on 4891 persons who fulfilled the criteria of the cohort. It was not possible to trace 133 of these for the whole period, but 5771 of the remaining 5025 were found to be still living in 1955 or later. Of the 147 known dead, cancer of the lung was considered as have been necessarily proved in nine and as be strongly suggested in three.

The members of the cohort were studied with respect to age, length of employment, a weighted average of their exposure, and their smoking habits. Four thousand, six hundred and seventy-three were found to be smokers within the definition of that term as used in this study. Thirty-four per cent of the cohort were more than 45 years of age, and 14% had been employed for longer than 25 years. Thirty per cent had a weighted exposure which placed them in category of highest exposure.

The mortality rate for lung cancer, as computed on the basis of nine "proved" deaths among the cohort was 12.3 per 100,000. When the three "suspected" cases were added, the "total" rate for the cohort rose to 12.8.

The importance of the suspected but unproved cases in determining those cases has been reiterated because it is likely that such cases would not be included in the statistics for the general population and because they influence the results so markedly.

According to the findings in this study, the mortality rate from lung cancer does not appear to increase with length of exposure or with degree of exposure, a fact which presents strong evidence against the carcinogenicity of asbestos.

Comparison of the experience among the asbestos miners with that of various segments of the unexposed, comparable population shows that the observed number of deaths among the miners is not significantly greater than the expected number. The rate for proved cases among the asbestos miners (25.3 per 100,000) compares well with the rate of 22.5 per 100,000 for the rest of the Province, and 22.5 per 100,000 for adult males throughout the Dominion of Canada. It also compares satisfactorily with rates of 17.2, 25.3, and 28.6 obtained from various sources for adult males in the United States. Finally, in this matter of comparison, it would appear that the world-wide experience of persons exposed to asbestos dust is not worse with respect to lung cancer than that of the unexposed population.

The counties surrounding the asbestos-producing areas, and in which it is presumed most of the asbestos miners live, have almost identical mortality rates with those of eight counties widely scattered through the Province, and are lower than those for the remainder of the Province, and much lower than the rate for Montreal.

Since 1960, there have been 15 cases in which the diagnosis of primary cancer of the lung may be considered to have been proved. Approximately half of these cases were associated with asbestosis. All but one died in the recognized 'cancer-age' and at least one-third had only the lightest exposure (category 1) to asbestos dust.

*On the basis of what are believed to be complete and reliable data, it seems fair to conclude that the asbestos miners in the Province of Quebec do not have a significantly higher death rate from lung cancer than do comparable segments of the general population.

Furthermore, the death rate from lung cancer in the areas contiguous to the asbestos operations is comparable to that in areas widely scattered throughout the Province of Quebec and is lower than in some urbanized areas within the Province.

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