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INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC

4400 FIFTH AVENUE

PITTSBURGH 13, PA



AN EPIDEMIOLOGICAL STUDY OF LUNG CANCER IN ASBESTOS MINERS

Report to

QUEBEC ASBESTOS MINING ASSOCIATION

Quebec, Canada

September, 1957

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Industrial Hygiene Foundation of America, Inc.
4400 Fifth Avenue
Pittsburgh 13, Pa.

AN EPIDEMIOLOGICAL STUDY OF LUNG CANCER IN ASBESTOS MINERS

For

QUEBEC ASBESTOS MINING ASSOCIATION

Quebec, Canada

July, 1956 to July, 1957

By

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September, 1957

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FOREWORD

The success of a study of the type herein reported depends very greatly upon the availability of data from many sources, and the assistance and cooperation of those in possession of these data. Industrial Hygiene Foundation was fortunate in having the wholehearted cooperation of the asbestos-producing companies, and particularly of their medical and nursing personnel who have the responsibility for maintaining the medical records of the workers. In this connection, we are especially indebted to Dr. Paul Cartier and his staff at the Thetford Industrial Clinic, and to Dr. T. R. Grainger and the nurses at Asbestos. All records in these two medical centers were put completely at our disposal, and the care and completeness with which they are maintained assisted considerably in the preparation of the material relative to the worker population.

Data on population figures and on the causes of death in the Province of Quebec were obtained with the utmost assistance and cooperation from Dr. Paul Parrot, Head of the Department of Demography in the Ministry of Health. Not only were all vital statistics and reports made readily available to us, but Dr. Parrot and his entire staff rendered valuable assistance in many ways, including the location and interpretation of death certificates. Especially helpful in this part of the work was Miss Gauthier of Dr. Parrot's staff. The same helpful

cooperation was rendered by Messrs. Hardy and Hopkins of the Sun Life Assurance Company of Canada in Montreal, who made available their records of the death claims paid under the group policy covering the workers at Asbestos.

Valuable suggestions for the conduct of the study were made by Dr. J. A. Vidal, Chairman of the Silicosis Board, and Dr. Guy, Pathologist for the Board, as well as Dr. Gregoire, Deputy Minister of Health for the Province of Quebec, and Drs. Simard, Dufresne, and Groulx, in Montreal.

Statistics for the mortality rates for the Dominion of Canada were obtained through the kindness of Dr. Dean F. Davies, Administrator for Research on Lung Cancer for the American Cancer Society, and those for the United States were graciously furnished by Miss Guralnick in the National Office of Vital Statistics, Department of Health, Education, and Welfare of the United States Government. Finally, the very great assistance rendered by Dr. Kenneth W. Smith, Medical Director of Johns-Manville Corporation, and Mr. Ivan Sabourin, General Counsel for the Association, in making the necessary contacts, in travel arrangements, and in so many other ways, is gratefully acknowledged.

The methodology of this research is believed to be unique among the reported studies of lung cancer as related to asbestosis and exposure to asbestos. Assistance in planning the study in such a way as

to assure a proper epidemiological approach, and all biostatistical applications of the findings were provided by Mr. T. David Truan, formerly of the Graduate School of Public Health, University of Pittsburgh, and the staff of the Industrial Hygiene Foundation.

The report is believed to present the findings in an objective manner and is respectfully submitted for the consideration of the Association.

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GLOSSARY

For the purpose of clarity and uniformity, the terms used in this report are herewith defined according to the manner of their use.

Asbestos workers: Workers exposed to asbestos dust in other than mining operations.

Asbestos miners: Workers engaged in the mining and preparation of asbestos in the areas under study.

Asbestosis: A generalized fibrosis of the lungs diagnosable by x-ray, or by microscopic examination of the lung tissue, but not necessarily accompanied by symptoms or by disability.

Cohort: A segment of the population, defined according to certain criteria, and representative of the whole population. Specifically in this study, a group of asbestos miners having at least five years of exposure in the industry and who were in the industry during 1950.

Lung cancer, cancer of the lung: A neoplasm of the lung or bronchus, wherever situated, and including adenocarcinoma, squamous cell, and undifferentiated, round, or "oat cell" histological types. Primary cancer of the lung means such a neoplasm originating in the lung, and not secondarily in the lung as the result of a metastasis from another primary location in the body.

Smoker: 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.

I. INTRODUCTION

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 compounds. In this connection, Smith [182] 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 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 [139] in 1935. Within the next ten years, about 15 additional cases were reported, and in 1946 Merewether [155] reviewed all deaths from asbestosis recorded in England since March, 1924. Lung cancer occurred, according

to Merewether, in 13.2% of these cases. Continuing this study to include December, 1954, Merewether counted 55 cases of cancer of the lung among 344 cases of asbestosis, raising the incidence to 16%. Gloyne,[92] whose work is also frequently referred to as establishing a connection between asbestosis and cancer of the lung, reported in 1951 the results of his findings on 1205 autopsied cases. This series included 132 asbestos workers, of whom 121 showed asbestosis. Cancer of the lung was present in 14.1% of these asbestosis cases. In 1941, Nordmann and Sorge[161] 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[122] 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[205] 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 the alleged association without reservation. Saupe[177] in 1939 had 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[104] expressed the opinion that the number of cases of asbestosis with lung cancer was too

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small for statistical evaluation. In 1947, Wegelius [200] 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, [95] 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.

Meanwhile, the Canadian Johns-Manville Company in Asbestos has been alert to the whole problem, and at the Thetford Industrial Clinic, Dr. Paul Cartier was studying the situation among a working population of about 6000, and made notable contributions to the literature just cited[42-44]. Between these two areas, a number of cases had been recognized and tabulated by the spring of 1956. At this time, at the suggestion of Dr. Kenneth W. Smith, Medical Director of the Johns-Manville Corporation, and Dr. Cartier, the Quebec Asbestos Mining Association approached Industrial Hygiene Foundation to determine whether it would be feasible to conduct an epidemiological study in order to discover whether the incidence of lung cancer was, in fact, greater among asbestos miners than among the general population, and whether there was a correlation between lung cancer and the disease asbestosis. The Foundation submitted, in March, 1956, a proposal for such a study based upon a preliminary survey of the type and accessibility of data which might be available. This proposal was accepted by the Association through its Secretary, Mr. W. H. Soutar, and its General Counsel, Mr. Ivan Sabourin, Esq.

II. CRITICAL REVIEW OF LITERATURE

A careful review of the published material on this subject 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 generalized beyond the scope of the works which they quote. Nowhere, 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. 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 (63), 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 [122] 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 in the previous section.

One of the most detailed studies and one which deserves the most serious consideration is that reported by Doll (63) 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.

It also seems that this review does not add any new cases to the literature, although Hueper in enumerating 99 cases reported prior to 1955, lists 11 discussed in it. Clearly, also, the paper is not dealing with asbestos miners.

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." An examination of these references leaves at least some question as to the strength of the evidence produced.

In 1951 Gloyne (92) 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. Presumably, all cases, including those of asbestosis, in which the findings were not considered unusual were never brought to Dr. Gloyne's attention. 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 those 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 [155] 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,[142] who with Smith[139] 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 of interest to note that Klotz[132] found only four instances of lung cancer in 478 cases of asbestosis, a series 11 times as large.

Behrens, as quoted in Merewether[156], 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 another case of generalizing an incidence obtained in a group of cases which were

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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 [192] who appears to have reviewed reports of 39 autopsies on persons with asbestosis among which six cases of lung cancer occurred. Information from those sources does not justify generalizations with regard to mortality rates.

Werber [205] who made the unequivocal statement that lung cancer would result in from 7% to 17% of cases of asbestosis, allowed himself considerable latitude by qualifying it, as regards time, to an interval of 1 1/2 to 20 years. Finally, mention should be made of some entirely unsupported statements which tend to build up a mistaken viewpoint through mere repetition. One example is a sentence in "Nontuberculous Diseases of the Chest" [76] where the authors say simply, "an excessive incidence of pulmonary cancer has occurred among workers in other occupations, such as asbestos industries, nickel-copper refineries, stokers in generator plants, etc." without substantiating reference.

As an illustration of the ease with which a few reports which merely suggest a certain conclusion can, through the lack of a sufficiently critical attitude, be summarized to produce the conclusion in a definite form, an editorial [69] in the Journal of the American Medical Association mentions the work of Wedler and the report of Merewether and then establishes the causal relation between asbestosis and cancer of the lung as settled. As a final convincing argument, it refers to "recent experimental

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observations (by) Nordmann and Sorge [161]". This is the experiment in which squamous carcinoma was said to have been produced in about a dozen white mice, and which has not been duplicated by any other investigator!

Perhaps no one has written so extensively or so dogmatically on the subject as has Hueper [109-124]. In 1955 he reviewed the cases [122] reported prior to that date and enumerated a total of 99. Eleven of these were those discussed by Doll [63] and appear to have been cases covered by other authors. Eight were discovered by Kennaway and Kennaway [131] 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 Gloyne contain some duplication with each other or with other English authors.

In the same paper, Hueper dismisses the idea of determining the frequency of pulmonary cancer among the total worker population of the asbestos industry on the grounds that it is immaterial how many workers in the industry develop lung cancer, since some of them have no exposure and therefore do not develop asbestosis!

III. PRINCIPLES OF THE EPIDEMIOLOGICAL METHOD

As has been indicated, 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. This has been 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.

Epidemiology is the method of investigating a specific disease in human populations in relation to certain variable characteristics, including the environment. In contrast to the clinical method which is primarily concerned with the characteristics of the disease in individuals, epidemiological research involves the investigation of the disease as a mass phenomenon. It seeks to discover what proportion of persons in a given set of circumstances will eventually develop the disease. Epidemiology cannot predict whether a given individual will fall victim to a specific disease, but it can predict the approximate number of cases of this disease which will develop in a population of specified size, composition, and subject to a given environment. It

proceeds by first carefully and accurately describing characteristics of the disease in different population groups and its essential objective is the formulation, testing, and verification of generalizations concerning the disease in question.

In order to apply this method of investigation to the problem under discussion, the Foundation was 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. Therefore, results of these studies cannot properly be generalized to include such people.

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 the Quebec Asbestos Mining Association is 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.

The frequency of cancer of the lung relative to the total of all types of cancer may be increased merely by reason of a decrease

in the incidence of cancer of other sites. This could be true even though the incidence of lung cancer remained constant, or if it decreased less rapidly than that of the other types.

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 because the relative frequency of cancer in other organs may be lower in the second group. 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 representative in any way of a larger group, and that in dealing with such samples, the observer may easily find more cases of any kind than would be found in a 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 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 in a later section, but the type of approach is considered to permit of fair comparisons and valid generalizations.

IV. 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. Similar information was obtained regarding all workers at the Canadian Johns-Manville Company in Asbestos. 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. Although the data in these two instances were not exactly similar in form, the inclusion of records from the personnel department at Asbestos covering employees who had retired, died or become disabled provided data sufficiently alike for the purpose of the study.

From this information it was possible to formulate for both Asbestos and Thetford Mines "cohorts" which could be well defined, should be representative of each 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 cohorts were defined as including every worker who had a total exposure of five or more years, and who was on the employment rolls at Asbestos or Thetford Mines in 1950. These cohorts were then followed by means of the annual physical examination records through a six-year interval, 1950 through 1955. All data regarding these groups were then tabulated in order to determine the characteristics of the cohorts. 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 cohorts 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 causes, total deaths from cancer of all types, 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 Canadian Johns-Manville 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 on the group at Asbestos, 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 workers 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 list of deaths was then verified individually by reviewing them with the physicians in charge at Canadian Johns-Manville Company and at Thetford Mines. 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 cohorts 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.

In order that the method by which these comparisons have been made may be more easily understood, it seems advisable to discuss briefly some of the fundamental statistical concepts which have been followed. The principle of calculating the probability of a given sample representing the true condition of a large group can be illustrated by imagining a container in which there are 1000 marbles of which 900 are white and 100 black. The actual probability of drawing a black marble is one in ten, or .1. However, should a sample of ten marbles be drawn

from the container, it would not be unlikely that two, three, or even no black marbles would be among them, even though the "expected" number would be one. On the other hand, if all ten were to be black, that sample would unquestionably be "extraordinary". The following tabulation shows a calculation of the probability that a given number of black marbles will be found in a sample of ten:

No. of Black Marbles in Sample	Probability
0	.3486784401
1	.3874204890
2	.1937102445
3	.0573956280
4	.0111602610
5	.0014880348
6	.0001377810
7	.0000087480
8	.0000003645
9	.0000000090
10	.0000000001
Total	1.0000000000

From these probabilities, it is evident that one might expect a sample of ten to include no black marbles or one, two, or three, but for the sample to consist entirely of black marbles would be expected only once in ten billion trials. Finding three black marbles in the sample would be expected in almost six samples out of 100, and it would be anticipated that the sample would contain four or more black

marbles in slightly more than one trial out of 100. The actual probability of this happening is .012795184, which is determined by adding the probabilities for 4 through 10. In practical applications of sampling, the percentage of "black marbles" is, of course, unknown and must be computed from the results found in the sample. There are limitations to the accuracy of such a computed value, but it is possible to state with a known probability that the true value lies within a certain range. If the range is wide enough, the probability may be practically 100%. The usual practice is to require 95% certainty.

In the present study, since the probability of having lung cancer is so small and since the sample size was fairly large, the Poisson distribution was used instead of the binomial distribution, which has just been described. This is a substitution frequently made under these conditions, because the Poisson distribution is tabulated and the differences between it and the binomial distribution are quite small. It is based on the equation:

$$\frac{e^{-np}(np)^x}{x!}$$

Where e = 2.71828 (the base of natural logarithms)
n = number of man years subject to risk
p = incidence rate
x = number of cases observed

The logic of the statistical approach may also justify a few words of clarification. Generally, in problems of this kind, one sets up a hypothesis, which in our case would be, "Asbestos miners do not

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have a higher rate of mortality from lung cancer than the general population." The hypothesis is then tested by means of the study of data on asbestos miners and on the general population, including the observed number of cases of lung cancer. From what has been said earlier, it is clear that even if the asbestos miners and general population had exactly the same lung cancer mortality rate, it is unlikley that in any single sample this identical rate would be found. Some difference is likely to be observed, but the important question is whether this difference is greater than might be expected merely as a matter of chance. In other words, we wish to know whether the difference is "statistically significant". If a sample should supply seven cases when the expected number (based on the rate for the general population) is five, one must inquire concerning the probability that this would occur purely as a matter of chance. It is this probability value which is calculated by the Poisson distribution. If, on this basis, a value is found in the sample which is so much larger than the expected value that it (or some larger value) would occur less than 5% of the time by chance, there is sufficient evidence to reject the original hypothesis. If, on the other hand, the value observed, even though larger than the expected value, is no greater than might occur by chance in fewer than 5% of trials, we have insufficient evidence to reject the original hypothesis.

Calculations and conclusions based on the results of the findings in this study have been made in conformity with these statistical concepts. They will be presented in the following section.

V. RESULTS AND INTERPRETATION

The two cohorts which were constructed according to the criteria described in the preceding section have been considered individually and compared with each other as well as with the general population. Description and comparison of these cohorts will be presented here as a preface to the results of the study.

A tabulated summary of each group and of the combined cohorts is shown below:

	Asbestos Cohort	Thetford Mines Cohort	Summary of Combined Cohorts
Original Cohort	2327	3764	6091
Lost Persons Deducted	54	79	133
Final Cohort	2273	3685	5958
Living in 1955 (working and retired)	2224	3547	5771
Dead by 1955	49	138	187
Ca. of lung	3	6	9
Questionable Ca. of lung	0	3	3
Other Causes	46	123	169
Unknown Causes	0	6	6
Smokers	1931	2742	4673
Nonsmokers	340	925	1265
Unknown	2	18	20

Tables 1, 2, 3, and 4 present age, number of years of employment, weighted average exposure and smoking habits of these two groups. It will be observed from Table 1 that the Thetford Mines workers had a higher average age than the Asbestos group (42 years vs. 39 years). Consistent with this finding, Table 2 indicates that they also had worked longer as asbestos miners (19 years as against 15 years).

A comparison of the exposure to asbestos dust is presented in Table 3. 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. Although it will be noted that the two cohorts had the same <u>average</u> exposure, a larger percentage of the Thetford Mines workers will be found in category II, while the Asbestos group occupy mainly the extremes of exposure. 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 4. A larger percentage of smokers is indicated here for the Asbestos cohort - 85.0% compared with 74.4%.

TABLE 1

Number and Percentage Distribution of Asbestos and Thetford Mines Cohorts by Age

Age	Asbestos No.	Asbestos %	Thetford Mines No.	Thetford Mines %	Combined No.	Combined %
20-44	1602	70	2299	62	3901	66
45-54	447	20	677	18	1124	19
55-64	185	8	430	12	615	10
65 +	39	2	276	8	315	5
Unknown	--	--	3	*	3	*
Totals	2273	100%	3685	100%	5958	100%
Av. Age	39		42		41	

* Less than .5%

TABLE 2

Number and Percentage Distribution of Asbestos and Thetford Mines Cohorts by Length of Employment

Length of Employment	Asbestos No.	Asbestos %	Thetford Mines No.	Thetford Mines %	Combined No.	Combined %
5-9	880	39	915	25	1795	30
10-19	864	38	1534	42	2398	40
20-29	342	15	580	16	922	16
30-39	168	7	435	12	603	10
40-49	17	1	168	4	185	3
50 +	2	*	53	1	55	1
Totals	2273	100%	3685	100%	5958	100%
Av. Yrs. of Employment	15		19		18	

* Less than .5%

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TABLE 3

Number and Percentage Distribution
of Asbestos and Thetford Mines Cohorts
by Exposure Category

Exposure Category	Asbestos No.	Asbestos %	Thetford Mines No.	Thetford Mines %	Combined No.	Combined %
I	969	43	1062	29	2031	34
II	564	25	1586	43	2150	36
III	735	32	1037	28	1772	30
Unknown	5	*	0	0	5	*
Totals	2273	100%	3685	100%	5958	100%
Av. Exposure	1.9		2.0		2.0	

* Less than .5%

TABLE 4

Number and Percentage Distribution
of Asbestos and Thetford Mines Cohorts
by Smoking Habits

Smoking Habits	Asbestos No.	Asbestos %	Thetford Mines No.	Thetford Mines %	Combined No.	Combined %
Smokers	1931	85	2742	74	4673	79
Nonsmokers	340	15	925	25	1265	21
Unknown	2	*	18	1	20	*
Totals	2273	100%	3685	100%	5958	100%

* Less than .5%

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This is a difference which could hardly occur by chance because of the large size of the sample. Therefore, it is likely that the difference is a real one unless the method of recording this information at the time of employment varies at the two locations.

In spite of the minor differences brought out by these comparisons, it would seem that the two cohorts are quite similar with regard to the variables of age, length of employment, degree of exposure and, although less so, in regard to smoking habits. These variables appear to us to be those most closely related to the problem, and will be taken into account in comparing the workers with the control groups.

Table 5 presents the year-by-year experience of the two cohorts 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.

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.

TABLE 5 - Part I

Study of the Asbestos Cohort

Year	No. Alive At Beginning of Year	Cause of Death: Proved Primary Ca. of Lung	Cause of Death: Suspected Primary Ca. of Lung	Cause of Death: Other Causes	Cause of Death: Unknown	Man-Years of Risk
1950	2273	0	0	6	0	2270
1951	2267	1	0	5	0	2264
1952	2261	0	0	9	0	2256.5
1953	2252	0	0	9	0	2247.5
1954	2243	0	0	12	0	2237
1955	2231	2	0	5	0	2227.5
Totals		3	0	46	0	13502.5

"Proved" cancer of lung death rate per 100,000 man-years of risk =

$$22.2\ (\frac{3}{13502.5})$$

TABLE 5 - Part II

Study of the Thetford Mines Cohort

Year	No. Alive At Beginning of Year	Cause of Death: Proved Primary Ca. of Lung	Cause of Death: Suspected Primary Ca. of Lung	Cause of Death: Other Causes	Cause of Death: Unknown	Man-Years of Risk
1950	3685	1	2	6	1	3680
1951	3675	1	0	12	1	3668
1952	3661	0	0	28	0	3647
1953	3633	2	1	25	0	3619
1954	3605	1	0	21	4	3592
1955	3579	1	0	31	0	3563
Totals		6	3	123	6	21769

"Proved" cancer of lung death rate per 100,000 man-years of risk =

$$27.6\ (\frac{6}{21769})$$

"Suspected" plus proved cancer of lung death rate per 100,000 man-years of risk = $41.3\ (\frac{9}{21769})$

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TABLE 5 - Part III

Study of Combined Cohorts

Combined death rates per 100,000 man-years of risk for Asbestos and Thetford Mines

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

"Suspected" plus proved cancer of lung death rate per 100,000 man-years of risk = $34.0\ (\frac{12}{35271.5})$

In two, no autopsy was performed but the clinical signs and symptoms were such that the death certificates read "cancer of the lung", and "suspected lung cancer". The third case came to autopsy but there was a difference of opinion between two pathologists as to whether lung cancer was present.

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 these two cohorts, and in which lung cancer is considered to have been proved as a cause, are shown in tabulated form on the next page. Also shown are three deaths in the Thetford Mines cohort which have been considered as "suspected" lung cancer cases.

ASBESTOS COHORT

"Proved" Cases of Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Au-topsy	Asbes-tosis
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

THETFORD MINES COHORT

"Proved" Cases of Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Au-topsy	Asbes-tosis
1. C. B.	59	Yes	32 Yrs. in Cat. I	8-20-50	Yes	No
2. A. S.	48	Yes	22 Yrs. in Cat. II	-51	Yes	Yes
3. W. F.	61	Yes	33 Yrs. in Cat. III	4-30-53	Yes	Yes
4. L. D.	56	Yes	30 Yrs. in Cat. II	11-22-53	Yes	Yes
5. E. L.	37	Yes	16 Yrs. in Cat. I	8- 5-54	Yes	No
6. A. R.	68	Yes	28 Yrs. in Cat. III	5- -55	Bronch.	No

"Suspected" Primary Cancer of the Lung

Name	Age	Smoker	Exposure	Died	Au-topsy	Asbes-tosis
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

At Asbestos there were no cases in which the diagnosis was questionable, with the result that the rate for "proved" cases in this cohort is the only one developed. At Thetford Mines, however, the three cases mentioned earlier were placed in the category of "suspected" primary cancer of the lung. An indication of the importance of these 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 Asbestos cohort is very close to the "expected" rate based on the general population figures for the Province as will be shown later, and on this basis, we should find five deaths from lung cancer among the Thetford Mines group. As was explained in the section on "Collection and Analysis of Data", it would then not be unlikely for six cases to occur in our sample. This is, in fact, the number of "proved" cases found in the Thetford Mines cohort. If, however, the three additional "suspected" cases are included, increasing this figure to nine, the whole situation changes from a statistical point of view. Since the 95% level of probability in this case falls between 9 and 10, we would reject the hypothesis that there is no difference between the incidence of lung cancer in miners and that in the general population if we found ten or more cases. On the other hand, having found nine cases we are not above the 95% level and are not justified in rejecting the hypothesis. Nevertheless, the occurrence of nine cases in this sample would show

an increase in rate 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 for the Thetford Mines cohort and the combined cohort have been calculated both ways.

Table 6, giving the rates by age groups, reveals different experiences for the two cohorts. It happens that all of the deaths in the

Asbestos cohort fall into one age group, so that the rate for that age category is exceptionally high. At Thetford Mines, a more even distribution of the deaths by age developed a series of rates which are less extraordinary and, as will be seen, are not widely divergent from the expected rates for each age category. The unusual rate in the Asbestos cohort for the age group 65 years and over, is the sort of thing which happens when the sample is small. For example, of these three deaths, two were exactly 65 years of age and would have been in another age group had the limits been increased by one year.

TABLE 6

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

Age Groups	Asbestos		Thetford Mines			Combined		
	Persons	Lung Cancer Deaths	Persons	Lung Cancer Deaths		Persons	Lung Cancer Deaths	
				Proved	Total		Proved	Total
20-44	1602	0	2299	1	1	3901	1	1
45-54	447	0	677	1	3	1124	1	3
55-64	185	0	430	3	3	615	3	3
65+	39	3	276	1	2	315	4	5
Unknown	0	0	3	0	0	3	0	0
Total	2273	3	3685	6	9	5958	9	12

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

Age Group	Asbestos	Thetford Mines		Combined	
	Total	Proved	Total	Proved	Total
20-44	0	7	7	4	4
45-54	0	25	74	15	44
55-64	0	116	116	81	81
65+	1282	60	121	212	265
Unknown	*	0	0	0	0
Over-all	22	27	41	25	34

* No one exposed

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The rates by length of employment (Table 7) show that the two groups were quite similar in this respect. 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 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 22 which appears later in this section indicates that the members of the cohorts did not die from lung cancer at a younger age than the general population.

The rates by weighted exposure are shown in Table 8, and it will be noted that they present strong evidence against asbestos being a carcinogenic agent. For the Asbestos cohort the rates actually decrease with increasing degree of exposure, and at Thetford Mines they appear completely independent of exposure, if we count only the "proved" cases.

TABLE 7

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

Length of Employment	Asbestos		Thetford Mines			Combined		
		Lung Cancer Deaths		Lung Cancer Deaths			Lung Cancer Deaths	
	Persons	Deaths	Persons	Proved	Total	Persons	Proved	Total
5-9	880	0	915	0	0	1795	0	0
10-19	864	0	1534	1	1	2398	1	1
20-29	342	1	580	2	2	922	3	3
30-39	168	2	435	3	5	603	5	7
40-49	17	0	168	0	1	185	0	1
50+	2	0	53	0	0	55	0	0
Total	2273	3	3685	6	9	5958	9	12

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

Length of Employment	Asbestos	Thetford Mines		Combined	
	Total	Proved	Total	Proved	Total
5-9	0	0	0	0	0
10-19	0	11	11	7	7
20-29	49	57	57	54	54
30-39	198	115	192	138	193
40-49	0	0	99	0	90
50+	0	0	0	0	0
Over-all	22	27	41	25	34

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TABLE 8

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

Exposure Category	Asbestos		Thetford Mines			Combined		
		Cancer		Lung Cancer Deaths			Lung Cancer Deaths	
	Persons	Deaths	Persons	Proved	Total	Persons	Proved	Total
I	969	2	1062	2	2	2031	4	4
II	564	1	1586	2	3	2150	3	4
III	735	0	1037	2	4	1772	2	4
Unknown	5	0	0	0	0	5	0	0
Total	2273	3	3685	6	9	5958	9	12

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

Exposure Category	Asbestos	Thetford Mines		Combined	
	Total	Proved	Total	Proved	Total
I	34	31	31	33	33
II	30	21	32	23	31
III	0	32	64	19	37
Unknown	0	*	0	0	0
Over-all	22	27	41	25	34

* No one exposed

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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. Tables 9, 10, and 11 which list the number of persons in various exposure categories by length of employment indicate that this error has not occurred. In fact, the average number of years of employment for each exposure category is almost identical.

TABLE 9

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

Asbestos

Length of Employment	Weighted Exposure Categories I	II	III	Unknown	Total
5-9	428	213	239	0	880
10-19	273	217	373	1	864
20-29	159	89	92	2	342
30-39	98	42	27	1	168
40-49	9	3	4	1	17
50 +	2	0	0	0	2
Total	969	564	735	5	2273
Av. Yrs. of Exposure	15.5	15.2	14.5	29.0	15.1

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TABLE 10

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

Thetford Mines

Length of Employment	Weighted Exposure Categories I	II	III	Unknown	Total
5-9	279	385	251	0	915
10-19	390	666	478	0	1534
20-29	155	274	151	0	580
30-39	149	176	110	0	435
40-49	67	64	37	0	168
50 +	22	21	10	0	53
Total	1062	1586	1037	0	3685
Av. Yrs. of Exposure	19.9	18.7	18.1		18.9

TABLE 11

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

Combined Asbestos and Thetford Mines

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
Total	2031	2150	1772	5	5958
Av. Yrs. of Exposure	17.8	17.8	16.6	29.0	17.5

Table 12, which develops the rates for smokers and nonsmokers, 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. A comparison of Tables 8 and 12 certainly suggests that smoking is a greater hazard than exposure to asbestos in the mining operations.

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 the difference between lung cancer death rates for smokers and nonsmokers.

TABLE 12

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

	Asbestos		Thetford Mines			Combined		
		Lung Cancer		Lung Cancer Deaths			Lung Cancer Deaths	
	Persons	Deaths	Persons	Proved	Total	Persons	Proved	Total
Smokers	1931	3	2742	6	9	4673	9	12
Nonsmokers	340	0	925	0	0	1265	0	0
Unknown	2	0	18	0	0	20	0	0
Total	2273	3	3685	6	9	5958	9	12

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

	Asbestos	Thetford Mines		Combined	
	Total	Proved	Total	Proved	Total
Smokers	26	36	55	32	43
Nonsmokers	0	0	0	0	0
Unknown	0	0	0	0	0
Over-all	22	27	41	25	34

TABLE 13

Number of Smokers and Nonsmokers by Age Groups

Age Groups	Asbestos			Thetford Mines			Combined		
	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known
20-44	1361	240	1	1839	449	11	3200	689	12
45-54	371	75	1	525	149	3	896	224	4
55-64	163	22	0	248	180	2	411	202	2
65+	36	3	0	128	147	1	164	150	1
Unknown	0	0	0	2	0	1	2	0	1
Total	1931	340	2	2742	925	18	4673	1265	20
Av. Age	38.5	38.1	41.0	39.8	46.4	40.7	39.3	44.2	40.7

Percentage Distribution of Smokers and Nonsmokers by Age Groups

Age Groups	Asbestos			Thetford Mines			Combined		
	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known
20-44	70.5	70.6	50.0	67.1	48.5	61.1	68.5	54.5	60.0
45-54	19.2	22.0	50.0	19.1	16.1	16.7	19.2	17.7	20.0
55-64	8.4	6.5	.0	9.0	19.5	11.0	8.8	16.0	10.0
65+	1.9	.9	.0	4.7	15.9	5.6	3.5	11.8	5.0
Unknown	.0	.0	.0	.1	.0	5.6	*	.0	5.0
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%

* Less than .05%

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TABLE 14

Number of Smokers and Nonsmokers by Length of Employment

Length of Employment	Asbestos			Thetford Mines			Combined		
	Smoker	Non-smoker	Unknown	Smoker	Non-smoker	Unknown	Smoker	Non-smoker	Unknown
5-9	720	159	1	688	218	9	1408	377	10
10-19	749	114	1	1218	312	3	1967	426	4
20-29	296	46	0	426	153	2	722	199	2
30-39	148	20	0	285	146	4	433	166	4
40-49	16	1	0	94	74	0	110	75	0
50+	2	0	0	31	22	0	33	22	0
Total	1931	340	2	2742	925	18	4673	1265	20
Av. Length of Employment	15.4	13.9	11.0	18.1	21.3	16.6	17.0	19.3	16.0

Percentage Distribution of Smokers and Nonsmokers by Length of Employment

Length of Employment	Asbestos			Thetford Mines			Combined		
	Smoker	Non smoker	Unknown	Smoker	Non-smoker	Unknown	Smoker	Non-smoker	Unknown
5-9	37.3	46.8	50.0	25.1	23.6	50.0	30.1	29.8	50.0
10-19	38.8	33.5	50.0	44.4	33.7	16.7	42.1	33.7	20.0
20-29	15.3	13.5	.0	15.6	16.5	11.1	15.4	15.7	10.0
30-39	7.7	5.9	.0	10.4	15.8	22.2	9.3	13.1	20.0
40-49	.8	.3	.0	3.4	8.0	.0	2.4	5.9	.0
50+	.1	.0	.0	1.1	2.4	.0	.7	1.8	.0
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%

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TABLE 15

Number of Smokers and Nonsmokers by Exposure Category

Exposure Category	Asbestos			Thetford Mines			Combined		
	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known
I	810	158	1	743	316	3	1553	474	4
II	483	80	1	1208	372	6	1691	452	7
III	634	101	0	791	237	9	1425	338	9
Unknown	4	1	0	0	0	0	4	1	0
Total	1931	340	2	2742	925	18	4673	1265	20
Av. Exposure Category	1.9	1.8	1.5	2.0	1.9	2.3	2.0	1.9	2.3

Percentage Distribution of Smokers and Nonsmokers by Exposure Category

Exposure Category	Asbestos			Thetford Mines			Combined		
	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known	Smoker	Non-smoker	Un-known
I	42.0	46.5	50.0	27.1	34.2	16.7	33.2	37.5	20.0
II	25.0	23.5	50.0	44.0	40.2	33.3	36.2	35.7	35.0
III	32.8	29.7	.0	28.9	25.6	50.0	30.5	26.7	45.0
Unknown	.2	.3	.0	.0	.0	.0	0.1	0.1	.0
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%

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The result of this additional analysis is that none of these factors appear to lessen the effect of Table 12, which is therefore strongly suggestive of the importance of smoking as compared to the other variables.

Asbestosis and Lung Cancer

When we attempt to relate the lung cancer deaths occurring in the cohort with the reported cases of asbestosis, we are immediately aware of a disturbing inconsistency. Various authors report the incidenc of asbestosis after 10 or 15 years of exposure as exceeding 50%, and in one study, as high as 87%. (133) (135) (147) (154) (195) However, data or cases of asbestosis from the cohorts at Thetford Mines and Asbestos produce a rate of only about 5%. It is true that these data are based on only those cases which have been proved at autopsy, and those whose most recent x-ray interpretation resulted in a diagnosis of asbestosis. This incidence may be far lower than if based on microscopic examination of the lung tissue. As a matter of fact, Dr. Cartier has estimated that there ar probably 300 workers who do not show radiological evidence of asbestosis but who have some degree of fibrosis. He also estimates that there are perhaps 40 workers who may have died or retired with this disease. Inste of 143 cases of asbestosis in the whole working force at Thetford Mines, we should then have perhaps 500, but even this would result in an over-all rate of less than 10%, which is far below those widely reported. In our

combined cohort, there are 1765 men who have had more than 20 years of employment, and 431 of these have worked in the heaviest average exposure. According to the records, we can account for only 138 cases of asbestosis in the combined cohorts. If even 25% of the workers with more than 20 years' exposure develop asbestosis, we should expect about 425 cases. This leads us to believe that there is a very considerable under-reporting of asbestosis. Such a hypothesis is easily conceivable when one considers that many chest x-rays in this group may be considered normal by comparison with others in the same group whereas, if they were to be compared with what are considered as normal chest x-rays elsewhere, they may be interpreted as showing fibrosis.

Cases of asbestosis which were accumulated from the autopsy records and from the periodical physical examinations result in a distribution which is shown in Table 16.

TABLE 16

Distribution of Recorded Asbestosis Cases

In Cohort	Asbestos	Thetford	Combined
Living	18	86	104
Dead	4	30	34
Total	22	116	138

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TABLE 17 - Part I

Number of Asbestosis Cases By Length of Employment and Exposure Category

Asbestos

Length of Employment	Exposure Category I	II	III	Unknown	Total
Less than 10	0	0	0	0	0
10-19	0	1	2	0	3
20-29	2	7	4	0	13
30-39	0	1	4	0	5
40-49	0	0	1	0	1
50 +	0	0	0	0	0
Total	2	9	11	0	22
Av. Yrs. of Employment	25	25	29		27

Percentages of Asbestosis Cases By Length of Employment and Exposure Category

Length of Employment	Exposure Category I	II	III	Unknown	Total
Less than 10	0	0	0	*	0
10-19	0	.5	.5	0	.3
20-29	1.3	7.9	4.3	0	3.8
30-39	0	2.4	14.8	0	3.0
40-49	0	0	25.0	0	5.9
50 +	0	*	*	*	0
Over-all	.2	1.6	1.5	0	1.0

* No one exposed in this group

TABLE 17 - Part II

Number of Asbestosis Cases By Length of Employment and Exposure Category

Thetford Mines

Length of Employment	Exposure Category I	II	III	Unknown	Total
Less than 10	0	0	0	0	0
10-19	0	1	7	0	8
20-29	2	5	21	0	28
30-39	2	15	33	0	50
40-49	0	6	20	0	26
50 +	0	2	2	0	4
Total	4	29	83	0	116
Av. Yrs. of Employment	30	36	34		34

Percentages of Asbestosis Cases By Length of Employment and Exposure Category

Length of Employment	Exposure Category I	II	III	Unknown	Total
Less than 10	0	0	0	*	0
10-19	0	.2	1.5	0	.5
20-29	1.3	1.8	13.9	0	4.8
30-39	1.3	8.5	30.0	0	11.5
40-49	0	9.4	54.1	0	15.5
50 +	0	9.5	20.0	*	7.5
Over-all	.4	1.8	8.0	0	3.1

* No one exposed in this group

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TABLE 17 - Part III

Number of Asbestosis Cases By Length of Employment and Exposure Category

Asbestos and Thetford Mines Combined

Length of Employment	Exposure Category I	II	III	Unknown	Total
Less than 10	0	0	0	0	0
10-19	0	2	9	0	11
20-29	4	12	25	0	41
30-39	2	16	37	0	55
40-49	0	6	21	0	27
50 +	0	2	2	0	4
Total	6	38	94	0	138
Av. Yrs. of Employment	28	33	33		33

Percentages of Asbestosis Cases By Length of Employment and Exposure Category

Length of Employment	Exposure Category I	II	III	Unknown	Total
Less than 10	0	0	0	*	0
10-19	0	.2	1.0	0	.5
20-29	1.3	3.3	10.3	0	4.4
30-39	.8	7.3	27.0	0	9.1
40-49	0	9.0	51.2	0	14.6
50 +	0	9.5	20.0	*	7.3
Over-all	.3	1.8	5.3	0	2.0

* No one exposed in this group

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A percentage incidence of asbestosis for each exposure category has been developed as well as for each period of employment. This information is shown in Table 17.

It will be noted that within an exposure category, the incidence rises with increased length of employment. It is also apparent that the incidences, even in the category of heaviest exposure, are far below the rates found by the authors previously referred to. It seems clear, that unless concentrations of asbestos dust to which the miners are exposed are very much lower than those which obtain in all the other studies, there has been a gross underreporting of the asbestosis cases. The obvious result is a higher relative frequency of lung cancer in association with asbestosis. Table 18 compares deaths due to lung cancer and fatal cases with asbestosis, alone and in combination with each other.

TABLE 18 - Part I

Statistical Analysis of the Causes of Death

Asbestos

Cause	Asbestosis	No Asbestosis	Total	Percentage
Lung Cancer	1 (.2)	2 (2.8)	3	6.1
No Lung Cancer	3 (3.8)	43 (42.2)	46	93.9
Total	4	45	49	
Percentage	8.2	91.8		

Figures in parenthesis are the "expected" numbers

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TABLE 18 - Part II

Statistical Analysis of the Causes of Death

Thetford Mines

Cause	Asbestosis	No Asbestosis	Total	Percentage
Lung Cancer	3(1.3)	3(4.7)	6	4.5
No Lung Cancer	25(26.7)	101(99.3)	126	95.5
Total	28	104	132	
Percentage	21.2	78.8		

Figures in parenthesis are the "expected" numbers

TABLE 18 - Part III

Statistical Analysis of the Causes of Death

Asbestos and Thetford Mines Combined

Cause	Asbestosis	No Asbestosis	Total	Percentage
Lung Cancer	4(1.6)	5(7.4)	9	5.0
No Lung Cancer	28(30.4)	144(141.6)	172	95.0
Total	32	149	181	
Percentage	17.7	82.3		

Figures in parenthesis are the "expected" numbers

Six deaths from unknown causes not included

The number of lung cancer deaths combined with asbestosis is larger than would be expected in each cohort and in the combined cohorts. This difference is significant at the 95% level using the chi-square test of significance. The importance of the under-reporting of asbestosis can be observed in Table 19.

TABLE 19

Statistical Analysis of the Causes of Death if
20 Nonasbestosis Cases had been Diagnosed as Asbestosis Cases

Cause	Asbestosis	No Asbestosis	Total	Percentage
Lung Cancer	4(2.6)	5(6.4)	9	5.0
No Lung Cancer	48(49.4)	124(122.6)	172	95.0
Total	52	129	181	
Percentage	28.7	71.3		

Figures in parenthesis are the "expected" numbers

In this table, it has been assumed that 20 of the cases which did not have lung cancer and which were reported to have no asbestosis did, in fact, have asbestosis, the diagnosis of which was missed. Although the cases of lung cancer with asbestosis are still higher than would be expected, the difference is no longer significant at the 95% level. This still is true if fewer than 20 cases were shifted but it is reasonable to expect that at least 20 of the 144 might have shown asbestosis had they been subject to autopsy. On the other hand, a shift of about 40 cases would produce an expected rate almost equal to the rate found. Explanation of this effect of under-reporting of asbestosis has been stressed because it seems so obvious that in under-reporting asbestosis the relationship between it and lung cancer has been made to appear more significant than it probably is.

Four of the proved cases of lung cancer and one of the suspected were associated with asbestosis. Since we have only 32 deaths in which asbestosis was present according to the records, the incidence in this series is 12.5%. While this is slightly lower than the rates found by Merewether, Gloyne, and Wedler, it is still much higher than could be expected if the asbestosis incidence were anywhere near the experience reported by other authors.

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 20 gives a tabulation of the number of deaths from lung cancer in the Province and in the two cohorts 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 Asbestos cohort is almost exactly the same as that for the Province, while the rate for "proved" cases in the Thetford Mines cohort is only slightly higher. When the "suspected" cases are included in the calculation, the rates for the Thetford Mines cohort rises to 41.4 per 100,000 which is nearly twice as high as the rate for the Province. This, it will be recalled from the previous discussion of the "suspected" cases, approaches but does not exceed the significant level.

One further interesting observation from Table 20 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 would tend to be low. This would appear to be substantiated by the fact that the reporting of cases in the combined cohort showed no such increase over the same period.

Table 21 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

TABLE 20

Comparison of Province of Quebec with Asbestos and Thetford Mines

	No. 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
Asbestos Cohort	2,261+								
Total		0	1	0	0	0	2	3	22.1
Proved		0	1	0	0	0	2	3	22.1
Thetford Mines Cohort	3,662+								
Total		3	1	0	3	1	1	9	41.0
Proved		1	1	0	2	1	1	6	27.3
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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confirmed by autopsy, surgery, or biopsy. The term "specified primary" refers to those cases in these same two categories in which the tumor was specified as having originated in the lung. It will be noted that, of the total cases certified in 1955, a much higher percentage than in 1954 was 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 21, and those for the cohort shown in Table 6. 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 22, 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 five deaths provide a figure which is almost significant at the 95% level. However, it should be noted that this number includes one of the suspected but unproved 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.

Before leaving this comparison of the Province 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 tabulation:

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

Age Group	Number	Percentage	Percentage Combined Cohorts
20-44	727,135	63	66
45-54	188,952	16	19
55-64	128,944	11	10
65 +	113,467	10	5
Total	1,158,498	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 23 indicates that the lung cancer rate generally decreases after age 70, and we could expect the rate for all people over 65 would be smaller than the rate for a group of 65 to 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 which are somewhat lower than if we had been able to exclude the general population over 75.

TABLE 21

Lung Cancer Deaths for the Province of Quebec
(Data from Death Certificates)

Age Group	Estimated * Population	1954 Total Certified Total	1954 Total Certified Proved	1954 Specified Primary Total	1954 Specified Primary Proved	1955 Total Certified Total	1955 Total Certified Proved	1955 Specified Primary Total	1955 Specified Primary Proved
20-44	777,000	17	13	11	9	17	9	17	9
45-54	202,000	67	36	43	29	60	35	56	32
55-64	137,000	100	38	69	32	117	57	116	57
65 +	121,000	111	33	68	29	148	54	148	54
Total	1,237,000	295	120	191	99	342	155	337	152

* Estimate for population obtained by applying 1951 percentages for age groups for males to the total population for 1954, as given in Rapport, Div. de la Demographie.

Annual Lung Cancer Death Rates per 100,000

Age Group	1954 Total Certified Total	1954 Total Certified Proved	1954 Specified Primary Total	1954 Specified Primary Proved	1955 Total Certified Total	1955 Total Certified Proved	1955 Specified Primary Total	1955 Specified Primary Proved
20-44	2.2	1.7	1.4	1.2	2.2	1.2	2.2	1.2
45-54	33.2	17.8	21.3	14.4	29.7	17.3	27.7	15.8
55-64	73.0	27.7	50.4	23.4	85.4	41.6	84.7	41.6
65 +	91.7	27.3	56.2	24.0	122.3	44.6	122.3	44.6
Over-all	23.8	9.7	15.4	8.0	27.6	12.5	27.2	12.3

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TABLE 22

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

Age Group	Province Total Specified Primary Rate per 100,000	No. of Miners	Expected+ No. of Deaths	Observed No. of Deaths Proved	Observed No. of Deaths Total
20-44	1.8	3901	0*	1	1
45-54	24.5	1124	2	1	3
55-64	67.6	615	2	3	3
65 +	89.3	315	2	4	5
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 22 also answers a question previously raised. It shows that the members of these cohorts 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 40 years of employment referred to on page 37.

A comparison between the asbestos miners and the population of the Dominion as a whole was made, using statistical material from several sources. In one source, Phillips [171] gave age- and sex-specific rates for Canada for three periods between 1931 and 1952. The rates for males are given in Table 23.

TABLE 23

Annual Death Rates per 100,000
for Cancer of the Lung in Canada*

Age Groups	Groups of Years 1931-1933	1941-1943	1950-1952
Under 30	0.2	0.3	1.0
30-34	0.9	0.9	0.8
35-39	2.0	3.2	3.0
40-44	3.0	5.4	6.5
45-49	5.2	12.5	16.7
50-54	8.2	18.9	37.2
55-59	12.7	27.0	59.7
60-64	12.5	33.7	77.8
65-69	15.1	34.5	102.9
70-74	10.7	30.6	86.3
75-79	15.8	30.0	83.9
80-84	8.2	27.9	59.7
85 +	11.4	14.3	71.0
All Ages	2.8	7.1	15.8

* "Mortality from Lung Cancer in Canada", 1931 to 1952.

These figures show strikingly the increase in rates between 1931 and 1952, and this increase is particularly marked after age 50, confirming an observation previously made, to the effect that 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 somewhat as follows:

Age Group	Rate
20-44	5
45-54	27
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 21)

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 20.8 per 100,000, an increase of 5 per 100,000 over Phillips' 1950-1952 rate, and compares with 25.5 per 100,000 for proved cases and 34.0 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 Quebec 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 24.

TABLE 24

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
20-44	24,544,000	883	3.6
45-54	8,065,000	2979	36.9
55-64	6,340,000	6254	98.6
65 +	5,670,000	6483	114.3
Total	44,619,000	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 1953, and 28.0 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 34 for total cases) obtaining among the asbestos miners.

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Returning 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. Hueper[122] 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 persons.

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

To compare lung cancer mortality rates in the counties surrounding the asbestos-producing areas with another group of counties in which no asbestos miners 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, Chateaugay, Montmagny, Portneuf, Richlieu, 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 25 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 Isle de Jesus has also been listed in order to provide further comparison.

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TABLE 25

Number of Lung Cancer Deaths and Rate per 100,000 Man-Years

Counties	Adult Male Population 1952	Male Lung Cancer Deaths*							
		1950	1951	1952	1953	1954	1955	Total	Rate per 100,000
Megantic County	13,100	3	1	3	3	1	4	15	18.9
Eight "Adjacent" Counties	97,600	6	3	9	16	4	16	54	9.4
Eight Selected Counties	83,000	2	10	5	18	5	9	49	9.8
Province of Quebec	1,198,000	196	220	245	303	303	357	1624	22.6
Province of Quebec less Eight "Adjacent" Counties	1,100,000	190	217	236	287	299	341	1570	23.8
Montreal et Isle de Jesus	394,000	3	7	158	192	185	225	770	32.3

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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 Megantic County has a rate nearly twice that of the combined eight selected counties, it is lower than the rate for the Province, and considerably lower than the rate for Montreal. The figure for Montreal would certainly be higher except for the very low numbers of deaths reported for 1950 and 1951, and it would appear that some error in reporting has undoubtedly been made. On the basis of the other years, 1950 and 1951 deaths would be expected to be about 200 greater, and this would result in a rate of 40 per 100,000.

The only possible conclusion from this comparison is that there is no evidence that the persons who live 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, at Asbestos and Thetford 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 statistical 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. All of these nine cases occurred at Thetford Mines. It is somewhat surprising that there is no record of any lung cancer deaths among the Asbestos group in the interval preceding the beginning of the study and equally so that no cases have been reported in 1956 and 1957. During the period covered by this investigation, there were six proved cases and three suspected cases at Thetford Mines, as well as three proved cases at Asbestos. Through 1956 and to date in 1957, there were eight deaths at Thetford Mines, six of which were merely suspected and included such diagnoses as mediastinal lymphosarcoma, mesothelioma, cancer of the leg with metastases to lung, absess 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 33 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 in both areas since 1940. Sixteen of these have been at Thetford Mines and only three at Asbestos, all of which occurred during the period of the study.

The proved cases averaged 59 years of age at death, and varied between 37 years and 68 years. Their working span covered

periods varying between a minimum of 14 years and maximum of 37 years. Only three men had less than 25 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.

Although they were subjected to post-mortem examination, there were three among these proved lung cancer cases in which we do not have information regarding the presence of asbestosis. Of the remaining 17, asbestosis was present in nine, although it was minimal in two, and two pathologists disagreed regarding its presence in one. Eight of the proved lung cancers, therefore, were not accompanied by asbestosis.

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VI. SUMMARY AND CONCLUSIONS

Interest in the question of whether there may be an association between lung cancer and asbestosis or 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. As additional cases in which the two diseases coexisted were reported, a causal association appears to have been gradually accepted by many authors, although a few workers considered the correlation to be inconclusive. Cases of lung cancer which had occurred among the asbestos miners in Quebec had been carefully recorded over the years, and the present study was commissioned in an effort to determine whether a causal relationship did, in fact, exist between exposure to asbestos and cancer of the lung.

Reference to the literature shows a remarkable uniformity both of method and of conclusions. In general, the method has been to study a circumscribed series of cases of asbestosis and to enumerate those in which lung cancer occurred. The series may consist of cases coming to autopsy or of death certificates mentioning asbestosis, and the total number has served as the denominator by which the number of lung cancer cases is divided to produce a certain "incidence rate". This rate, as reported by various authors has been consistently high, and its uniformity is indicated by the following tabulation.

Author	Asbestosis Deaths	Cancer of Lung	Percentage Incidence
Merewether	344	55	16.0
Wedler	92	15	16.3
Wyers	115	17	14.8
Lynch & Cannon	40	3	7.5
Gloyne	121	17	14.1
Totals	712	107	15.0

The notable characteristic of all previous publications is the adherence to the development of a percentage relationship in a relatively small and very selected group of cases. Only Doll,[63] among all of these authors, has described a representative population group and studied it for the mortality rate from lung cancer and compared this rate with that for a control group. His investigation dealt with only 113 men in the study population.

Since most earlier studies had been limited to enumerating the lung cancers found in certain 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 medical records at the two main locations

of these operations. Cohorts were defined according to certain criteria and all workers who met these criteria were included in the study. Through their medical records, 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 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 its 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 in section IV.

Records were obtained on 6091 persons who fulfilled the criteria of our cohorts. It was not possible to trace 133 of these for the whole period, but 5771 of the remaining 5958 were found to be still living in 1955 or later. Of the 187 known dead, cancer of the lung was considered to have been reasonably proved in nine and to be strongly suggested in three.

The members of the cohorts 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 percent of the cohort were more than 45 years of age, and 30% had been employed for longer than 20 years. Thirty percent had a weighted exposure which placed them in category III.

The mortality rates for lung cancer, as computed on the basis of six "proved" deaths among the Thetford Mines cohort and three "proved" deaths among the Asbestos cohort, were 27.6 per 100,000 for the Thetford Mines group, and 22.2 per 100,000 for the Asbestos group. When the three "suspected" cases were added, the "total" rate for the Thetford Mines cohort rose to 41.3. The rate for the combined cohort was 25.5 per 100,000 for "proved" cases, and 34 per 100,000 for "proved" and "suspected" cases. The importance of the suspected but unproved cases in determining these rates has been reiterated because it is likely that such cases would not be included in the statistics for the general population.

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. On the other hand, the study indicates that cigarette smoking is a very important factor in the incidence of cancer of the lung.

A comparison of relative frequency of lung cancer and asbestosis is less reassuring, but we believe that this is because of an

under-reporting of asbestosis cases. The incidence of asbestosis indicated by the medical records is far below that which would be expected on the basis of all previously published figures. Naturally, when the cases of lung cancer are compared with an artificially low figure, its relative incidence will be higher than it should. However this may be, 12.5% of the recorded cases of asbestosis in this study developed lung cancer, a figure slightly lower than those quoted by authors who confined themselves to this type of comparison.

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. The rate for proved cases among the asbestos miners (25.5 per 100,000) compares well with the rate of 22.5 per 100,000 for the rest of the Province, and 20.8 per 100,000 for adult males throughout the Dominion of Canada. It also compares satisfactorily with rates of 37.2, 25.3, and 28.0 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 1940, there have been 19 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 I) to asbestos dust.

Conclusions

On the basis of a careful and detailed study of what are believed to be complete and reliable data, it seems fair to conclude that the asbestos miners at Thetford Mines and Asbestos in the Province of Quebec do not have a significantly higher death rate from lung cancer than do comparable segments of the general population. Despite this, the results suggest that a miner who develops the disease asbestosis does have a greater likelihood of developing cancer of the lung than a person without this disease. We suspect, however, that underreporting of asbestosis cases had led to a fallacious finding in this connection.

The death rate from lung cancer in the areas continguous 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.

The present study indicates that the effect of cigarette smoking is a much more important consideration in the production of lung cancer than is exposure to asbestos, and in this respect, it tends to confirm recent studies dealing with the effect of smoking.

The value of this investigation would be considerably enhanced by continuing the observation of the cohorts formulated herein on a year-by-year basis. It is strongly recommended that the chest x-rays of all workers be submitted to an independent reading for the diagnosis of asbestosis, since an inaccurately low incidence rate for this disease creates an artifically high relative incidence for lung cancer.

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